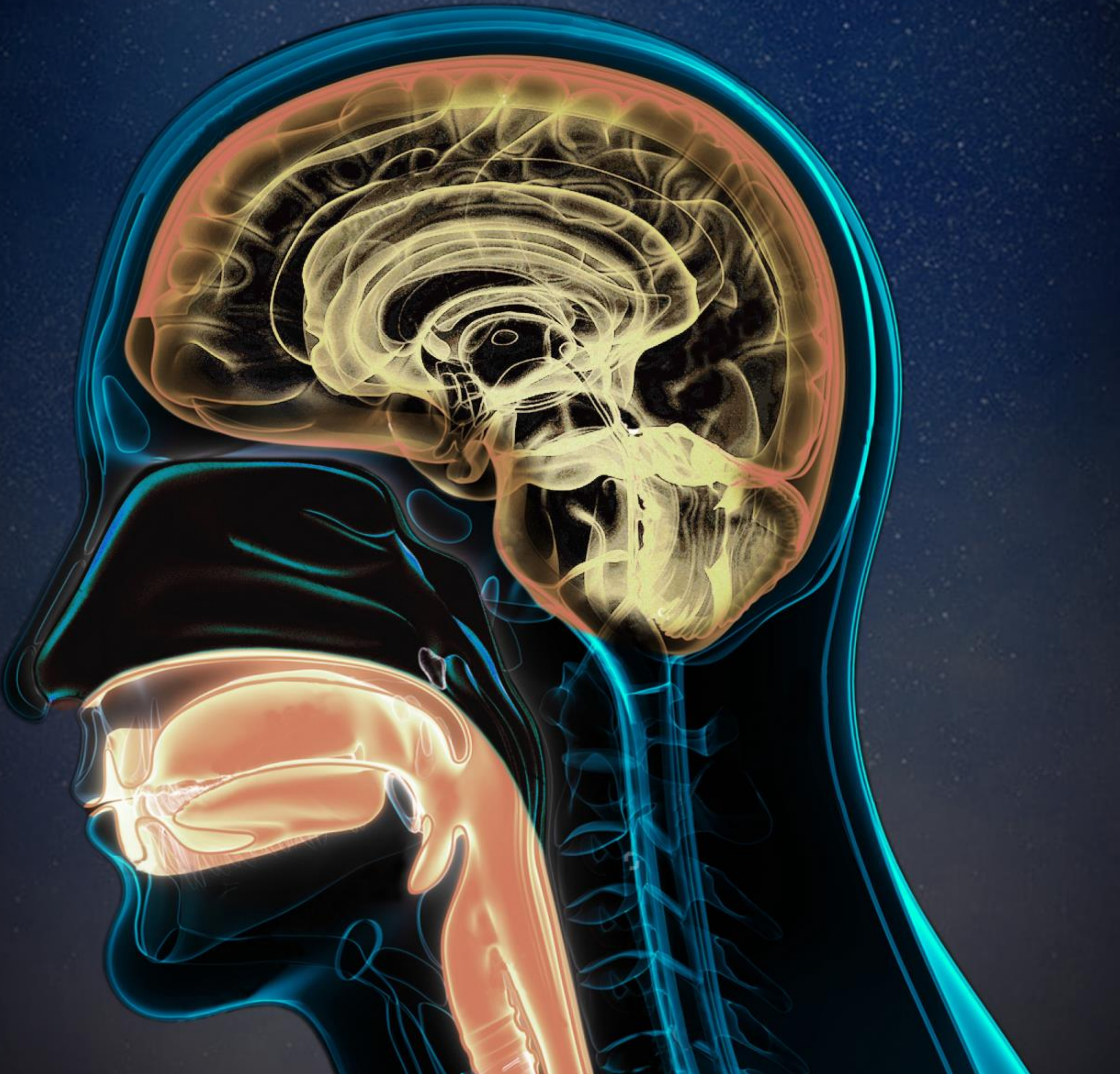
CONTRIBUTION TO THE STUDY OF THE LINKS BETWEEN CONSCIOUSNESS AND SWALLOWING

Thèse présentée en vue de l'obtention du grade de Docteur en Sciences Médicales



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Contribution to the study of the links between consciousness and swallowing

Under the supervision of
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A Bijan et tous les autres patients
présentant des troubles de la conscience
ainsi qu'à leurs proches qui les accompagnent
au quotidien.

CONTENT

ABSTRACT

Following severe brain injuries (e.g., traumatic or anoxic brain injury, stroke), a small proportion of patients will remain in an altered state of consciousness. Patients with prolonged (> 28 days post-insult) disorders of consciousness (DOC) can open their eyes (sometimes showing electrophysiological sleep/wake cycles) and the majority no longer need invasive ventilation. However, most of them receive artificial feeding, suggesting that consciousness affects swallowing capacities.

The aim of this thesis is to **contribute to the study of the links between consciousness and swallowing**. The hypotheses are that swallowing capacities are linked to level of consciousness, and that the presence of some components of swallowing constitutes a possible sign of consciousness.

Based on a literature review, we show that the sequencing of the components of swallowing falls on a continuum of voluntary to reflex behaviors. Components of the oral phase may be considered as voluntary behaviors because they are controllable and suppressible (although largely automated), components of the pharyngeal phase as somatic reflexes, and components of the esophageal phase as autonomic reflexes. The triggering of the swallowing reflex inhabits the border region between voluntary behaviors and somatic reflexes, while the opening of the upper esophageal sphincter divides somatic from autonomic reflexes. If voluntary behaviors are considered possible signs of consciousness, the presence of components of the oral phase of swallowing should be considered as revealing conscious behaviors. Moreover, we show that a range of cortical areas (mainly the primary sensorimotor cortex, premotor cortex and supplementary motor area, anterior part of the cingulate cortex, insula and cerebellum) are involved in both volitional and non-volitional swallowing tasks.

In two retrospective studies analyzing swallowing in patients with DOC diagnosed by means of repeated behavioral assessment and neuroimaging, we demonstrate that almost all such patients present at least one dysfunction in the oral and/or pharyngeal phase. Patients who do not show behavioral signs of consciousness (unresponsive wakefulness syndrome – UWS) do not present an efficient oral phase of swallowing allowing oral feeding with solid food. Consequently, the preservation of components of the oral phase of swallowing should be

considered as a sign of consciousness and be one of the diagnostic criteria for consciousness. The absence of an efficient oral phase of swallowing in patients with UWS and its presence in only a small proportion of minimally conscious (MCS) patients explain why no “typical” patients with UWS (i.e., with behavioral and neuroimaging assessments pointing in the same direction) can be fed entirely orally while no patients with MCS can eat ordinary textured food.

Furthermore, in the studied group, level of consciousness is linked to components of the pharyngeal phase (reflected by the absence of a tracheostomy, pharyngo-laryngeal secretions or saliva aspiration) and to the cough reflex. Indeed, more patients with MCS than UWS present efficient spontaneous saliva management and a cough reflex, although these components are present in some patients with UWS. For that reason, these components seem to represent cortically mediated behavior but do not constitute signs of consciousness as such.

Finally, this work highlights the lack of appropriate tools to assess and treat swallowing for patients with DOC. A protocol study for the validation of a swallowing assessment tool for patients with DOC is therefore proposed.

RESUME

A la suite d'atteintes cérébrales sévères telles que des accidents vasculaires cérébraux, des traumatismes crâniens ou anoxies cérébrales, une petite proportion de patients conserve une altération de l'état de conscience. Les patients avec des états de conscience altérée (ECA) dits « prolongés » (>28 jours post-accident) ouvrent leurs yeux (certains présentant des cycles éveil/sommeil) et la majorité d'entre eux ne bénéficient plus d'une ventilation invasive. En revanche, la plupart des patients ECA sont nourris artificiellement, suggérant un impact de la conscience sur les capacités de déglutition.

L'objectif de ce travail de thèse est de **contribuer à l'étude des liens entre conscience et déglutition**. Nos hypothèses sont que les capacités de déglutition sont en lien avec le niveau de conscience et que la présence de certains composants de la déglutition constitue un signe possible de conscience.

Sur base d'une revue de littérature, nous montrons que l'enchaînement des composants de la déglutition s'inscrit sur un continuum allant de comportements volontaires à réflexes. Les composants de la phase orale peuvent être considérés comme volontaires car davantage contrôlables et suppressibles (bien que largement automatisés), les composants de la phase pharyngée comme des réflexes somatiques et les composants de la phase œsophagienne comme des réflexes autonomes. Le déclenchement du réflexe de déglutition se situe quant à lui à la frontière entre comportement volontaire et réflexe somatique et l'ouverture du sphincter supérieur de l'œsophage sépare réflexe somatique et autonome. Si nous considérons les comportements volontaires comme de possibles signes de conscience, la présence de composants de la phase orale de la déglutition peut être considéré comme un comportement conscient. Nous montrons en outre qu'un grand nombre d'aires corticales (principalement le cortex sensorimoteur primaire, le cortex prémoteur, l'aire motrice supplémentaire, le cortex cingulaire antérieur, l'insula et le cervelet) sont impliquées à la fois dans des tâches de déglutition dites « volontaires » et « non-volontaires ».

Nous démontrons dans deux études rétrospectives analysant la déglutition de patients ECA diagnostiqués à l'aide d'évaluations comportementales répétées et d'examens de neuroimagerie, que la très grande majorité des patients ECA présentent une atteinte de la phase orale et/ou pharyngée.

Les patients ne montrant pas de signes comportementaux de conscience (état d'éveil non-répondant – EENR) ne présentent pas non plus de phase orale efficace autorisant une alimentation en texture solide. En conséquence, la préservation de composants de la phase orale de la déglutition devrait donc être envisagée comme un signe de conscience et faire partie des critères diagnostiques des patients ECA. L'absence de phase orale efficace chez les patients EENR et sa présence chez seulement une faible proportion de patients en état de conscience minimal (ECM) expliquent pourquoi aucun patient EENR « typique » (examens comportementaux et de neuroimagerie pointant dans la même direction) ne peut être nourri exclusivement per os ainsi que le fait qu'aucun patient ECM n'est nourri oralement en texture ordinaire.

En outre, dans le groupe de patients étudiés, le niveau de conscience est en lien avec certains composants de la phase pharyngée (reflété par l'absence de trachéotomie, de sécrétions pharyngo-laryngées ou de fausses-routes salivaires) ainsi qu'avec le réflexe de toux. En effet, il y a davantage de patients ECM comparés aux patients EENR qui présentent une gestion salivaire efficace et une toux réflexe bien que ces composants soient aussi présents chez certains patients EENR. Pour cette raison, ces éléments semblent constituer des « comportements sous contrôle cortical » sans pour autant constituer des signes de conscience en tant que tel.

Enfin, ce travail souligne le peu d'outils et de techniques de prise en charge de la déglutition adaptés aux patients ECA. Un protocole de validation d'un outil d'évaluation de la déglutition pour les patients ECA est dès lors proposé.

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Scientific publications

The present thesis is based on the following publications:

Links between swallowing and consciousness: Insight from behavioral and neuroimaging studies

Mélotte, E., Maudoux, A., Panda, R., Kaux, J.-F., Lagier, A., Herr, R., Belorgeot, M., Laureys, S., & Gosseries, O. (submitted).

Is oral feeding compatible with an unresponsive wakefulness syndrome?

Mélotte, E.[+], Maudoux, A.[+], Delhalle, S., Martial, C., Antonopoulos, G., Larroque, S. K., Wannez, S., Faymonville, M.-E., Kaux, J.-F., Laureys, S.*, Gosseries, O.*, & Vanhaudenhuyse, A.* (2018). *Journal of Neurology*, 265(4), 954-961. https://doi.org/10.1007/s00415-018-8794-y

Swallowing in individuals with disorders of consciousness: A cohort study

Mélotte, E., Maudoux, A., Delhalle, S., Lagier, A., Thibaut, A., Aubinet, C., Kaux, J.-F., Vanhaudenhuyse, A., Ledoux*, D., Laureys, S.*, & Gosseries, O*. (2020). *Annals of Physical and Rehabilitation Medicine* (in press). https://doi.org/10.1016/j.rehab.2020.04.008

The development and validation of the SWADOC tool: A study protocol for a multicentric prospective cohort study

Mélotte, E.[+], Belorgeot, M. [+], Herr, R. [+], Simon, J., Kaux, J.-F., Laureys, S., Sanz R.D., L., Morsomme, D., Lagier, A., Pellas, F.*, & Gosseries, O*. *Frontiers in Neurology* (accepted).

Other publications:

Article (as co-author)

Swallowing function after severe COVID-19: early videofluoroscopic findings

Lagier, A., Mélotte, E., Poncelet M., Remacle S., Meunier P. (2020). European Archives of Oto-Rhino-Laryngology

Book chapter (as co-author)

Feasibility of Oral Feeding in Patients with Disorders of Consciousness

Maudoux, A., Breuskin, I., Gosseries, O., Mélotte, E., Schnakers, C., & Vanhaudenhuyse, A. (2017). In Schnakers C. & Laureys, S. (eds), *Coma and Disorders of Consciousness* (p. 137-153). Springer International Publishing.

+ contribute equally to the work as first author

* contribute equally to the work as last author

Glossary

ABI	Acquired Brain Injury
CAMMRI	Comprehensive Measure for the Minimally Responsive Individual
CIs	Confidence Intervals
CPG	Central Pattern Generator
CRS-R	Coma Recovery Scale-Revised
DOC	Disorders Of Consciousness
DOCS	Disorders Of Consciousness Scale
DTI	Diffusion Tensor Imaging
EEG	Electroencephalography
EMCS	Emergence from the Minimally Conscious State
ENT	Ear, Nose and Throat
FDG-PET	Fluorodesoxyglucose Positron Emission Tomography
FILS	Food Intake Level Scale
fMRI	Functional Magnetic Resonance Imaging
FEES	Fiberoptic Endoscopic Evaluation of Swallowing
FOIS	Functional Oral Intake Scale
FOTT	Facial Oral Tract Therapy
FOTT-SAS	Facial Oral Tract Therapy Swallowing Assessment of Saliva
FOUR	Full Outline of UnResponsiveness
GCS	Glasgow Coma Scale
IDDSI	International Dysphagia Diet Standardisation Initiative
LIS	Locked-In-Syndrome
MCS	Minimally Conscious State
MRI	Magnetic Resonance Imaging
NVOST	Non-volitional swallowing task
ORs	Odds Ratios
PDOC	Prolonged Disorders of Consciousness
RLA	Ranchos Los Amigos Scale
SECONDs	Simplified Evaluation of CONsciousness Disorders
SMART	Sensory Modality Assessment and Rehabilitation Technique
SS	Spontaneous swallowing
SLT	Speech and Language Therapists
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
SWADOC	SWallowing Assessment in Disorders of Consciouness
TBI	Traumatic Brain Injury
UES	Upper Esophageal Sphincter
UWS/VS	Unresponsive Wakefulness Syndrome/Vegetative State

VFSS	VideoFluoroscopic Swallowing Study
VOST	Volitional swallowing task
VS	Voluntary swallowing
WHIM	Wessex Head Injury Matrix

List of tables and figures

Tables

Figures

GENERAL INTRODUCTION

Humans swallow several hundred times per day (Tanaka et al., 2013). Swallowing occurs spontaneously during wakefulness and sleep, and most of the time, without our being aware of it. Swallowing is one of the most essential physiological mechanism since it allows us to manage saliva and secretions.

We can all remember the sensation of food or liquid going down the wrong way, although the incidence of choking episodes is actually very low in the healthy population (Hemsley et al., 2019). In contrast, several acquired and chronic neurological conditions lead to swallowing problems (Hemsley et al., 2019). Depending on the disease, the incidence of dysphagia can be very high[1] (Arnold et al., 2016; Dunn & Rumbach, 2019; Guan et al., 2015; Kalf et al., 2012; Michel et al., 2018; Takizawa et al., 2016) and different components of the swallowing sequence can be affected.

After an acquired brain injury, we can reasonably assume that, the more severe the brain injury, the more severe the dysphagia (Formisano et al., 2004; Mackay et al., 1999a, 1999b). However, the question of what factors (e.g., lesion localization and volume, type of brain injury, consciousness) most affect the severity of dysphagia following brain injury has not yet been completely elucidated.

Level of consciousness has an impact on a variety of abilities such as language (Aubinet et al., 2018), motor function (Thibaut et al., 2015), sphincter function (Foxx-Orenstein et al., 2003) and feeding (Brady et al., 2006). Most patients with disorders of consciousness (DOC) are fed by enteral feeding tube. However, the true impact of consciousness on swallowing abilities remains poorly understood.

Consciousness allows us to experience things inside and outside us (Damasio & Meyer, 2009) and is classically defined by two components: arousal and awareness. Modifications of consciousness can be pathological (DOC) or non-pathological (sleep or anesthesia).

DOC represent different states along a continuum from coma (no arousal and no awareness) to being conscious and awake (preserved arousal and

[1] Stroke: 20.7% (Arnold et al., 2016), 9.1%–80% (Takizawa et al., 2016); Non-traumatic subarachnoid hemorrhage: 31.6% (Dunn & Rumbach, 2019); Multiple sclerosis: 36% (Guan et al., 2015); Parkinson's disease: 35% with subjective measurements and 82% with objective measurements (Kalf et al., 2012), 11%–81% (Takizawa, 2016); Older patients with dementia: 86.6% (Michel et al., 2018); Traumatic brain injury: 27%–30% (Takizawa et al., 2016); Community-acquired pneumonia: 91.7% (Takizawa et al., 2016).

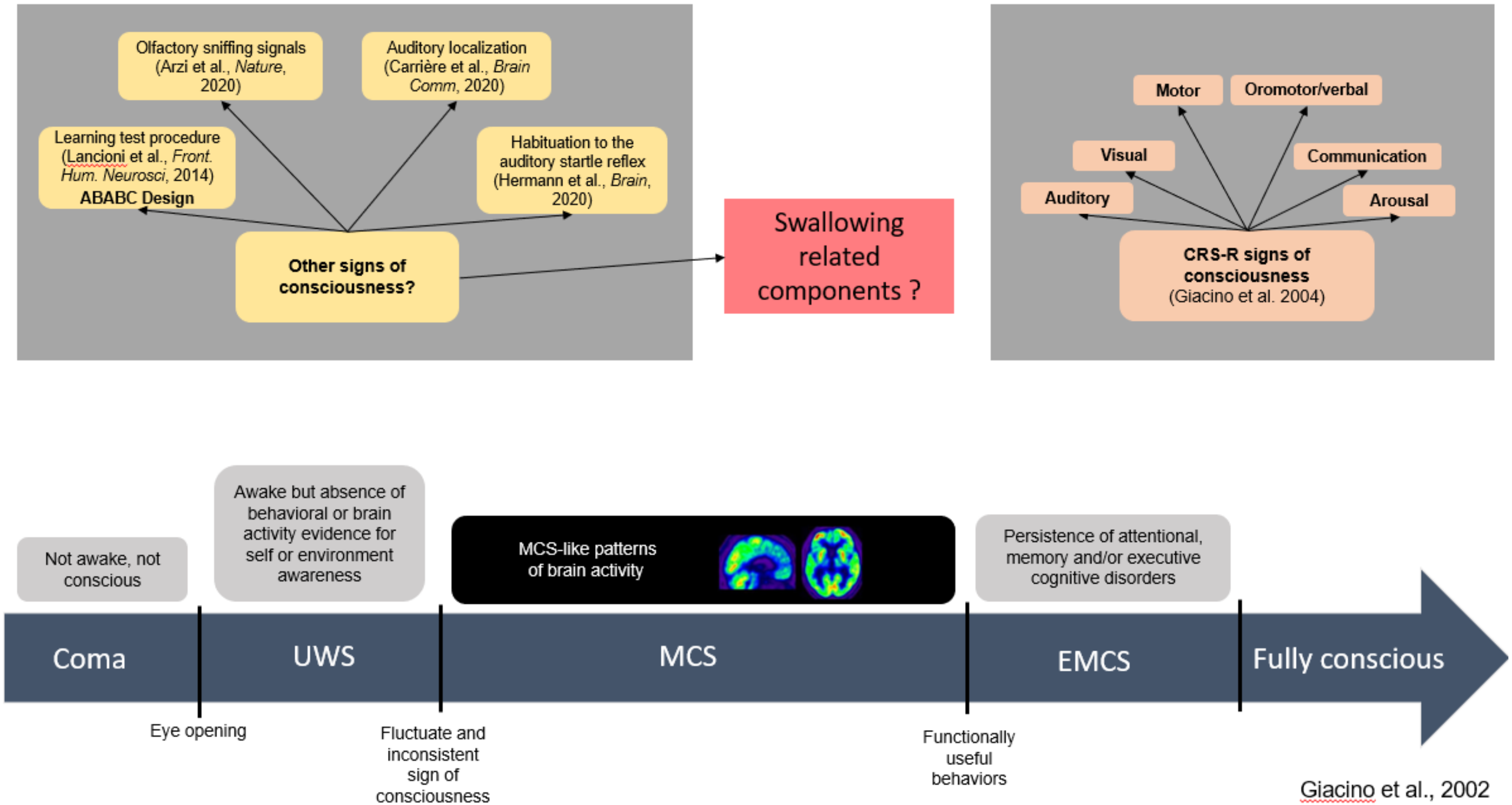
awareness). Between the two extremes, unresponsive wakefulness syndrome (UWS, previously termed vegetative state) is defined by recovery of arousal in the absence of any sign of awareness (Laureys et al., 2010), whereas minimally conscious state (MCS) refers to preserved arousal and reproducible but inconsistent signs of consciousness (Giacino et al., 2002). The MCS entity can be subdivided into minimally conscious MINUS (MCS–) and PLUS (MCS+) based on the presence (MCS+) or absence (MCS–) of behaviors indicating at least partial preservation of language abilities (Bruno et al., 2011; Thibaut et al., 2020). When patients recover the ability to functionally communicate or to use two objects appropriately, we consider that they are emerging from the minimally conscious state (EMCS) (Giacino et al., 2002). Patients with locked-in syndrome (LIS) have woken from their coma and are fully conscious but are unable to show behavioral signs of consciousness except by eye movements (Gosseries et al., 2009).

Misdiagnosis can have serious medical and ethical consequences for patients and their families. Indeed, functional outcomes and prognoses are better for MCS than UWS (Luaute et al., 2010; Noé et al., 2012). Moreover, response to treatment seems to be better in patients with MCS (Thibaut et al., 2014). Regarding pain management, noxious stimuli seem to elicit a larger cerebral response in patients with MCS than in UWS, suggesting that patients with MCS may be more likely to feel pain than those with UWS (Boly, Faymonville, et al., 2008; Demertzi et al., 2009, 2013). Finally, level of consciousness influences end-of-life decisions (Bernat, 2008; Demertzi et al., 2011)

Recent guidelines for the diagnosis of patients with DOC recommend that one use valid, reliable standardized neurobehavioral assessments of consciousness (Giacino et al., 2018a, 2018b; Kondziella et al., 2020). The Coma Recovery Scale – Revised (CRS-R) is the reference standard for the clinical bedside evaluation of consciousness (Giacino et al., 2004), as it fulfills all the Aspen Neurobehavioral Workgroup criteria (Seel et al., 2010). The diagnostic criteria for consciousness in the CRS-R are classified in six categories (auditory, visual, motor, oromotor/verbal, communication, arousal) (see **Appendix 1.1**). Beyond behaviors assessed using the CRS-R, some authors have identified other criteria linked to level of consciousness (Chatelle et al., 2018; van Ommen et al., 2018) and other possible signs of consciousness (Arzi et al., 2020;

Carrière et al., 2020; Hermann et al., 2020; Lancioni et al., 2014) (see **Figure 1** & **Appendix 1.2**).

Figure 1. CRS-R and possible other signs of consciousness along the continuum from coma to recovery of consciousness



Note: CRS-R=Coma Recovery Scale-Revised; UWS=Unresponsive Wakefulness Syndrome; MCS=Minimally Conscious State; EMCS=Emergence of minimally conscious state

Hermann et al. (2020) emphasized the importance of expanding the range of signs of consciousness that can be tested at the bedside.

Until now, swallowing capacities have not been included in the diagnostic criteria for consciousness (Giacino et al., 2002) and it has not been clearly established whether the level of consciousness is related to the presence or absence of certain components of swallowing.

Our hypotheses are that swallowing capacities are linked to level of consciousness, and that the presence of some components of swallowing constitutes a possible sign of consciousness.

As clinicians, at the beginning of this thesis project, our ambition was to work on the management of dysphagia in patients with DOC. However, there was no real understanding of the impact of consciousness on swallowing or the pathophysiology of swallowing in patients with DOC, nor were there any assessment tools. For that reason, we chose to devote this work to establishing the basis of the links between swallowing and consciousness.

To lead off, **Chapter 1** presents a theoretical introduction in the form of a literature review on the links between swallowing and consciousness. In that section, we identify several thematic areas addressing the relationships between swallowing and consciousness.

In **Chapter 2**, we retrospectively explore the possibility of oral feeding in a group of 68 patients without behavioral signs of consciousness.

To extend our understanding of the possibility of oral feeding and, more broadly, the pathophysiology of swallowing in all patients with DOC, in **Chapter 3,** we retrospectively document the incidence and characteristics of dysphagia in 92 patients with DOC (UWS and MCS), and describe the links between level of consciousness and different components of swallowing.

Finally, **Chapter 4** presents the protocol study for the development and validation of a new instrument: the SWallowing Assessment in Disorders Of Consciousness (SWADOC).

This thesis takes the form of a collection of scientific papers. The figures and tables have been renumbered and all references are now presented in a single list at the end of the thesis.

01

CHAPTER

LITERATURE REVIEW

LINKS BETWEEN SWALLOWING AND CONSCIOUSNESS: INSIGHT FROM BEHAVIORAL AND NEUROIMAGING STUDIES

Submitted.

Evelyne Mélotte, Audrey Maudoux, Rajanikant Panda, Jean-François Kaux, Aude Lagier, Roxanne Herr, Marion Belorgeot, Steven Laureys, Olivia Gosseries

ABSTRACT

This literature review focuses on swallowing and associated brain mechanisms from the perspective of consciousness. Swallowing phases operate on a continuum ranging from voluntary (oral components) to somatic (pharyngeal) and autonomic (esophageal) reflex behaviors. Moreover, cortical activations seem to be similar in volitional and non-volitional swallowing tasks, although volitional swallowing activates a larger cortical area than non-volitional swallowing. These cortical areas are, however, not specific to swallowing but common to related motor tasks and consciousness networks. The efficacy of the oral phase seems to be the most robust sign of consciousness related to swallowing. Components of the pharyngeal phase (in terms of abilities of saliva management) and cough reflex are cortically mediated behaviors but not necessarily signs of consciousness. This review also highlights the critical lack of tools and techniques to assess and treat dysphagia in patients with disorders of consciousness.

INTRODUCTION

Consciousness is a complex phenomenon. In the field of clinical science, researchers define consciousness based on two components: wakefulness (arousal) and awareness (subjective experience) (Laureys, 2005). Consciousness allows us to be aware of objects and events, inside and outside our body (Damasio & Meyer, 2009; Laureys, 2005). Wakefulness and awareness are generally correlated. Although healthy people are aware when they are awake, during coma and in most cases during general anesthesia, patients are neither awake nor aware. Modifications of consciousness can be pathological (disorders of consciousness) or nonpathological (sleep or anesthesia) and can alter cognitive, language and motor functions, and also swallowing capacities (Schnakers, 2017).

In healthy individuals, swallowing is such an automated sensorimotor mechanism that, apart from episodes of food “going down the wrong way” due to distraction, no one consciously experiences their swallowing. An exception exists with mindfulness and we can consciously experience our swallowing if we decide to voluntarily pay attention to it. Depending on the disease, the prevalence of dysphagia can be very high in neurological populations (Arnold et al., 2016; Dunn & Rumbach, 2019; Guan et al., 2015; Kalf et al., 2012; Michel et al., 2018). In acquired brain injury, we can reasonably assume that, the more severe the brain injury, the more severe the dysphagia (Formisano et al., 2004; Mackay et al., 1999b).

The severity of brain injury is classically defined, among other things, according to the Glasgow Coma Scale (GCS) (Teasdale & Jennett, 1974), on admission and coma duration (Asikainen et al., 1998). Some comatose patients die because of the severity of their brain injuries or subsequent complications, while others open their eyes and initially present disorders of consciousness (DOC) before recovering partial or complete consciousness (Schnakers, 2017).

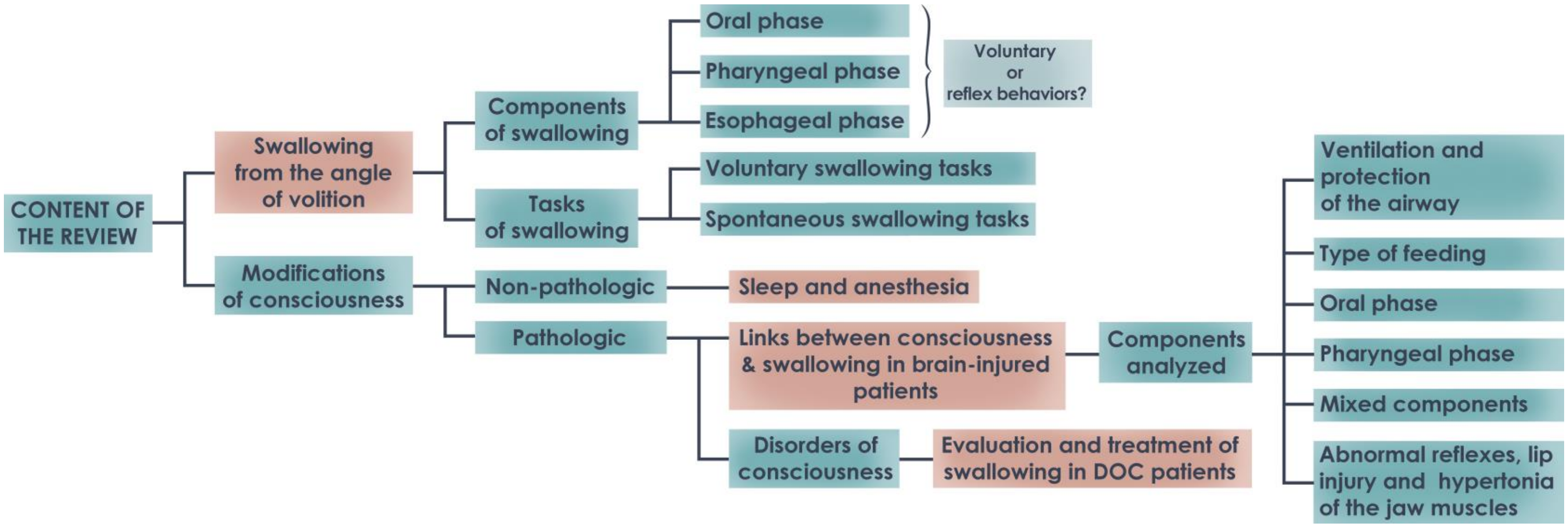
Based on the presence of reflexive or conscious behaviors, level of consciousness can reflect three different clinical entities (Gosseries et al., 2014): *coma,* which is characterized by no arousal and no awareness; *unresponsive wakefulness syndrome* (UWS, previously termed vegetative state), characterized by eye opening and reflexive movements only (Laureys et al., 2010); and *minimally conscious state* (MCS), identified by reproducible but inconsistent signs of consciousness, such as visual pursuit or response to commands (Giacino et al., 2002). MCS can be subdivided into minimally conscious MINUS (MCS–) and PLUS (MCS+) based on the presence (MCS+) or absence (MCS–) of behaviors indicating at least partial preservation of language abilities (Bruno et al., 2011; Thibaut et al., 2020). When patients recover the ability to functionally communicate or to use two objects appropriately, they are emerging from MCS (EMCS) (Giacino et al., 2002). UWS and MCS are usually transitional states between coma and higher levels of consciousness. However, some patients present prolonged, chronic DOC.

Recent guidelines for the diagnosis of patients with DOC recommend using valid, reliable standardized neurobehavioral assessments of consciousness (Giacino et al., 2018a, 2018b; Kondziella et al., 2020). Behavioral assessments of consciousness in brain-injured patients aim to identify the presence or absence of voluntary behaviors versus reflexive behaviors (Fischer & Truog, 2015). In the last 20 years, an increasing number of researchers have focused their work on the identification of signs of consciousness. In 2002, the Aspen Neurobehavioral Workgroup outlined the clinical features associated with coma, UWS, MCS and Locked-in syndrome across seven categories (consciousness, sleep/wake, motor, auditory and visual functions, communication and emotion) and defined the diagnostic criteria for MCS (Giacino et al., 2002). The development of diagnostic criteria for the MCS led to the revision of the Coma Recovery Scale (CRS) and the development of its current version, the Coma Recovery Scale – Revised (CRS-R) (Giacino et al., 2004). The CRS-R is considered the gold standard for clinical bedside evaluation of signs of consciousness (Giacino et al., 2004), as it fulfills all the Aspen Workgroup criteria (Seel et al., 2010). Beyond the behaviors assessed using the CRS-R, other possible signs of consciousness include the learning test procedure (Lancioni et al., 2014), resistance to eye opening (van Ommen et al., 2018), olfactory sniffing signals (Arzi et al., 2020), auditory localization (Carrière et al., 2020) and auditory habituation (Hermann et al., 2020).

It is relatively clear to therapists working in dysphagia rehabilitation that level of consciousness influences swallowing abilities. However, the links between swallowing and consciousness have not yet been examined to any great extent.

Because of the scarcity of studies directly related to swallowing and consciousness, in this article we chose to explore a wide range of themes addressing the links between swallowing and consciousness rather than focusing on one topic or answering one specific question (see **figure 2**). For this reason, we present the results of our research in the form of a literature review instead of a systematic review.

Figure 2. Summary of the research fields explored in this review



Note. Orange rectangles indicate the main fields covered by the literature review. Abbreviations: DOC=disorders of consciousness

SECTION 1: Swallowing from the perspective of volition

The approach historically used to determine whether or not a patient is conscious consists in the comparison of reflexive and voluntary behaviors (Giacino et al., 2002). However, the difference between conscious and reflexive behaviors remains ambiguous (Fischer & Truog, 2015). In fact, there are no empirical characteristics that allow us to reliably distinguish reflexive behaviors from conscious behaviors (Fischer & Truog, 2015).

Prochazka et al. (2000) demonstrated that the distinction between *voluntary and reflex* differs depending on the approach. The Prochazka/Loeb/Rothwell position (Prochazka et al., 2000) describes ***voluntary behaviors*** as those that proceed under conscious control (Loeb) and that we can interrupt, influence (Rothwell) and suppress at will (Prochazka) and ***reflex behaviors*** as those that are automatic and hard to suppress (Prochazka) and that cannot be modified voluntarily. Some researchers (D'Ostilio & Garraux, 2012; Sumner & Husain, 2008) also agree that all voluntary behaviors contain ***automatic processes*** contributing to their rapidity and flexibility. Moreover, two types of reflexes are involved in swallowing: somatic and autonomic reflexes (see below) (Miller, 2002). Somatic reflexes implicate striated/skeletal muscles, and autonomic reflexes target smooth muscles.

Based on these characteristics (see **table 1**), we will analyze the different components of swallowing and try to distinguish voluntary from reflex behavior.

Table 1. Characteristics of voluntary behavior and somatic and autonomic reflexes

	Voluntary behavior	**Somatic reflex**	**Autonomic reflex**
Type of peripheral efferent nervous system	Somatic nervous system	Somatic nervous system	Autonomic nervous system
Characteristics	Under conscious control Can be interrupted Can be influenced Can be suppressed at will	? Cannot be interrupted Can be influenced to some degree Hard to suppress	Not conscious Cannot be interrupted Cannot be influenced Cannot be suppressed
Type of muscles	Striated/skeletal muscles	Striated/skeletal muscles	Smooth muscles

Swallowing is classically divided into three phases: oral, pharyngeal and esophageal (Shaker, 2013). The oral phase has two stages. Stage I consists of the transport of ingested food from the incisal area to the molar region and the reduction of food with mastication to a “swallowable” condition. Stage II consists of the movement of the bolus from the oral cavity through the pillars of the fauces to the oropharynx (Hiiemae & Palmer, 1999). The duration of the oral phase depends on several parameters, such as the consistency and volume of the bolus (Hiiemae et al., 1996).

In the pharyngeal phase, the bolus is transferred from the base of the tongue to the esophagus with successive rapid mechanisms (nasopharyngeal closure, elevation of hyoid bone and pharynx with laryngeal elevation, laryngeal closure, downward movement of the epiglottis and esophageal sphincter relaxation).

Finally, during the esophageal phase, the bolus is pushed into the stomach through a series of peristaltic contractions.

1.1. Components of swallowing

As we have seen, swallowing is divided into three phases (oral, pharyngeal, esophageal), each one comprising several components.

The oral phase is classically described as the voluntary phase of swallowing while the pharyngeal and esophageal phases are the reflexive phases (Ertekin & Aydogdu, 2003). To confirm this assumption, we will now discuss the different components in each phase of swallowing in light of the characteristics of voluntary versus reflex behaviors (**figure 3,** page 40).

1.1.1. Oral phase

Although we chew and transport food without consciously controlling each orofacial movement, the oral phase is the only phase of swallowing that can be entirely interrupted and consciously controlled. In that respect, the modifiable and suppressible character of the oral phase categorizes this phase as ***voluntary behavior***. In addition, several studies have demonstrated that consciously controlling the oral phase modifies its sequencing (Ashiga et al., 2019; Furuya et al., 2014; Palmer et al., 2007). Indeed, the chewing sequence can be significantly lengthened (almost twice as long) with volition (e.g., chewing with a conscious effort, or a specific number of chews) than without volition (i.e., eating normally). These data emphasize the role of automatic processes in natural feeding conditions. In other words, most of the time, the various lip and tongue movements occur without volition but rather as semiautomatic periodic or rhythmic movements, which explains why, in "controlled" conditions, the oral phase lasts longer.

The notion of semiautomatic periodic or rhythmic movements is not a recent one (Dubner et al., 1978). Many studies, especially those by Sessle's team (Martin et al., 1997; Sessle et al., 2005, 2007; Yao et al., 2002), have explored the neural control of orofacial movements in primates using intracortical microstimulations. They indicated that the primary motor cortex dedicated to the orofacial area is involved in voluntary movements but also in the control of semiautomatic movements, such as tongue and mastication movements. Studies of oral reflexes also showed that diffuse stimuli to the palate in decerebrated and anesthetized cats elicited rhythmic tongue activity (Miller, 1982). Moreover, in the field of epilepsy, one study showed that electrical stimulation of the right inferior frontal gyrus (fronto-opercular cortex) leads to oroalimentary automatisms (lip movements, chewing) (Maestro et al., 2008).

The oral phase of swallowing can be classified as a voluntary behavior but, like any another motor activity, it includes some automatic processes. As described by Humbert and German (2013), during feeding, the different components of the oral phase can moved along the continuum of low to high voluntary control depending on the degree of attention dedicated specifically to them. The pattern-generating circuits for chewing and licking are located in the brainstem but receive direct cortical inputs (Moore et al., 2014).

1.1.2. Pharyngeal phase

The triggering of what is commonly called the "swallowing reflex" heralds the end of the oral phase and the beginning of the pharyngeal phase. This reflex is a somatic reflex because it involves striated/skeletal muscles.

In "natural" conditions, the swallowing reflex occurs in response to saliva accumulation or to the presence of liquid or food in the oropharyngeal space (i.e., area of the soft palate, faucial pillars, pharyngeal surface of the epiglottis, dorsal pharyngeal wall). Indeed, when a sensory input (presence of saliva or a liquid or solid bolus) reaches a certain threshold, it triggers the swallowing reflex, which elicits the start of the sequence leading to protection of the airway and transportation of the bolus to the esophagus (Nishino, 2013). The timing of the initiation of the swallowing reflex is influenced by the waking state (see **section 2**), type of bolus (shortest with liquids) (Palmer et al., 1992) and cognitive functions (Dodderi & Larisa, 2016; Dodderi et al., 2018; Troche et al., 2014).

Although the swallowing reflex is usually triggered without conscious perception, it can be evoked voluntarily. Moreover, the swallowing reflex can be artificially initiated in humans by air pulses (Theurer et al., 2009) or electrical stimulations (Takatsuji et al., 2012; Tsukano et al., 2012) of the pharyngeal area. Whereas the execution of the oral phase can be stopped at any time, the swallowing reflex is hard to suppress for a long time during feeding or at rest.

If we refer to the definitions of Prochazka et al. (2000), the swallowing reflex can be triggered voluntarily but is usually automatic and is hard to suppress. It is thus ***on the borderline between a voluntary behavior and a reflex***. Moreover, we can postulate that the transition between a voluntary behavior and a somatic reflex takes place somewhere between the beginning of the stage II oral phase transport and the triggering of the swallowing reflex.

On the other hand, the proceedings occurring after the trigger of the swallowing reflex (pharyngeal phase) cannot be suppressed voluntarily, unlike the oral phase and, to a lesser extent, the triggering of the swallowing reflex. However, some studies have shown that the pharyngeal phase can be influenced voluntarily to some extent; for example, patients can learn maneuvers that change swallowing physiology and help to reduce aspirations (e.g., Mendelsohn maneuver or effortful swallow) (Humbert & German, 2013; Shaker, 2013; Wheeler-Hegland et al., 2008). The process of the pharyngeal phase is mainly a ***somatic reflex***.

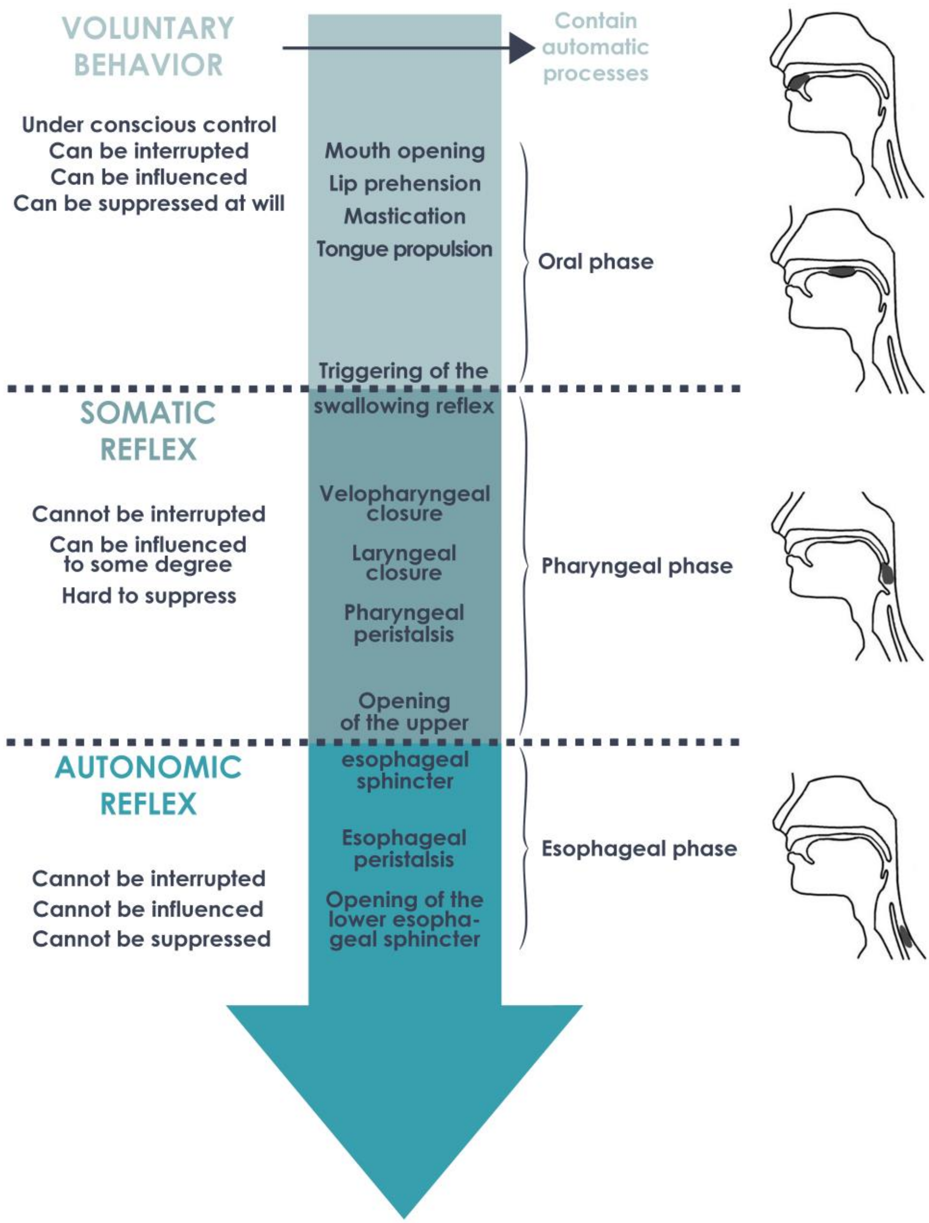
1.1.3. Esophageal phase

The opening of the upper esophageal sphincter (UES) marks the end of the pharyngeal phase and the start of the esophageal phase. The UES is also called the inferior pharyngeal sphincter (Shaker, 2013). Muscles involved in the upper third of the esophagus (mainly the UES) are striated muscles under the control of vagal cholinergic motoneurons in the nucleus ambiguus of the brainstem (partly with the vagus cranial nerve X). In the lower two thirds of the esophagus, which is composed of smooth muscles, neural control switches to the autonomic/vegetative (enteric) nervous system through motoneurons situated in the ganglia (Broussard & Altschuler, 2000; Musgrove et al., 2020; Richards & Sugarbaker, 1995; Shaker, 2013).

The esophageal phase cannot be voluntarily triggered or suppressed. The only possible influence on the esophageal phase is a passive effect on the UES. In fact, Shaker et al. (2002) showed that head-raising exercises improve the UES, among other things. The mechanism at play is a passive stretch of the UES and/or an improvement of pharynx propulsion, which facilitates the opening of the UES.

For these reasons, the esophageal phase can be considered as an ***autonomic reflex***. Given anatomical considerations (Meyer et al., 1986), we can assume that the transition between a somatic and an autonomic reflex (and consequently between striated and smooth muscles) takes place somewhere in the upper third of the esophagus.

Figure 3. Classification of the oral, pharyngeal and esophageal phases of swallowing on the continuum of voluntary to reflexive behaviors



Note. The transition between a voluntary behavior and a somatic reflex takes place somewhere between the beginning of the stage II oral phase transport and the triggering of the swallowing reflex. The transition between a somatic and an autonomic reflex (and consequently between striated and smooth muscles) takes place somewhere in the upper third of the esophagus.

1.2. Swallowing tasks

In the last 20 years, several researchers have explored the different stages of swallowing in healthy participants and in patients with dysphagia. Swallowing has been studied in several conditions (saliva, liquid or food swallowing) and, in addition to the voluntary or reflexive nature of each component of swallowing, some authors also distinguish swallowing tasks depending on the influence of volition.

Ertekin et al. (2001) distinguished between reflexive swallows (water introduced to the back of the tongue with a syringe), nasopharyngeal swallows (water introduced through a canula at the level of the uvula), spontaneous swallows (accumulation of saliva in the mouth that triggered spontaneous swallowing) and voluntary swallows (1–3 ml of water swallowed voluntarily) in an electrophysiological study. They showed, among other things, that the time interval between the onset of submental EMG and the onset of upward deflection of the larynx was significantly shorter for reflexive, nasopharyngeal and spontaneous swallows than for voluntary swallows. Kern, Jaradeh, et al. (2001) compared reflexive (rapid injection of water into the pharynx) and voluntary swallows (cued to swallow saliva volitionally once every 30 s by a tactile cue) in a neuroimaging study. While reflexive swallowing was associated with bilateral activity concentrated in the primary sensory/motor regions, volitional swallowing was represented bilaterally in the insula, prefrontal, cingulate, and parietooccipital regions in addition to the primary sensory/motor cortex.

One decade later, Ertekin (2011) dedicated a literature review to a comparison of *spontaneous swallowing* (SS) and *voluntary swallowing* (VS). He described SS as a “type of protective reflex action that occurs to ensure safety of the upper airway tract against any escape of food particles or saliva, or as an emotion-related reflex activity occurring during stressful conditions” (2011, p. 184). SS occurs without awareness while one is awake or asleep. The oral phase is bypassed in most cases, although there may be partial excitation. SS is also sometimes called “reflexive swallowing” or “non-nutritive swallowing.” On the other hand, he described VS (also called “conscious swallowing”) as sequential eating or drinking voluntarily initiated or facilitated by the cerebral cortex during the awake and aware state (Ertekin, 2011).

In **table 2**, we describe several types of volitional (VOST) and non-volitional swallowing tasks (NVOST) related to the concept of reflexive (RS), spontaneous (SS) and voluntary swallowing (VS). Because of the potentially different brain activations and different physiological mechanisms at play during nutritive compared to non-nutritive swallowing, we also make a distinction between these two types of swallowing tasks.

To examine this distinction in light of neuroimaging data, we did a qualitative analysis of studies exploring cerebral areas activated during RS, SS or VS task in healthy subjects (see **Appendix 2.1** for research strategy and selected criteria).

Table 2. *Description of the different types of swallowing tasks*

	Non-volitional tasks (NVOST)		**Volitional tasks (VOST)**
	Reflexive swallowing (RS)	Spontaneous swallowing (SS)	Voluntary swallowing (VS)
Non-nutritive	Triggering of the swallowing reflex with tactile stimulation in the pharyngo-laryngeal area	Saliva swallowing without visual or verbal instruction to swallow	Saliva swallowing under visual or verbal instruction to swallow
Nutritive	Injection of small amounts of water or food directly into the pharynx	Swallowing of water or food without visual or verbal instruction to swallow	Swallowing of water or food with visual or verbal instruction to swallow

Note. Reflexive swallowing refers to triggering of the swallowing reflex by an external stimulus (tactile or with the injection of a bolus). In this case, the participation of the oral phase is diminished but not completely bypassed considering the involvement of the tongue in any swallowing process. Non-nutritive spontaneous swallowing refers to the management of saliva and secretions that are produced spontaneously by all healthy humans, while nutritive spontaneous swallowing is associated with eating and drinking. Volitional swallowing tasks refer to tasks occurring further to an internal or external request.

In the 31 studies identified (see **Appendix 2.2** for description of studies and results), the majority (n=28) focused on VS tasks using water or saliva and compared the induced brain activity with that induced by other tasks, such as motor imaging of swallowing, speaking out loud, tongue movement or finger tapping. One author compared RS with VS (Kern, Jaradeh, et al., 2001), another compared SS with VS (Martin et al., 2001) and one study (Paine et al., 2011) focused on SS task but compared their results with another study analyzing VS tasks (Malandraki, 2009).

Only four studies (Hamdy & Rothwell, et al., 1999; Harris et al., 2005; Zald & Pardo, 1999, 2000) used positron emission tomography (PET); the majority used functional magnetic resonance imaging (fMRI) (n=27). Regarding brain location, the majority of the studies (n=24) focused on whole brain analysis whereas five targeted regions of interest (Lowell et al., 2012; Luan et al., 2013; Malandraki et al., 2010; Mihai et al., 2014; Toogood et al., 2017), and one focused specifically on the brainstem (Komisaruk et al., 2002). The small number of studies focusing on the brainstem may reflect the technical challenges of imaging this area (Sclocco et al., 2018).

We did a qualitative analysis of areas involved in volitional (VS) compared to non-volitional (RS and SS) swallowing tasks, based on the brain areas and Brodmann areas mentioned in studies. Each brain area identified was linked with brain areas in the AAL2 Atlas (Rolls et al., 2015), implemented in Surf Ice (https://www.nitrc.org/projects/surfice/) (**figure 4**).

Numerous cortical and subcortical areas are involved in the control of **VOST tasks** (**figure 4**). Based on the 30 studies using VOST tasks, we found that the main brain regions (identified in at least 50% of the studies) involved in VOST tasks are the primary motor cortex (n=26), insula (n=24), primary somatosensory cortex (n=22), premotor cortex and supplementary motor area (n=19) and anterior cingulate cortex (n=19) (right>left). Regions identified in at least 25% of studies are the cerebellum (n=13) (left>right), superior temporal gyrus (n=11), posterior cingulate cortex (n=10), thalamus (n=10), inferior parietal lobule (n=9), precuneus (n=9), putamen (n=9) (left>right) and superior frontal gyrus (n=8). The other regions (identified in less than 25% of studies) are the frontal operculum (n=7), inferior frontal gyrus (n=7), cuneus/lingual gyrus (n=7), middle frontal gyrus (n=5), middle cingulate gyrus (n=5) and middle temporal gyrus (n=5) (**figure 4**).

The three studies exploring **NVOST tasks** (Kern, Jaradeh, et al., 2001; Martin et al., 2001; Paine et al., 2011) showed that the activated regions were not specific to NVOST as they were all also activated in **VOST tasks**.

However, some brain areas (i.e., precuneus, inferior, middle and superior frontal cortex, frontal operculum, putamen and middle cingulate cortex) were activated during VOST tasks but not NVOST tasks.

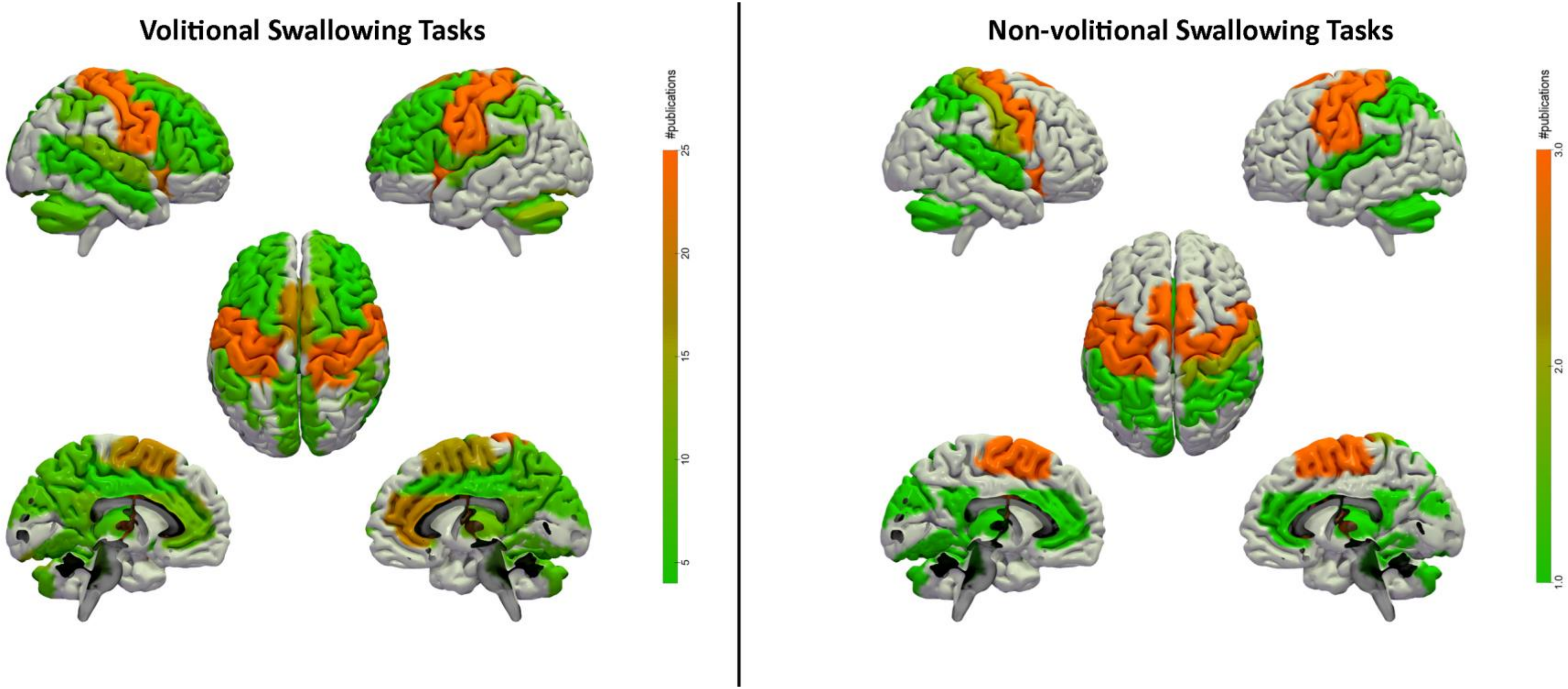
In the **two studies directly comparing VOST and NVOST tasks** (Kern, Jaradeh, et al., 2001; Martin et al., 2001), the authors reported that some areas were activated in VOST tasks and not in NVOST tasks; the insula and the prefrontal, anterior cingulate, and parieto-occipital regions in the Kern study and the anterior cingulate cortex in the Martin study. Kern et al. also argued that NVOST (RS) is characterized by greater cortical activation in the left hemisphere, whereas VOST shows greater volume activation in the right hemisphere.

Paine et al. (2011) compared their results obtained with naive saliva swallowing (SS) with the results of another study (Malandraki et al., 2009), which used voluntary water swallowing (VS). They showed that regions activated in both tasks were almost identical. Indeed, regions related to motor control, sensory input and somatosensory integration were significantly activated in both SS and VS conditions. However, the authors reported that the significant activations from the SS study were much more localized in motor control areas.

Finally, swallowing tasks and specific oral (e.g., jaw clenching, tongue movements) or pharyngeal (i.e., throat clearing) tasks share areas of activation. Indeed, the main brain areas activated during swallowing were also activated during isolated oral or pharyngeal tasks.

All these studies were done during wakefulness, but we will see now what impact sleep and anesthesia have on swallowing.

Figure 4. Brain areas activated by volitional and non-volitional swallowing tasks



Note. Colors refer to the number of studies that mentioned the depicted area. For studies using volitional tasks, brain areas mentioned in at least five studies are illustrated in the figures. For the non-volitional tasks, all areas are depicted because of the low number of studies (n=3). The main regions activated in **volitional tasks** are the bilateral primary somatosensory cortex and bilateral insula, followed by the bilateral supplementary motor area and the right anterior cingulate cortex. The other regions activated at least in five studies are the bilateral cerebellum (left>right), bilateral superior temporal cortex, bilateral posterior cingulate cortex, bilateral thalamus, bilateral inferior parietal cortex, bilateral precuneus and cuneus, bilateral inferior frontal cortex and frontal operculum, left putamen, bilateral superior frontal cortex, left middle frontal cortex, bilateral middle cingulate cortex and right middle temporal cortex. Brain areas activated in **non-volitional tasks** are the primary sensorimotor cortex, supplementary motor cortex and insula, followed by the bilateral anterior and posterior cingulate cortex, bilateral cerebellum, left cuneus, bilateral thalamus, bilateral inferior and superior parietal cortex and bilateral superior temporal cortex.

Section 2: Nonpathological modifications of consciousness: sleep and anesthesia

Investigating swallowing in nonpathological modifications of consciousness such as sleep or anesthesia allows to explore swallowing without the ambiguity of conscious control. Indeed, sleep and anesthesia are associated with reduced consciousness and lack of volition, enabling volitional versus nonvolitional swallowing to be distinguished.

Sleep is classically divided into three stages of nonrapid eye movement (NREM) sleep (N1, N2 and N3) and rapid eye movement (REM) sleep. As described by Sanders et al. (2012), in NREM sleep individuals are generally considered unconscious, disconnected and not responsive, but people recall dreams after being woken from NREM sleep in 23% to 74% of cases. In contrast, during REM sleep, individuals are sometimes considered conscious (in approximately 80% of REM sleep awakenings) and report vivid dreams, but they do not experience their environment. They are disconnected and not responsive.

During sleep and in the case of DOC, the absence of consciousness does not lead to a complete absence of swallowing. Several studies have explored spontaneous saliva swallowing in healthy adults during sleep (Guiu Hernandez et al., 2019; Kelly et al., 2007; Lichter & Muir, 1975; Okuno et al., 2016; Pohl et al., 2013; Sato et al., 2011, 2016; Sato & Nakashima, 2006). During sleep, swallowing is episodic, absent for long periods and influenced by sleep stage (Sato et al., 2011, 2016; Sato & Nakashima, 2006). The deeper the sleep stage, the lower the mean swallowing frequency. Swallowing occurs almost in association with movement arousals in both REM and NREM sleep (Lichter & Muir, 1975; Sato et al., 2016; Sato & Nakashima, 2006). Some authors reported no (Sato et al., 2016) or very few (Sato & Nakashima, 2006) swallows during deep sleep (NREM stage N3). Regarding the efficacy of the pharyngeal phase, healthy adults have lower velopharyngeal and hypopharyngeal swallowing pressures when asleep (Guiu Hernandez et al., 2019). In their study, Kelly et al (2007) showed that breathing-swallowing coordination differed between volitional (saliva swallowing on command) and nonvolitional swallowing (spontaneous saliva swallowing without cuing) conditions but not between their two nonvolitional conditions (spontaneous saliva swallowing during waking and sleep). Moreover, during a functional test (instillation of water in the pharynx), more aspirations after swallowing were observed during sleep than during wakefulness, as well as more repetitive swallowing and coughing after swallowing (Okuno et al., 2016).

Patients with neurological impairments (cerebral atrophy or lacunar infarct) demonstrated a delayed response between the delivery of water in the pharynx and the triggering of swallowing when asleep, compared to when awake, while the healthy group showed no significant difference between wakefulness and sleep (Pinto et al., 1994). In Parkinson's disease patients, the mean duration of sleep decreases while the number of spontaneous saliva swallowings increases compared to healthy subjects (Uludag et al., 2016). Moreover, patients present more multiple swallows than healthy subjects.

Anesthesia can also be considered as a way of exploring consciousness but cannot be considered simply as an "absence of consciousness" (Bonhomme et al., 2019). Different consciousness states can be observed during general anesthesia, depending on the anesthetic agent and dose: (1) a complete absence of subjective experience (unconsciousness); (2) conscious experience without perception of the environment (disconnected consciousness, as in dreaming); or (3) episodes of oriented consciousness with awareness of the environment (connected consciousness) (Bonhomme et al., 2019).

Some authors (D'Angelo et al., 2014; D'Honneur et al., 1994; Gemma et al., 2016; Rimaniol et al., 1994; Taylor et al., 1972) have shown that general anesthetics (e.g., propofol, sevoflurane, ketamine and midazolam), which generally cause some form of unconsciousness (Sanders et al., 2012), can alter swallowing. Thus, during general anesthesia, the frequency of spontaneous saliva swallowing decreases and the number of pathological swallows (characterized by inspiration or followed by an inspiration) increases (D'Angelo et al., 2014). Moreover, studies analyzing the efficacy of swallowing after the injection of a liquid at the back of the tongue or the pharynx during anesthesia showed that the latency between the injection and the initiation of the swallowing reflex (D'Honneur et al., 1994; Nishino et al., 1987; Rimaniol et al., 1994), and the number of aspirations (Gemma et al., 2016) increase while laryngeal reflexes are depressed (Taylor et al., 1972). Moreover, coordination between respiration and swallowing can change with deep sedation or during the recovery period from general anesthesia (Cedborg et al., 2015; Nishino & Hiraga, 1991).

All this information (see **Appendix 2.1** for research strategy and selected criteria) shows that the frequency, speed of initiation of the swallowing reflex, efficacy of the pharyngeal phase of swallowing (mainly the number of aspirations) and coordination between respiration and swallowing are influenced by the level of consciousness during sleep and general anesthesia.

In the next section, we will see how consciousness affects swallowing in patients with brain injuries.

Section 3: Links between consciousness and swallowing in brain-injured patients

The prevalence of dysphagia further to severe brain injury is very high (Mélotte et al., 2020), mainly due to the large number of brain areas dedicated to swallowing (see above), any of which can be severely damaged by a brain injury. A large majority of patients with DOC require artificially delivered hydration and nutrition, mainly through a gastrostomy feeding tube (Mélotte et al., 2020; Royal College of Physicians, 2003a). The aim of this section is to examine the extent, variety and characteristics of swallowing disabilities in patients with acquired brain injury (ABI), and to identify which swallowing components are related to consciousness. To better understand these links, we reviewed studies analyzing swallowing in relation to consciousness level (see **Appendix 2.1** for research strategy and selected criteria).

We found 18 studies that describe a link between consciousness and swallowing abilities (see **table 3** for characteristics of the studies). Nine studies explored swallowing abilities for all etiologies (Brady et al., 2006, 2009; Bremare et al., 2016; Godet et al., 2017; Kjaersgaard et al., 2015; Mélotte et al., 2018, 2020; Millwood et al., 2005; Wang et al., 2019, while nine focused solely on traumatic brain injury (TBI) (Hansen, Engberg, et al., 2008; Hansen, Larsen, et al., 2008; Mackay et al., 1999a, 1999b; Mandaville et al., 2014; O'Neil-Pirozzi et al., 2003; Terré & Mearin, 2007, 2009; Winstein, 1983).

The studies are quite heterogeneous in terms of the swallowing components described, the consciousness scales used, the range of consciousness level considered, and the design of studies.

Twelve studies reported the results of swallowing in patients diagnosed with the *Rancho Los Amigos (RLA) Scale* (Hagen et al., 1987), four with *the Coma Recovery Scale – Revised (CRS-R)* (Giacino et al., 2004), one with the *Wessex Head Injury Matrix (WHIM)* (Shiel et al., 2000) and one with the *Full Outline of UnResponsiveness (FOUR)* (Wijdicks et al., 2005) (see **Appendix 2.3** for description of scales).

We will present the results based on the type of swallowing components studied (i.e., ventilation and protection of the airway, type of feeding, oral phase, pharyngeal phase, abnormal reflexes, lip injury and hypertonia of the jaw muscles, and mixed components of the oral and pharyngeal phase). **Table 4** summarizes the results of the different studies.

Table 3: Characteristics of studies exploring the relation between level of consciousness and swallowing-related abilities in patients with severe brain injury

Author, year of publication	Study year	Type of cohort study	Level of evidence[a]	Number of participant and etiology	Time since injury	Consciousness evaluation	Level of consciousness (mean and/or range)	Swallowing components studied
Winstein, 1983	Jan 1980–Sept 1981	Retrospective chart review	2b	55 TBI	"Non-acute"	RLA	Level III – V	Enteral or oral feeding (and type of feeding)
Mackay et al., 1999a	1992–1995	Prospective	2b	54 severe TBI with initial GCS score < 9	17.6 days post-injury (range: 3–72 days)	RLA	In admission: 2,8 ± 0,7 Level II – IV	- VFSS: normal or abnormal swallowing[2] and presence or absence of aspiration - Length of ventilation - Time until initiation of oral feeding, achievement of exclusively oral feeding and time between the two
Mackay et al., 1999b	1992–1995	Prospective	2b	Same as Mackay et al., 1999a	Same as Mackay et al., 1999a	RLA	In admission: Level II – IV	Same as Mackay et al., 1999a
O'Neil-Pirozzi et al., 2003	Not mentioned	Prospective	2b	50 severe TBI with tracheostomy: 12 DOC (RLA II or III) and 38 without DOC Initial GCS score < 9	Mean days post-injury: 78.6 (range: 31–306 days) Median: 42.5 days	RLA	Level II – III	VFSS: presence or absence of aspiration t and food and/or drink recommended
Millwood et al., 2005	12-month period	Not mentioned	2b	45 ABI (VS/UWS or MCS) patients	Mean of 8 months	SMART	VS/UWS MCS	Presence or absence of abnormal reflexes and lip injury
Brady et al., 2006	30 month timeframe	Retrospective	3b	25 ABI	Mean time from the injury until inpatient rehabilitation admission: 89 days	RLA	Level II – III	- Diet levels - FEES or VFSS (pharyngeal swallowing components: presence or absence of aspiration, laryngeal

[2] Swallowing mechanism was identified as abnormal if any oral or pharyngeal deficits were noted.

								penetration, and pharyngeal residue)
Terré & Mearin, 2007	Jan–Dec 2004	Prospective	2b	48 TBI GCS score < 6	Neurorehabilitation unit: *Mean time from TBI to admission = 2 months (range: 1–5 months) *Mean time from TBI to discharge = 6 months (range: 4–11 months)	RLA	Group 1 (n=15): level II–III Group 2 (n=19): level IV–V Group 3 (n=14): level VI–VIII	- Clinical evaluation - VFSS at admission (oral and pharyngeal components such as impaired tongue control, oral transit time, aspiration, penetration) - Type of feeding at discharge
Hansen, Engberg, et al., 2008	Oct 2000–Dec 2005	Retrospective chart review	2b	173 TBI Initial GCS score 9–13	Mean time until admission in the rehabilitation unit: 86 days	RLA	Level I – VIII	FOIS
Hansen, Larsen, et al., 2008	Oct 2000–Dec 2005	Retrospective chart review	2b	Same as Hansen, Engberg, et al., 2008	Same as Hansen, Engberg, et al., 2008	RLA	Level I – VIII	Risk of pneumonia
Brady et al., 2009	July 2002–June 2006	Retrospective	2b	35 ABI	62.3 days ±71.1 days post-insult	RLA	Group 1: Level II–III Group 2: >Level III	FEES or VFSS (aspiration and laryngeal penetration rates)
Terré & Mearin, 2009	Jan 2005–June 2007	Prospective	3b	26 severe TBI GCS score < 6	12 months post-admission to the rehabilitation unit	RLA	Mean = 4 Level II – VII	VFSS (presence or absence of aspiration)
Mandaville et al., 2014	June 2006–June 2011	Retrospective	2b	219 severe TBI Initial GCS score < 9	Admission and discharge from a trauma unit of the hospital Mean time at admission = 10 days	RLA	Initial RLA: 4.5 ± 1.9	Presence or absence of feeding tube
Kjaersgaard et al., 2015	June 2009–Apr 2011	Retrospective	2b	118 ABI	10–2845 days Median control group: 36 days Median intervention group: 35 days	RLA	Level III–VIII	Initiation of oral feeding Return to total oral feeding

Bremare et al., 2016	Dec 2013–June 2014	Prospective	3b	11 ABI = GCS score 3–13	69.3 ± 26.3 days post-insult	WHIM	5–57	- Type of feeding (oral or enteral) on admission - Clinical functional swallowing test (oral and pharyngeal swallowing components) - FEES (pharyngeal swallowing components) - FOIS (based on the clinical functional swallowing test and the FEES)
Godet et al., 2017	June 2013–Feb 2015	Prospective	1b	140 ABI GCS<13	Acute (Intensive Care Unit)	CRS-R FOUR	Group extubation success: CRS-R total score 10–19; FOUR total score 11–13 Group extubation failure: CRS-R total score 8–15; FOUR total score 10–13	Extubation failure
Mélotte et al., 2018	Dec 2006–May 2017	Retrospective	2b	68 ABI	Median: 30 months	Repeated CRS-R and neuroimaging	UWS	Type of feeding
Wang et al., 2019	Not mentioned	Prospective	1b	19 ABI	Median: 4 months (range 1–12)	Repeated CRS-R	UWS and MCS–	Initiation of mouth opening
Mélotte et al., 2020	Jan 2010–August 2018	Retrospective	2b	92 ABI	UWS: 30±22 months MCS: 40±34 months	Repeated CRS-R and FDG-PET	UWS and MCS	- Type of feeding - Presence or absence of tracheostomy - 8 components related to swallowing based on FEES

Note. [a] Level of evidence of the study based on the Oxford Centre for Evidence-based Medicine for "Differential diagnosis/symptom, prevalence study": 1b = Prospective cohort study with good follow-up; 2b = Retrospective cohort study, or poor follow-up; 3b = Nonconsecutive cohort study, or very limited population. https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/

DOC=disorders of consciousness; TBI=traumatic brain injury; ABI=acquired brain injury; UWS=unresponsive wakefulness syndrome; MCS=minimally conscious state; GCS=Glasgow Coma Scale; FDG-PET=fluorodeoxyglucose-positron emission tomography

Level of consciousness assessments: CRS-R=Coma Recovery Scale – Revised; FOUR=Full Outline of UnResponsiveness; RLA=Rancho Los Amigos Scale; SMART=Sensory Modality Assessment and Rehabilitation Technique; WHIM=Wessex Head Injury Matrix

Swallowing assessments: FEES=fiber-optic endoscopic evaluation of swallowing; VFSS=videofluoroscopic swallowing study; FOIS=Functional oral intake scale

3.1. Ventilation and protection of the airway

Mackay et al. (1999a) did not find a significant correlation between RLA score and **length of ventilation** in 54 patients with severe acute TBI. However, the second study on the same data set by the same authors (Mackay et al., 1999b) showed that the time on ventilation was approximately three times longer for patients with lower RLA scores. One decade later, Hansen et al. (2008) found an association between RLA scores and the **risk of pneumonia** after adjustment for age and sex in 173 patients with TBI in a rehabilitation center.

More recently, a large study with 140 patients with acute ABI determined the predictors of **extubation failure** (Godet et al., 2017). They used a single administration of the CRS-R and the FOUR to assess the level of consciousness. In the univariate analysis, visual functions, brainstem and arousal capabilities on the FOUR and CRS-R differentiated success from failure. None of the motor functions was significant. The communication and oromotor subscales of the CRS-R did not appear to discriminate between groups. In the multivariate analysis, the CRS-R visual subscale was independently associated with extubation failure.

In the study by Bremare et al. (2016), three out of four patients with UWS had a tracheostomy with inflated cuff. The fourth did not have a tracheostomy, but he could swallow on request and as such should not be considered as having UWS. Of the six patients with MCS, only one did not have a tracheostomy and the five others had a tracheostomy with inflated cuff.

Finally, our retrospective study of 92 patients with DOC found that **the presence of a tracheostomy** and of a **cough reflex** were significantly associated with DOC diagnosis (UWS or MCS) in the multivariate analysis (taking into consideration the etiology and time since insult) (Mélotte et al., 2020). These findings suggest that the level of consciousness may influence the ability to correctly manage saliva and cough sensitivity.

3.2. Type of feeding

Two studies analyzed the type of feeding in patients with acute TBI. In a prospective study of 54 patients with severe acute TBI receiving exclusively oral feeding, Mackay et al. (1999a) found significantly different RLA scores in patients with normal swallowing than in patients with abnormal swallowing according to the VFSS. A second paper by the same authors (Mackay et al., 1999b) showed that RLA score is the most important independent predictor of the delay until exclusively oral feeding is achieved. In a retrospective study with 219 patients with severe acute TBI, Mandaville et al. (2014) found a statistically significant association (univariate and multivariate analysis adjusted for age) between initial RLA score and the use of a percutaneous **endoscopic gastrostomy tube** at discharge.

Eight other studies focused on patients admitted to rehabilitation centers or chronic facilities. Winstein (1983) did a retrospective chart review on swallowing in severe brain injury, focusing on 57 patients with TBI admitted to a rehabilitation center. He reported a trend between RLA score and type of feeding (enteral or oral feeding and type of oral feeding). On admission, 77% of the patients with enteral feeding had at best an RLA level IV and the majority were at level II or level III. For patients with oral feeding and dysphagia, 70% were at level V or higher and 30% were at level III. At discharge, patients remaining on enteral feeding were at the cognitively unresponsive level (level I), or at best the generalized response level (level II), and demonstrated severe oral-facial hypersensitivity or primitive responses. No statistical analysis was done to assess the link between type of feeding and RLA score. In the same vein, in their retrospective chart review, Hansen, Engberg, et al. (2008) found a significant correlation between RLA score and type of feeding in 173 patients with TBI admitted to a rehabilitation center. Patients admitted with RLA levels I to II had a 24% chance of engaging **exclusively in ordinary oral feeding**, whereas 77% of the patients admitted with RLA level III, 88% of the patients with RLA levels IV to V, and 100% of the patients with RLA levels VI to VIII achieved unrestricted feeding at the unit.

Brady et al. (2006) studied swallowing retrospectively in 25 patients with TBI hospitalized in a rehabilitation center and divided them into two groups. In group 1, oral feeding was initiated at RLA III, and in group 2 oral feeding was not initiated until the patient reached RLA IV or was never initiated. The authors showed that the two groups did not differ according to diet levels (three meals daily) at the time of discharge, suggesting that beginning oral feeding early in recovery from coma does not influence the final type of feeding at discharge. In another retrospective study, Brady et al. (2009) found a difference in diet level in a group of ABI patients with RLA level II/III (group 1) compare to a group in a RLA level IV to VI (group

2). After baseline swallow examination with FEES or VFSS, therapeutic feeding was introduced in 76% of the patients in group 1 and 17% in group 2 and modified diet with 3 meals was introduced in 55,5% of patients in group 2 and not initiated in group 1.

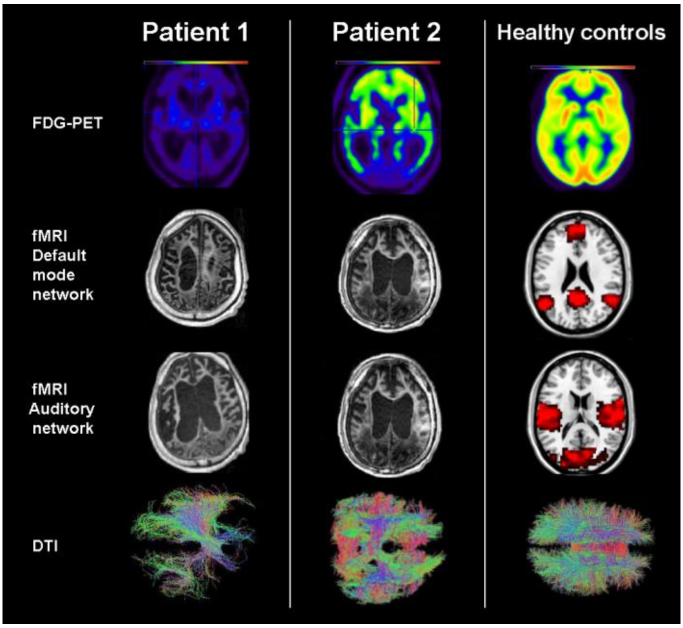
In a prospective study of 48 patients with TBI in a neurorehabilitation unit, Terré and Mearin (2007) found that the type of **feeding mode at discharge** was substantially correlated with RLA scores (range from II to VIII) at admission and at discharge. Kjaersgaard et al. (2015) retrospectively explored the links between RLA scores and the **time of initiation and return to exclusive oral feeding** based on the results of a FEES in 118 patients with ABI (RLA levels III to VIII). They did not find a significant association between the two.

In a consecutive cohort study, Bremare et al. (2016) described 11 patients with ABI (mixed etiologies) in the prolonged phase. The level of consciousness was established based on a single administration of the WHIM (Shiel et al., 2000) and swallowing was assessed with a clinical swallowing evaluation and a functional swallowing test when deemed possible. No statistical analysis was done due to the small number of patients. At admission to their rehabilitation center, according to the WHIM, four (36.4%) patients were considered to be in UWS, six (54.5%) in MCS, and one (9.1%) in a confusional state. In their cohort, one patient considered to be in UWS (score WHIM=4) could swallow on request, which is incompatible with UWS based on the DOC diagnosis criteria (command following) (Giacino et al., 2002). Regarding the type of feeding, all patients were fed by enteral tube on admission. Of the eight patients with severe TBI, four (50%) resumed oral feeding 3 months after admission to the specialized rehabilitation unit. However, we do not know if there was a link to the level of consciousness assessed with the WHIM.

In two other studies, we analyzed the links between type of feeding and level of consciousness measured with repeated CRS-R assessments (Mélotte et al., 2018, 2020). First, a retrospective analysis of type of feeding was conducted on patients with chronic UWS (> 3 months) (Mélotte et al., 2018, **Chapter 2**). Of 68 patients, only two were able to resume oral feeding (3%). Patient 1 could engage in oral feeding with liquid and semiliquid textures only, in addition to gastrostomy feeding, while patient 2 achieved full oral feeding with liquid and mixed solid food. The neuroimaging and neurophysiology results were compatible with the diagnosis of UWS for patient 1, but atypical for patient 2: they were more compatible with a diagnosis of MCS (**figure 5**). Given the dissociation between the behavior and the neuroimaging findings, the authors hypothesized that patient 2 could be considered to be in MCS* (Gosseries et al., 2014) or in a state of cognitive motor dissociation (Schiff, 2015). These terms refer to a patient who is diagnosed as having UWS or MCS– at the bedside but who presents fMRI or electrophysiological evidence of preserved brain activity compatible with MCS and/or is able to follow commands. We also suggested that resuming full oral feeding may be related to the recovery of some brain functions, which probably leads to a higher level of consciousness than in UWS, and that the recovery of a full, complex oral phase of swallowing (including solid food) should be considered as a sign of consciousness.

Finally, we did a recent retrospective study with 92 patients with DOC in the prolonged condition (> 28 days) with a DOC diagnosis based on the CRS-R and confirmed by fluorodeoxyglucose-positron emission tomography (FDG-PET) (Mélotte et al., 2020, **Chapter 3**). We did not find a significant association between type of feeding (exclusively enteral feeding or not) and DOC diagnosis (UWS or MCS); 88% of the patients with UWS and 73% of those with MCS received exclusively enteral feeding.

Figure 5. Neuroimaging results (sagittal and axial views) of the two UWS patients who were able to swallow and of healthy controls



Note. Patient 1 (left panel): FDG-PET showed a 79% drop in brain metabolism with hypometabolism in the global lateral and medial frontoparietal network and preservation of the brainstem and cerebellum. Structural MRI revealed global bilateral atrophy of the cerebral and cerebellar hemispheres. DTI showed diffuse alteration of white matter connections. Patient 2 (central panel): 47% drop in brain metabolism with hypometabolism in the bilateral parietotemporal associative areas but relative preservation of the brainstem, cerebellum and frontal and occipital cortex. Structural MRI revealed global cerebellar vermis atrophy, bilateral mesencephalic atrophy, and parieto-occipital cortex and basal ganglia (principally left thalamic) atrophy. DTI showed loss of white matter in the dorsal posterior area bilaterally and disorganization of fibers in the parietal cortex.
Functional MRI, performed with sedation, showed no spontaneous brain activity in either patient's default mode network or auditory network.
Abbreviations: FDG-PET=fluorodeoxyglucose positron emission tomography; fMRI=functional magnetic resonance imaging; DTI=diffusion tensor imaging
Adapted with permission from Mélotte et al. (2018).

3.3. Oral phase of swallowing

Terré and Mearin (2007) showed that **impaired tongue control and oral transit time** (assessed by clinical and VFSS examination of swallowing) correlated significantly with RLA scores in 48 patients with TBI in a rehabilitation unit.

A recent prospective study tested **initiation of mouth opening** in 19 patients with DOC (UWS and MCS–) diagnosed with repeated CRS-R with five different stimuli (Wang et al., 2019): (1) on command ("open your mouth"); (2) placing a spoon in front of the patient's mouth without a command; (3) placing a spoon filled with water in front of the patient's mouth without a command; (4) one command ("there is a spoon; open your mouth") with a spoon in front of the patient's mouth; and (5) one command ("there is a spoon with water; open your mouth") with a spoon filled with water in front of the patient's mouth. While none of the patients with DOC responded to the first four stimuli, six of them (five MCS− and one UWS) initiated mouth opening with the fifth stimulus. Of these six patients (five MCS− and one UWS), five had a good outcome 6 months later (i.e., MCS− had progressed to MCS+ and UWS was now MCS−).

We found that a partial oral phase of swallowing (e.g., tongue and chewing-like movements) was observed in all patients with DOC (UWS and MCS) (Mélotte et al., 2020, **Chapter 3**). However, an **effective oral phase of swallowing** (adequate lip prehension, tongue propulsion and no post-swallowing oral stasis) was not detected in any of the patients with UWS, and in only a small minority (21%) of those with MCS. This component was significantly correlated with the level of consciousness in multivariate analysis (adjusted for etiology and time since insult). Based on this result, and as already suggested in our previous study (Mélotte et al., 2018, **Chapter 2**), an effective oral phase should be considered as a sign of consciousness.

3.4. Pharyngeal phase of swallowing

In a cohort of 54 patients with severe TBI in a rehabilitation unit, Mackay et al. (1999b) showed that as the RLA score upon admittance decreased, **the rate of aspiration** (different bolus and consistencies) later identified by VFSS increased (the VFSS was conducted only when the patient was awake and alert to the therapist and the presentation of food and demonstrated automatic or volitional responses to the presentation of food or a spoon). For patients with admitting RLA levels II, III, and IV, the corresponding percentages of aspiration were 50%, 21%, and 0%. Another study using RLA scores found no statistically significant differences in percentage of aspiration (based on VFSS) between a group of subjects with DOC (n=12, RLA levels II and III) and a group of subjects without DOC (n=38, RLA > III) (O'Neil-Pirozzi et al., 2003).

Two other studies (Terré & Mearin, 2007, 2009) with 48 and 26 patients with chronic TBI following severe brain injury found a significant relationship between RLA scores and, respectively, **penetration** of the laryngeal vestibule (at admission) (Terré & Mearin, 2007) and **aspiration** 12 months post-admission to the rehabilitation unit (Terré & Mearin, 2009), assessed by VFSS (pudding, nectar and liquid viscosities) in both studies. The lower the RLA score, the more penetrations or aspirations there were. However, Brady et al. (2009) did not find a difference in the percentage of aspiration or laryngeal penetration in a FEES or a VFSS between patients in RLA level II/II and patients in RLA level IV to VI.

In the study by Bremare et al. (2016), of the seven subjects tested with compote texture (2 UWS based on the WHIM but one with command following, 3 MCS, 2 confusional state), two had aspirations (1 MCS, 1 UWS) and one (MCS) had pharyngeal residues. Of the four subjects tested with liquid texture (2 UWS but one with command following, 1 MCS, 1 confusional state), two had aspirations (2 UWS) and none had pharyngeal residues. Despite its clinical relevance, this study is affected by methodological bias regarding the diagnosis of DOC. In fact, the WHIM does not provide a reliable diagnosis, patients benefited from only one evaluation and no neuroimaging exam was done to confirm the diagnosis.

If we look at our study of 92 patients with DOC (UWS or MCS) diagnosed using the CRS-R and FDG-PET, the presence of pharyngo-laryngeal secretions (UWS=58%; MCS=29%) and saliva aspiration (UWS=46%; MCS=21%) correlates with DOC diagnosis in univariate analysis (Mélotte et al., 2020, **Chapter 3**). However, the presence of aspiration with cream (UWS=12%; MCS=13%) or liquid (UWS=17%; MCS=36%) textures was not linked to the DOC diagnosis.

3.5. Mixed components (including oral and pharyngeal swallowing components)

Mackay et al. (1999a) analyzed the difference in RLA scores at admission between patients with **normal and abnormal swallowing** (oral or pharyngeal deficits) based on an objective swallowing assessment (VFSS) in 53 patients with severe acute TBI. They found significantly lower RLA scores in the abnormal swallowing group compared to the normal swallowing group at the time of exclusively oral feeding but not at admission. Moreover, they found no significant evolution of RLA between initial and exclusive oral feeding. In the same vein but at a later point (2 months post-injury), Terré and Mearin (2007) explored swallowing with clinical examination and VFSS in 48 patients with severe TBI. A relationship was found between RLA scores and **swallowing impairments** (oral or pharyngeal deficits) assessed by videofluoroscopy, but not between RLA scores and the clinical bedside examination.

3.6. Abnormal reflexes, lip injury and hypertonia of the jaw muscles

One study explored the link between the presence or absence of oral reflexes and lip injury in patients with ABI (VS/UWS or MCS) with a level of consciousness diagnosis based on the Sensory Modality Assessment and Rehabilitation Technique (SMART; Gill-Thwaites & Munday, 1999). The authors found no association between scores for awareness, oral reflexes, and lip biting. Similarly, our retrospective cohort study of 92 patients with DOC found no statistical association between hypertonia of the jaw muscles and DOC diagnosis (UWS or MCS) **(Mélotte et al., 2020, Chapter 3**).

A few studies (n=4) explored components related to swallowing in patients with DOC. We will see in the next section that there are very few tools and techniques for appraising and managing swallowing components.

Table 4. Summarized results of studies analyzing the link between level of consciousness and swallowing components

Consciousness evaluation scale	Author, Date	Respiration and protection of the airway	Type of feeding	Oral phase of swallowing	Pharyngeal phase of swallowing	Mixed components	Abnormal reflexes, lip injuries and hypertonia of the jaw muscles
RLA	*Winstein, 1983*		+ (enteral or oral feeding and type of oral feeding)				
	Mackay et al. 1999a	- - (length of ventilation)			+ (presence or absence of aspiration based on the VFSS)	++ (normal vs. abnormal swallowing based on the VFSS)	
	Mackay et al. 1999b	+ (ventilation days)	+++ (delay before achievement of exclusively oral feeding)				
	O'Neil Pirozzi et al., 2003				- - (percentage of aspiration based on the VFSS)		
	Brady et al., 2006		- - (diet levels at time of discharge)				
	Terré & Mearin, 2007		++ (feeding mode at admission and at discharge)	++ (impaired tongue control) ++ (oral transit time)	++ (presence or absence of penetration based on the VFSS)	- - (clinical evaluation) ++ (VFSS)	
	Hansen, Engberg, et al., 2008		++				
	Hansen, Larsen, et al. 2008	++ (risk of pneumonia)					
	Brady et al., 2009		+		- (aspiration and laryngeal penetration)		
	Terré & Mearin, 2009				++ (presence or absence of aspiration based on the VFSS)		
	Mandaville et al., 2014		+++ (initial RLA score and presence of an endoscopic gastrostomy tube at discharge)				

	Kjaersgaard et al., 2015		- - (time until initiation of oral intake and ability to return to total oral intake based on the results of a FEES)					
SMART	*Millwood et al., 2005*							- - (presence or absence of oral reflexes and lip injury)
WHIM	*Bremare et al., 2016*	?	?		?			
FOUR	*Godet et al., 2017*	++ (extubation failure)						
CRS-R	*Godet et al., 2017*	+++ (extubation failure)						
	Mélotte et al., 2018		+ (type of feeding of patients with UWS)					
	Wang et al., 2019			+ (initiation of mouth opening)				
	Mélotte et al., 2020	+++ (tracheostomy) +++ (cough reflex)	- - - (presence or absence of exclusively enteral feeding in patients with UWS and MCS)	+++ (efficacy of the oral phase)	++ (pharyngo-laryngeal secretions) ++ (saliva aspiration)			- - - (hypertonia of the jaw muscles)

Note. Presence of a link between score on the consciousness scale and swallowing: Quantitative: +; Univariate: ++; Multivariate: +++
Absence of a link between score on the consciousness scale and swallowing: Quantitative: –; Univariate: – –; Multivariate: – – –
? = Not clearly determined
UWS=unresponsive wakefulness syndrome; MCS=minimally conscious state; CRS-R=Coma Recovery Scale – Revised; FOUR=Full Outline of UnResponsiveness; RLA=Rancho Los Amigos Scale; SMART= Sensory Modality Assessment and Rehabilitation Technique; WHIM=Wessex Head Injury Matrix; FEES=fiber-optic endoscopic evaluation of swallowing; VFSS=videofluoroscopic swallowing study

Section 4: Evaluation and treatment of swallowing in patients with DOC

See **Appendix 2.1** for research strategy and selected criteria

4.1. Assessment of swallowing

Determining the efficacy of swallowing in patients with DOC is difficult and challenging because they may not respond to commands (UWS, MCS–) and their responses may fluctuate. Most such patients are fed by enteral nutrition because of severe dysphagia (Mélotte et al., 2020, **Chapter 3**). Understanding swallowing disorders in this population will help clinicians determine the nature and judge the efficacy of the therapy to be applied. Moreover, a better understanding of the pathophysiology of swallowing in patients with DOC will also contribute to our understanding of the links between consciousness and swallowing.

Classically, we distinguish between clinical bedside assessments and objective swallowing assessment (e.g., FEES and VFSS).

A series of screening protocols or bedside assessments have been developed in the last 20 years to explore swallowing (Martino et al., 2013). However, most of them require the patient to participate actively (respond to commands) and therefore are not suitable for assessing swallowing in patients with DOC.

Three behavioral assessments developed for patients with DOC include a swallowing subscale or item: the Disorders of Consciousness Scale (DOCS) (Pape et al., 2005; Pape et al., 2011), the Comprehensive Assessment Measure for the Minimally Responsive Individual (CAMMRI) (Gollega et al., 2015) and the CRS-R (Giacino et al., 2004).

One of the eight DOCS subscales is called “Taste & Swallowing” (Pape et al., 2005; Pape et al., 2011). It evaluates patient response to pre-swallowing stimulation (when we explain that we will apply the stimulation) and the ability to swallow within 15 to 20 seconds of a stimulation. The taste stimulation consists in touching the lips and gums with a cotton swab soaked in orange juice and observing the patient’s reactions (no response, generalized response or localized response). This item has the advantage of avoiding a functional swallowing test, which can expose the patient to a high risk of inhalation.

The CAMMRI includes a 7-item dysphagia rating scale ranging from "profound dysphasia" to "functional swallowing" (Gollega et al., 2015). It consists of a checklist that requires clinicians to evaluate oral motor impairment, pharyngeal phase of swallowing, cough reflex, secretion management, risk of aspiration and type of feeding. To be objective, this scale requires a FEES or VFSS to be performed. The CAMMRI also has an oral/facial sensitivity subtest that assesses reaction to firm and soft touch on the face and inside the mouth (Gollega et al., 2015).

The CRS-R includes baseline observations of spontaneous behaviors including sticking out the tongue and opening and closing the mouth. On the motor function scale, in the "automatic motor response" item, if the patient does not show episodes of automatic motor behaviors, the examiner can propose to test mouth-opening ability when a spoon is presented. However, this item is proposed only if the examiner judges that the patient presents an inability to move their limbs and is not able to perform a wave sign. Moreover, the item tests the ability to inhibit the automatic motor behavior of opening the mouth when a spoon is presented because we ask the patient not to move at all.

Bicego et al. (2014) developed an observation chart based on the Facial Oral Tract Therapy (FOTT) tool. The FOTT is a rehabilitation approach that can be used with patients with DOC as it does not require active participation (Hansen, Engberg, et al., 2008). This tool contains a series of items related to head and body posture, orofacial area (e.g., lip and jaw position, aperture of the jaw, appearance of the lips, tongue and cheeks), oral and perioral sensitivity, saliva swallowing, respiration, and cough and orofacial reflexes. They also proposed a bolus swallowing test. Although it is appropriate for patients with DOC, this tool is only available in French and has not been validated with a cohort of patients with DOC.

Similarly, we recently submitted a protocol study that aims to validate the SWallowing Assessment in Disorders Of Consciousness (SWADOC). This bedside assessment has been developed to assess components related to swallowing in patients with DOC (Mélotte et al., submitted, **Chapter 4**). The SWADOC was inspired by Bicego et al.'s (2014) assessment. It includes both qualitative and quantitative items. Items are grouped into 11 categories: (1) Arousal; (2) Resting position of the head, eyes, mandibles and lips; (3) External facial stimulations; (4) Initiation of mouth opening; (5) Mouth cavity observations; (6) Initiation of the saliva swallowing reflex; (7) Stimulation of the saliva swallowing reflex; (8) Lip prehension, tongue propulsion and reactions to 1 mL functional test; (9) Respiration; (10) Voice, speech, language; and (11) Tonicity and sensitivity profiles. A subsection of the SWADOC, the "SWADOC-scored," includes only 8 quantitative items (four items related to the oral phase and four to the pharyngeal phase). Items of the SWADOC-scored must be scored as one of the four severity levels indicated for each item (scores from 0 to 3). The SWADOC-scored allows one to calculate three performance scores: the oral phase subscore, the pharyngeal phase subscore and the total swallowing score (maximum 24). Concurrent validity is assessed with the Facial Oral Tract Therapy Swallowing Assessment of Saliva (FOTT-SAS) (Mortensen et al., 2016). This scale has seven questions: if items 1 to 4 are answered "Yes" and items 5 to 7 are answered "No," oral intake should be initiated (see **table 5**).

Table 5. The Facial Oral Tract Therapy Swallowing Assessment of Saliva (FOTT-SAS) (adapted from Mortensen et al., 2016)

Items	Yes	No
1. Conscious and/or respond to verbal address?		
2. Able to sit upright with some degree of head control?		
3. Oral transport of saliva?		
4. Spontaneous or facilitated swallowing of saliva?		
5. Coughing following swallowing of saliva?		
6. Gurgling breath sound following swallowing of saliva?		
7. Difficulties breathing following swallowing of saliva?		
Based on the above questions, should oral intake be initiated? (Oral intake should be initiated if items 1 to 4=Yes and items 5 to 7=No)		

Clinical bedside assessments are essential in day-to-day clinical work to gain an initial idea of a patient's swallowing capacity, guide therapy and track progress. However, they remain subjective because hypotheses are made based on external signs of dysphagia (e.g., cough, voice changing). To objectively determine the efficacy of the pharyngeal phase of swallowing, an objective swallowing assessment is mandatory (FEES or VFSS). Such swallowing assessments, performed by experienced clinicians, constitute the gold standard tools to assess dysphagia in patients at high risk of inhalation (Carnaby-Mann & Lenius, 2008; Swan et al., 2019). They allow the mechanisms at play during swallowing to be analyzed more precisely and possible silent aspiration to be detected. The high prevalence of silent aspiration in patients with DOC (Mélotte et al., 2020, **Chapter 3**) makes the combination of a bedside clinical assessment with an objective swallowing assessment essential.

Objective swallowing assessments can be challenging to do with patients with DOC. In Mackay et al.'s (1999a) study, one of the inclusion criteria to perform a VFSS was a level IV RLA score (corresponding approximately to EMCS). Moreover, a VFSS was performed only if patients were able to show automatic or volitional responses to presentation of food or a spoon (i.e., mouth opening). In contrast, Brady et al. (2009) showed that FEES and VFSS are feasible in patients at levels II and III. In another study (O'Neil-Pirozzi et al., 2003) with acute tracheostomized patients with severe DOC following TBI, the authors argued that "these patients may be poor candidates when: i) swallows are not observed spontaneously and cannot be elicited using digital stimulation to the laryngeal area; ii) a profound bite reflex is present; and/or iii) the patient cannot tolerate an upright position for a minimum of 15 minutes" (p. 396). We also showed recently that an objective swallowing assessment can be successfully completed in patients with DOC but that a functional swallowing test (food or liquid testing) can be difficult if patients have severe trismus (lockjaw) or completely lack an oral phase of swallowing (Mélotte et al., 2020, **Chapter 3**). Together, this information suggests that three criteria are necessary when performing a functional swallowing test (liquid or solid food testing) with an objective swallowing assessment (FEES or VFSS): (1) semi-seated position for a minimum of 15 minutes; (2) mouth opening (automatic response to presentation of food or spoon or active opening without severe hypertonia of the jaw muscles); and (3) at least minimal tongue propulsion.

4.2. Treatment of orofacial area and swallowing

Swallowing has not been studied much in patients with DOC, and swallowing treatment is even less studied.

In 2010, the National Italian Consensus Conference drew up recommendations on rehabilitation programs for patients with severe ABI in the intensive hospital phase (De Tanti, 2015). These recommendations include some indications concerning swallowing (see **table 6**).

Table 6. Indications concerning swallowing adapted from the National Italian Consensus Conference

1. Precise assessment of swallowing in all patients with ABI, even with LCF < 4.
2. Bedside assessment of swallowing by the blue dye test by a doctor or an expert speech therapist.
3. Detailed diagnosis by fiber-optic endoscopic evaluation of swallowing (FEES) and/or videofluorography, especially in cases suspected of silent aspiration. FEES is preferable for low-compliance patients.
4. Swallowing training may be initiated in sufficiently wakeful patients (LCF 4 or more)
5. Dysphagia should be treated by a speech therapist experienced in this disorder and may include the use of appropriate measures of compensation.
6. Use of a phonation valve for swallowing training in patients with tracheostomy, in the absence of contraindications.
7. Inform family members about the timing of weaning to minimize the risk of inappropriate feeding.

Note. Abbreviations: LCF= Rancho Los Amigos – Level of Cognitive Functioning

Other researchers have given some directions on how to manage swallowing in patients with DOC, such as using a nonfeeding program (O'Neil-Pirozzi et al., 2003; Winstein, 1983). A **nonfeeding program** consists in stroking, stretching, applying firm pressure or providing thermal and taste stimulations to desensitize inappropriate orofacial responses and facilitate more normal swallowing and intraoral responses. Brady et al. (2006; Brady & Pape, 2011) suggest that, if patients do not demonstrate aspiration in an objective swallowing assessment, **therapeutic feedings** can be used. Therapeutic feedings consist of giving small amounts of food to stimulate the oral and pharyngeal phases of swallowing and provide a positive experience for the patient. Recently, Jakobsen et al. (2019) proposed a treatment protocol for patients with severe brain injuries that aims to facilitate swallowing by intensifying the FOTT program (Hansen & Jakobsen, 2010). They found a tendency to improvement of specific swallowing parameters (frequency of swallowing, elevation of larynx and speed of laryngeal elevation) in the intervention group (Jakobsen et al., 2019).

A modified Delphi study requested speech language therapists' (SLT) opinions about best practices to assess and treat patients with DOC (Roberts & Greenwood, 2019). For the first time, an expert panel of 36 SLTs reached a consensus on 67 statements covering assessment, management and service delivery for patients in prolonged DOC. This study constitutes the starting point for developing SLT guidelines when working with patients with DOC. In **Table 7,** we report the statements related to the assessment or treatment of dysphagia and the percentage of agreement.

The Delphi study addressed the use of the FOTT (Hansen & Jakobsen, 2010) as part of the SLT intervention for patients with DOC but reported that only a small percentage of speech therapists are trained in its use. Moreover, only half of the participants agreed that SLTs should use the FOTT with patients in prolonged DOC. The authors also emphasized the lack of English language papers on that topic and the study design's limitations (Konradi et al., 2015; Seidl et al., 2007). Recently, a practice-oriented book on the FOTT was published that allows clinicians to learn more about this approach (Nusser-Müller-Busch & Gampp Lehmann, 2021).

Table 7. Percentage of agreement of 40 speech and language therapists with several items linked to the assessment and treatment of dysphagia in patients with prolonged disorders of consciousness (extracted from Roberts & Greenwood, 2019, p. 7-8)

Assessment	**Percentage of agreement**
SLT assessment should include assessment of oral hypersensitivity/oral reflexes of patients in PDOC (n = 34)	100
SLT assessment should include assessment of the ability of patients in PDOC to manage their oral secretions	100
SLT assessment should include assessment of the ability of patients in PDOC to tolerate cuff deflation and speaking valve (for tracheostomy patients) (n = 32)	100
SLT assessment should include bedside assessment of swallowing of medically stable patients in a MCS/suspected MCS (if yet to be diagnosed)	97.2
SLT assessment should include instrumental assessment of swallowing of patients in PDOC (n = 35)	80
SLTs working with patients in PDOC should refer to a speaking valve as a one-way valve (n = 29)	79.3
SLT assessment should include bedside assessment of swallowing of medically stable patients in a VS/UWS/suspected VS/UWS (if yet to be diagnosed)	77.8
Patients in PDOC are frequently able to tolerate videofluoroscopy (n = 31)	29.1
Patients in PDOC are frequently able to tolerate fiberoptic endoscopic evaluation of swallowing (n = 28)	60.7
All patients in PDOC should have an instrumental swallowing assessment before commencing oral trials/therapeutic feeding (n = 35)	40
SLTs should offer cough reflex testing for patients in PDOC	38.9
Treatment	
SLTs should provide programs to manage oral hypersensitivity in patients in PDOC (n = 35)	100
SLTs should be involved in decision-making regarding the management of oral secretions of patients in PDOC (n = 40)	100
SLTs should be involved in planning tracheostomy weaning of patients in PDOC (n = 32)	100
SLTs should be involved in decision-making regarding the use of botulinum toxin for management of bite reflex	86.1
SLTs should provide FOTT to patients in PDOC (n = 35)	54.3

Note. Abbreviations: SLT = speech and language therapists; PDOC = prolonged disorders of consciousness; VS/UWS = vegetative state/unresponsive wakefulness syndrome; MCS = minimally conscious state; FOTT = Facial Oral Tract Therapy

Discussion

Synthesis and interpretation of the results

The different phases of swallowing are multifaceted, having both volitional and reflexive components. The entire sequence of swallowing (from the oral phase through the esophageal phase) represents a continuum from voluntary to reflexive behaviors. The oral phase can be considered as a voluntary behavior containing automatic processes. The swallowing reflex is positioned at the border between voluntary and reflexive behaviors. The pharyngeal phase can be considered a somatic reflex. Finally, the esophageal phase can be considered an autonomic reflex.

Many neuroimaging studies have explored cortical activation during swallowing in healthy subjects using volitional tasks (VOST) but very few used non-volitional tasks (NVOST); thus, comparisons of volitional and non-volitional tasks are unreliable. The main areas activated during VOST tasks are the primary sensorimotor cortex, premotor cortex and supplementary motor area, anterior cingulate cortex, insula and cerebellum. The anterior cingulate plays a role in volitional movement (Winterer et al., 2002). It is activated at the early stage of swallowing and could be related to the cognitive processes of swallowing (Watanabe et al., 2004). The insula, for its part, has reciprocal connections with the sensorimotor network upstream and with the thalamus and the nucleus tractus solitarius of the brainstem downstream (Daniels & Foundas, 1997; Sörös et al., 2009, 2011). The insula certainly plays a role in controlling the initiation of swallowing and modifying the swallowing pattern in association with peripherical inputs (Daniels & Foundas, 1997; Sörös et al., 2009, 2011). Finally, the cerebellum plays a role in the control and coordination of movements. There is increasing evidence of the efficacy of noninvasive brain stimulation of the cerebellum to improve neuromotor control of swallowing (Jayasekeran et al., 2011; Rangarathnam et al., 2014; Sasegbon et al., 2019).

It seems that VOST tasks activate a larger cortical area than NVOST tasks, but further studies are still needed. Moreover, the activation of frontal areas in VOST tasks but not in NVOST tasks could be linked to the recruitment of an attentional network that participants use to perform a voluntary action.

Some cortical areas activated during swallowing tasks are not specific to swallowing but are also activated during related motor tasks (e.g., lip pursing, mastication, tongue movement) (Al-Toubi et al., 2011; Kern, Birn, et al., 2001; Martin et al., 2004). Studies exploring the networks of consciousness have associated consciousness with the frontoparietal network, precuneus and adjacent posterior cingulate cortex, mesial frontal, midbrain and central thalamic systems (Boly et al., 2008; Crone et al., 2014; Steven Laureys & Schiff, 2012). There seem to be some similarities between the swallowing areas identified and consciousness networks but only if we look at the secondary activated areas (posterior cingulate cortex, inferior parietal lobule, precuneus, superior frontal gyrus).

Analyses of swallowing in the context of nonpathological modifications of consciousness such as sleep and anesthesia told us that consciousness affects the initiation of the swallowing reflex, pharyngeal phase and coordination between respiration and swallowing. However, the number of studies exploring swallowing during sleep or general anesthesia is limited.

As for pathological modifications of consciousness, the current literature shows some links between swallowing and consciousness in patients with ABI. However, the heterogeneity of the swallowing-related components described, the level of consciousness considered, the various study designs and the lack of clear diagnoses of DOC in a large majority of studies mean we must be cautious when interpreting the results. Regarding **ventilation and protection of the airway**, a connection has been described between extubation failure and CRS-R visual subscale in acute patients (Godet et al., 2017) and between risk of pneumonia and RLA score in patients in rehabilitation. In patients with DOC, the presence of a tracheostomy and the cough reflex are also linked to the level of consciousness in multivariate analysis (Mélotte et al., 2020, **Chapter 3**). Concerning **type of feeding and the oral phase of swallowing**, six out of eight studies of patients with severe ABI found a link between type of feeding and RLA scores (Winstein, 1983; Mackay et al. 1999b; Terré & Mearin 2007; Hansen, Engberg, et al., 2008; Brady et al. 2009; Mandaville et al., 2014). Moreover, in one study (Terré & Mearin, 2007), impaired tongue control and oral transit time were also linked to RLA scores. In studies with strictly patients with DOC diagnosed with the CRS-R, the swallowing components of the oral phase (initiation of mouth opening, efficacy of the oral phase) and, consequently but to a lesser extent, the patient's type of feeding were linked to level of consciousness (Mélotte et al., 2018, 2020; Wang et al., 2019). However, neither the **oral reflexes** (bite reflex, bruxism, etc.) and **lip injury**, nor the **hypertonia of the jaw muscles** seemed to be linked with the level of consciousness in patients with DOC (Mélotte et al., 2020; Millwood et al., 2005). No study analyzed the link between level of consciousness and the swallowing reflex in terms of frequency of triggering. Finally, regarding the **pharyngeal phase of swallowing**, three out of four studies (Mackay et al., 1999b; O'Neil-Pirozzi et al., 2003; Terré & Mearin, 2007, 2009) found a link between RLA score and the rate of aspiration and penetration in a functional swallowing test. In patients with DOC diagnosed with the CRS-R and FDG-PET, pharyngo-laryngeal secretions and saliva aspiration are linked to level of consciousness (Mélotte et al., 2020, **Chapter 3**) but liquid or cream aspiration is not.

An ear, nose and throat (ENT) examination is relevant for patients with DOC regardless of their level of consciousness, whether to discuss the utility of maintaining a tracheostomy, document the value of botulinum toxin to improve saliva management, or assess the feasibility of therapeutic feeding. Clinicians also need some clinical bedside swallowing evaluations to measure patients' progress and assess the efficacy of the therapy. The use of an adapted swallowing tool to assess dysphagia will also help clinicians to implement appropriate dysphagia treatment.

Because most patients with DOC cannot communicate, which makes it hard to understand how they really experience stimulations, clinicians must be very mindful of any behavioral response following stimulations. Similarly, although we tend to think that any patient would like to eat and/or drink, we have to remember that some patients may perceive the introduction of food into the mouth as an unpleasant sensation.

Even though evidence regarding the benefits of stimulation is still scanty, there is growing evidence that patients with DOC need intensive rehabilitative interventions (Whyte & Nakase-Richardson, 2013; Willems et al., 2015). These kinds of care can benefit patients who make functional progress but also those who do not, by reducing later acute care hospital readmissions and enhancing comfort (Whyte & Nakase-Richardson, 2013).

Study limitations and perspectives

First, a systematic review of the literature, rather than a literature review, might have allowed the presentation of stronger evidence for some parts of this work. However, this would have given us a less comprehensive view of this fascinating but little explored subject.

One other limitation that might be emphasized is the absence of statistical analysis for the brain-imaging review. However, the lack of spatial coordinates in 12 studies ruled out a statistical analysis; alternatively, we would have had to set aside all these studies.

The influence of consciousness on swallowing components requires further study to be better understood. For example, the impact of level of consciousness on the presence or absence of pharyngo-laryngeal secretions, saliva aspiration and tracheostomy is not clear based on existing studies. We can postulate that one reason for the presence or absence of these components is the frequency of initiation of the swallowing reflex. In other words, a significant reduction in the frequency of spontaneous saliva swallowing might potentially explain why a patient presents pharyngo-laryngeal secretions and saliva aspirations that necessitate maintenance of a tracheostomy for a prolonged period. Another explanation could be a pharyngeal propulsion deficit (due to amyotrophy or a motor control disorder) or a combination of both deficits (low frequency of initiation of swallowing and a pharyngeal propulsion disorder). To test the hypothesis regarding the role of consciousness and cortical areas in modulating the frequency and/or efficacy of the spontaneous saliva swallowing, it would be interesting to study frequency of spontaneous swallowing during wakefulness and sleep in patients with DOC in relation to level of consciousness. Jakobsen et al. (2019) showed that measuring the frequency of swallowing is feasible in patients with severe brain injury. Indeed, it constitutes a simple, noninvasive measure of swallowing that can give us valuable information about spontaneous saliva management.

In addition, sensitivity to evoked coughing also seems to be influenced by level of consciousness and should be further explored in the future. Several cough reflex techniques have been developed and they are quick and easy to use in clinical practice (Lee et al., 2014; Miles et al., 2013; Monroe et al., 2014; Perry et al., 2019).

Conclusion

Based on this review, we can conclude that a link between swallowing and consciousness exists but is understudied and poorly understood. If we consider voluntary behaviors as possible signs of consciousness, the swallowing components of the oral phase should be considered conscious behaviors. Neuroimaging analysis of voluntary and spontaneous swallowing tasks have shown that oral and pharyngeal swallowing components are cortically mediated behaviors. The main areas activated during swallowing tasks are the primary sensorimotor cortex, supplementary and premotor cortex, anterior cingulate cortex, insula and cerebellum.

In patients with severe brain injury, the level of consciousness is associated with several components related to swallowing, such as the possibility of extubation, risk of pneumonia, type of feeding or components directly related to swallowing such as oral or pharyngeal abnormalities. Only four studies analyzed swallowing-related components specifically in patients with DOC diagnosed with a validated repeated behavioral scale. Both oral and pharyngeal phases of swallowing can be impaired in patients with DOC. Altered consciousness seems to influence voluntary swallowing behaviors (i.e., oral phase components). Based on existing studies, the **efficacy of the oral phase** and the **possibility of exclusive oral feeding** seem to be the most robust sign of consciousness. Indeed, until now, no typical patients with UWS are described as having a complex oral phase of swallowing enabling the preparation and mastication of solid food or as receiving exclusive oral feeding. There also seems to be a difference between patients with UWS and MCS regarding pharyngeal components of swallowing. However, these links are still not clear. As Naccache (2018) described, cortical activity is not specific to conscious states. In this context, we hypothesize that the presence of an efficient oral phase of swallowing and/or the ability to receive exclusive oral feeding are conscious, cortically mediated behavior while components of the pharyngeal phase and cough reflex are cortically mediated behaviors but not necessarily signs of consciousness based on existing data.

Further prospective studies will help refine our understanding of these associations and determine which swallowing behaviors suggest consciousness in patients with DOC. To succeed, therapists need assessment protocols adapted to this population. Moreover, it would be very interesting to implement a quick and easy test of oral phase components (mouth opening, lip prehension, tongue propulsion) in all behavioral assessments of consciousness.

The research field on the links between swallowing and consciousness deserves our attention, and there is an urgent need for clinical guidelines focusing on assessment and treatment of dysphagia in patients with DOC.

Declarations of competing interest

None.

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Author contributions

EM reviewed the literature and drafted the article with the help of AM and OG. All authors reviewed it critically for important intellectual content and gave final approval of the revised manuscript.

02

CHAPTER

IS ORAL FEEDING COMPATIBLE WITH AN UNRESPONSIVE WAKEFULNESS SYNDROME?

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ABSTRACT

Objective: The aim of the study is to explore the possibility of oral feeding in unresponsive wakefulness syndrome/vegetative state (UWS/VS) patients.

Method: We reviewed the clinical information of 68 UWS/VS patients (mean age 45 ± 11; range 16–79 years) searching for mention of oral feeding. UWS/VS diagnosis was made after repeated behavioural assessments using the Coma Recovery Scale—Revised. Patients also had complementary neuroimaging evaluations (positron emission tomography, functional magnetic resonance imaging and electroencephalography and diffusion tensor imaging).

Results: Out of the 68 UWS/VS patients, only two could resume oral feeding (3%). The first patient had oral feeding (only liquid and semi liquid) in addition to gastrostomy feeding and the second one could achieve full oral feeding (liquid and mixed solid food). Clinical assessments concluded that they fulfilled the criteria for a diagnosis of UWS/VS. Results from neuroimaging and neurophysiology were typical for the first patient with regard to the diagnosis of UWS/VS but atypical for the second patient.

Conclusion: Oral feeding that implies a full and complex oral phase could probably be considered as a sign of consciousness. However, we actually do not know which components are necessary to consider the swallowing conscious as compared to reflex. We also discussed the importance of swallowing assessment and management in all patients with altered state of consciousness.

Background

The unresponsive wakefulness syndrome (UWS/VS) is a disorder of consciousness characterized by the presence of eye-opening and reflexive movements, without conscious behaviours (Laureys et al., 2010). In patients in UWS/VS, cortical white and grey matters are severely affected (Royal College of Physicians, 2003). Fluorodesoxyglucose positron emission tomography (FDG-PET) studies show impairment of metabolism in the polymodal associative cortices but relatively preserved metabolism in the brainstem (Laureys et al., 1999; Laureys, 2004).

Swallowing is a complex sensorimotor function, which is either initiated voluntary or occurs spontaneously (reflex swallowing). Each type of swallowing activates different cortical regions. Neuroimaging studies demonstrated that while the central pattern generator (CPG; localized in the brainstem) mediates the reflexive component of swallowing, many cortical regions are involved in voluntary as well as in reflex swallowing (Ertekin & Aydogdu, 2003; Hamdy, Mikulis et al., 1999; Kern, Jaradeh, et al., 2001; Martin et al., 2001). However, even if both forms of swallowing involve cortical regions activation, the network of brain regions activated during reflexive swallowing is different from that observed during volitional swallowing (Ertekin & Aydogdu, 2003; Hamdy, Mikulis, et al., 1999; Kern, Jaradeh, et al., 2001; Martin et al., 2001). More specifically, fMRI studies in healthy volunteers showed that cerebral cortical representation of saliva and water reflexive swallow mainly involved bilateral primary sensorimotor cortices and insular cortices (Kern, Jaradeh, et al., 2001; Martin et al., 2001). On the other hand, during saliva and water bolus volitional swallows, there is an activation of the primary sensorimotor, premotor, prefrontal, frontal opercular, temporal and insular cortices, anterior cingulate gyrus and precuneus with a most consistent cortical activation in the primary sensorimotor cortex (Hamdy, Mikulis, et al., 1999; Kern, Jaradeh, et al., 2001; Martin et al., 2001). In the case of UWS/VS, patients classically receive hydration and nutrition through an enteral feeding tube. The possibility of resuming oral feeding in the UWS/VS population is greatly debated (ANA, 1993; Australian Government National Health and Medical Research Council, 2003; Bernat, 1992; Royal College of Physicians, 2003; The Multi-Society Task Force on PVS, 2011), and it is actually unclear if the presence of oral feeding is compatible with the diagnosis of UWS/VS or if this observation should lead to a modification of diagnosis (i.e., minimally conscious state). In this article, we document the feasibility of oral feeding in patients in UWS/VS.

Method

We retrospectively reviewed the clinical information of 68 chronic patients in UWS/VS. These patients were sent by their institution, doctor or family to be hospitalized for a one-week multimodal assessment in the University Hospital of Liege. From December 2006 to May 2017, 68 chronic patients in UWS/VS underwent this hospitalization week. The inclusion criteria were a chronic state (>3 months after onset) and a diagnosis of UWS/VS. Diagnosis of UWS/VS was made after repeated behavioural assessments by trained and experienced neuropsychologists using the Coma Recovery Scale–Revised (CRS-R, Giacino et al., 2004). The CRS-R consists of six subscales (auditory, visual, motor, and oromotor functions as well as communication and arousal) giving us 23 items ordered by degree of complexity, ranging from reflexive to cognitively mediated behaviours.

We also performed complementary clinical neuroimaging assessments. FDG-PET data were normalized to signal intensity of the skin (Stender et al., 2016). The mean value of skin voxels was selected as intensity scaling index for each volume. The skin was chosen due to the fact that it is not affected by the brain injury and metabolic activity can easily be extracted. For resting state functional Magnetic Resonance Imaging (fMRI), spontaneous BOLD signal correlations were measured between different brain regions for the default mode, auditory, visual, sensorimotor, salience and frontoparietal networks (Demertzi et al., 2014). We also used Diffusion Tensor Imaging (DTI) to quantify the orientation and directional uniformity of water diffusion in brain tissue (Gomez et al., 2012). Finally, clinical electroencephalograms (EEG) using 19 electrodes were also acquired and interpreted by a certified neurologist. Among the 68 patients in UWS/VS (mean age 45 ± 11; range 16-79 years), etiology was traumatic in 17 cases and non-traumatic in 51 cases (anoxic encephalopathy (n=34), ischemic or hemorrhagic stroke (n=8), mixed etiology (n=4), others (n=5)). Median interval since insult was 30 months (Q1 = 9 and Q3 = 39).

Results

Out of the 68 UWS/VS patients included in this study, according to the medical records and the questionnaires fulfilled by the family, the doctor and the nurses, only two patients could resume oral feeding (3%). The first patient received oral feeding (i.e., liquid and semi liquid) in addition to gastrostomy feeding, with a functional swallowing based on an otorhinolaryngological examination, and the second patient had full oral feeding (i.e., liquid and mixed solid food).

Case report 1

Medical history: A 17-year-old man was admitted to intensive care unit after an ethylic coma complicated by a pneumopathy caused by gastric liquid inhalation. The situation was evolving positively, allowing the patient to leave the hospital after a few days. However, a couple of days after the discharge, the patient suffered from a cardiorespiratory arrest occurring after an effort at home. Cardiorespiratory resuscitation was performed and ventilation was needed. An unconscious state was observed with a lack of evolution. One month later, the patient was discharged from intensive care unit with a diagnosis of UWS/VS and returned to his parent's home without any period in a rehabilitation centre. He received nurse care each day and physical therapy thrice a week, but no swallowing care. Fourteen years after the brain injury, he came to the University Hospital of Liège. He was still considered as UWS/VS.

Oral feeding: When the patient came at the University Hospital of Liege, he was entirely fed by mouth with thick to thin liquid texture (corresponding to level 0 to 4 in the International Dysphagia Diet Standardisation Initiative - IDDSI Framework (Cichero et al., 2016). However, the patient still had the gastrostomy tube for complementary nutrition of about 0.5 litre per day. Otorhinolaryngological exam were performed. The fiberoptic endoscopic evaluation showed preserved laryngeal mobility and cough reflex, as well as no salivary or secretions stasis. Semi-liquid and liquid test was performed. For semi-liquid, the patient could open his mouth when the spoon touched his lips but he was not able to close it around the spoon. Antero-posterior movements of the tongue were observed and there was no buccal stasis. The initiation of swallowing reflex was delayed but no inhalation occured. Liquid was given with a syringe on lingual basis. A posterior leakage was observed, the initiation of swallowing reflex was delayed but ventricular bands close to protect the larynx and no inhalation occured.

Multimodal diagnosis assessment: CRS-R total scores ranged from 4 to 7 depending on the day (total of 6 evaluations). The patient showed spontaneous eye opening, head and legs movements, auditory startle reflex, no response to command, no visual fixation, no visual pursuit, bilateral abnormal flexion in response to noxious stimulations, oral reflex movements and vocal productions but no communication. The total CRS-R score the day of the otorhinolaryngological exam was 5. Clinical assessments concluded that he fulfilled the criteria for a diagnosis of UWS/VS. Neuroimaging results also pointed in that direction (**figure 6**). FDG-PET showed a drop in brain metabolism of 79% as compared to healthy controls, with hypometabolism in the global lateral and medial fronto-parietal network and a preservation of the brainstem and cerebellum (fig 6A and 6B). MRI revealed a global bilateral atrophy of the cerebral and cerebellar hemispheres (fig 6C and 6D). fMRI showed no spontaneous brain activity in the different resting state networks (fig 6C-6F). DTI showed diffuse alteration of white matter connections (fig 6G and 6H). Clinical electroencephalograms (EEG) suggested a severe encephalopathy.

Case report 2

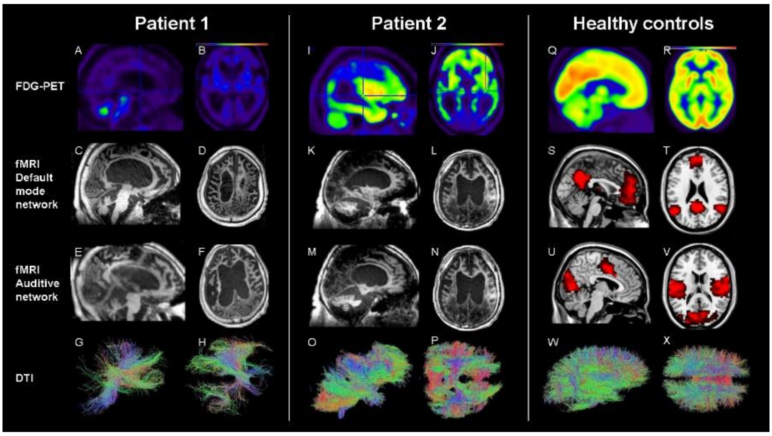
<u>Medical History</u>: A 35-year-old man was admitted to the hospital as a result of a motor road accident (moped knocked down by a car). There was no loss of awareness or neurologic symptoms but some fractures in the hand and kneecap. Three days later, he was admitted to the intensive care unit after a cardiac arrest during a kneecap surgery. He sustained an anoxic brain injury and remained comatose during the following 10 weeks. He then recovered spontaneous eye opening and startle reflexes to loud sound and bright light. Three weeks after the brain injury, computed tomography revealed cerebral collapse on basal ganglia. He was tracheostomized during the first three months then oral feeding was gradually started. At the discharge, neurological examination retained the diagnosis of “permanent vegetative state” based on the absence of any behavioural sign of consciousness. The patient returned back home four months after the anoxic brain injury with a naso-gastric tube feeding. Nineteen years after the insult, the patient came to the University Hospital of Liège for a multimodal diagnosis assessment.

<u>Oral feeding</u>: Oral liquid and solid food feeding were gradually continued by the mother after the initial hospitalization and enteral feeding was stopped two weeks after the discharge. The patient never received swallowing therapy. When he came to our center, the patient was entirely fed by mouth. He also orally received hydration and medications. Solid food corresponded to the level 5 (minced and moist) in the IDDSI

Framework (Cichero et al., 2016). Three meals per day were administrated by the mother or the nurse with normal utensils. The patient opened his mouth when the spoon was touching his lips but was not able to close his lips around the spoon. There was no history of lung infection and his body weight was stable. The nutritional status measured by albumin indicator was normal (43gr/L - norms 38-49).

Multimodal diagnosis assessment: Behavioural examinations confirmed the diagnosis of UWS/VS. The CRS-R total scores ranged from 6 to 7 depending on the day (total of 6 evaluations) and showed spontaneous eyes opening, auditory startle reflex, no response to command, no visual fixation or pursuit, no blink to threat, bilateral flexion responses to noxious stimulations, oral reflex movements and vocalizations without any communication. However, neuroimaging examinations (FDG-PET, DTI and EEG) looked atypical (**figure 6**). FDG-PET showed a drop in brain metabolism of 47% as compared to healthy controls with relative metabolic preservation of the brainstem, cerebellum, frontal and occipital cortices, and hypometabolism in the bilateral parieto-temporal associative areas (fig 6I and 6J). MRI revealed global cerebellar vermis atrophy, mesencephalic bilateral atrophy, parieto-occipital cortex and basal ganglia (principally left thalamic) atrophy. There was also a hyperintense signal in the midbrain and the pons compatible with a wallerian degeneration. A quadriventricular dilatation was also noted as well as bilateral white matter diffuse lesions encompassing parietal and cingulate posterior cortices and precuneus (fig 6K and 6L). fMRI showed no spontaneous brain activity in any of the resting state networks (fig 6K-6N). DTI showed a loss of white matter in dorsal posterior area bilaterally and disorganisation of fibers in parietal cortex (fig 6O and 6P). EEG depicted symmetrical areactive slow theta activity, suggesting of a medium and diffuse cerebral suffering.

Figure 6. Neuroimaging results (PET, fMRI Default mode Network, fMRI Auditory Network and DTI) of the two patients and healthy controls



Note: Patient 1 (left panel): FDG-PET showed a drop in brain metabolism of 79% with hypometabolism in the global lateral and medial fronto-parietal network and a preservation of the brainstem and cerebellum (A and B). MRI revealed a global bilateral atrophy of the cerebral and cerebellar hemisphere in patient 1 (C and D). DTI showed diffuse alteration of white matter connections (G and H). Patient 2 (central panel): drop in brain metabolism of 47% with hypometabolism in the bilateral parieto-temporal associative areas but relative preservation of the brainstem, cerebellum and frontal and occipital cortex (I and J). MRI revealed a global cerebellar vermis atrophy, a mesencephalic bilateral atrophy, a parieto-occipital cortex and basal ganglia (principally left thalamic) atrophy (K and L). DTI showed loss of white matter in dorsal posterior area bilaterally and disorganisation of fibers in parietal cortex (O and P). In fMRI, performed with sedation, patient 1 and 2 showed no spontaneous brain activity in the different resting state networks (C-F and K-N, respectively).

Discussion

In our population, only two out of 68 patients in UWS/VS could safely resume oral feeding. This is thus a rare observation (3%) among patients in UWS/VS. We see that the period between the accident and the assessment in our center is very long. It reflects the failure of most health care system to adequately care for DOC patients after the acute phase. A previous retrospective study showed that in 260 patients diagnosed as "permanent vegetative state", 8% could perform oral feeding (Lin et al., 2008). However, no information was given about how the diagnosis of UWS/VS was made and if standardized behavioural assessments were used. Indeed, repeated behavioural assessment is essential to make a proper diagnosis. A recent study shows that performing a single CRS-R assessment could lead to up to 35% of misdiagnosed UWS/VS (Wannez et al., 2017). In our study, repeated clinical assessments (n=6) matched with the diagnosis of UWS/VS in both patients according to actual behavioral diagnosis criteria. For patient 1, neuroimaging results are in line with the UWS/VS diagnosis. However, atypical results were observed for patient 2 (relative metabolic preservation of frontal and occipital cortices, relatively preserved DTI and theta activity but no spontaneous resting state fMRI networks). Given the dissociation between the behavior and the neuroimaging findings, patient 2 could be considered as being in a functional locked-in (Bruno et al., 2011; Formisano et al., 2013) or in a MCS* (Bodart et al., 2017; Gosseries et al., 2014), or even maybe in a state of cognitive motor dissociation (Schiff, 2015). However, advanced diagnostic techniques during a swallowing task or by means of mental imagery tasks should be performed to confirm this alternative diagnosis. Considering that the diagnosis of UWS/VS implies the absence of any voluntary behaviour, the observation of functional swallowing in these two patients raises many questions and reflexions.

As we described above, swallowing can either occurs spontaneously (reflex swallowing) or be initiated voluntary (for a review see Ertekin, 2011). Reflex swallowing is classically described as an irrepressible swallowing movement occurring despite the intention to avoid swallowing, without volitional input for initiation (Kern, Jaradeh, et al., 2001) and without conscious control (Hamdy, Mikulis, et al., 1999). Reflex swallowing is classically assessed with injection of minute amounts of water directly into the pharynx (Kern, Jaradeh, et al., 2001) or "naïve" saliva swallow (Martin et al., 2001). According to the classical view of the initiation of reflex swallow, the oral phase is bypassed. Reflex swallowing is observed as early as the 12th gestational week, before the cortical and subcortical structures have totally developed (Jean, 2001). It has also been reported that swallowing can be observed in the human anencephalic foetus (Peleg & Goldman, 1978; Prtichard, 1965). On the other hand, voluntary swallowing corresponds to sequential eating or drinking voluntarily initiated or facilitated by the cerebral cortex (Ertekin, 2011). Materials in the mouth (food or saliva) and the cortical drive to the tongue and the submental muscles are necessary for initiation of voluntary swallowing (Ertekin, 2011). In voluntary swallowing studies, water or food was injected in the mouth without any verbal instruction to swallow (Hamdy, Mikulis, et al., 1999; Martin et al., 2001) or subjects were cued to swallow volitionally their saliva (Kern et al., 2001; Martin et al., 2001).

As described in the introduction, the network of brain regions activated during reflexive swallowing is different from that observed during volitional swallowing (Hamdy, Mikukis, et al., 1999; Kern, Jaradeh, et al., 2001; Martin et al., 2001; Mosier, Patel, et al., 1999; Zald & Pardo, 1999). In previous studies, voluntary and reflex swallow can be differentiated in terms of state of awareness, wakefulness, and to what extent the oral phase is involved (Ertekin, 2011a; Ertekin & Aydogdu, 2003a; Hamdy, Mikulis, et al., 1999; Kern et al., 2001; Martin et al., 2001). However, because swallowing was never studied in DOC population, we actually do not know what is sufficient to consider swallowing as conscious compared to reflex swallowing in this population of patients. In terms of the oral phase of the swallowing, are lip closure, mastication, tongue manipulation and propulsion necessary to consider the swallowing a conscious action? This issue is still debated and future studies are needed to define what is a “conscious” swallowing and what is a reflex swallowing in DOC patients. Given the retrospective character of this study, we are not able to analyze precisely the efficacy of the oral phase. However, we can make prediction by looking at the food texture that these two patients received. The first patient was able to swallow liquid and semi-liquid textures, which does not necessarily imply a complex oral phase. On the other hand, patient 2 received solid food and this type of texture definitely implies some form of functional oral phase to propel the food. We can then consider that the swallowing of patient 2 probably reflects higher level of conscious swallowing than the swallowing of patient 1. Interestingly, these observations are in line with the atypical neuroimaging results found in patient 2. Furthermore, given that voluntary swallowing is initiated or facilitated by the cerebral cortex, we can suppose that the preservation of some cortical areas (principally in the frontal cortex) in patient 2 can contribute to better swallowing results. However, based on the current neuroimaging results, we should be careful in saying that swallowing is reflex or conscious. This precise information can only be obtained with functional imaging performed during swallowing.

The swallowing abilities of the patients with DOC should be systematically assessed and compared among the different states of consciousness. This is critical as misdiagnosis can have serious medical and ethical consequences for the patients and their family. Indeed, prognosis, treatment decisions (particularly pain treatment) and medico-legal judgements (especially end-of-life decision-making) are influenced by the diagnosis (Bernat, 2008; Demertzi et al., 2011).

Neuropathological studies seem to indicate that a correlation exists between the level of consciousness and swallowing function: the higher the cognitive function, the better the chance to achieve oral feeding (Formisano et al., 2004; Hansen, Engberg, et al., 2008a; Mackay et al., 1999a; Winstein, 1983). Based on this, the atypical brain activation observed in patient 2 in addition to his capacity to perform full oral feeding should prompt us to be more careful and rethink our initial clinical UWS/VS diagnosis.

Finally, this case study emphasizes the importance of systematic observations of swallowing capacities in all patients with altered consciousness. Indeed, as shown in our study, even patients with no evident sign of consciousness can sometimes demonstrate some functional swallowing. More than 30 years ago, it was demonstrated that some assessments (pre-feeding assessment and functional assessment) could be performed in severe head-injured patients (Winstein, 1983). Since then, other studies showed that objective swallowing assessments (realized with instrumental assessments such as fiberoptic endoscopic exam (FEES) or videofluoroscopy (VFSS)) could be performed safely in patients regardless their level of consciousness (Brady et al., 2006; Bremare et al., 2016; O'Neil-Pirozzi et al., 2003). Brady et al. (2006) considered that the decision to introduce oral food or liquid in DOC patients should only be made after the completion of an objective swallowing evaluation. We share Brady's opinion and we insist on the importance of the realization of a systematic swallowing evaluation including instrumental assessments of swallowing such as VFSS or FEES, as they are the only reliable way to identify silent aspiration due to poor cough reflex (Miles et al., 2013). Combined to VFSS or FEES, swallowing function clinical evaluation will give complementary information on the pre-swallowing and swallowing abilities (Brady et al., 2006; Bremare et al., 2016).

Clinicians working with DOC patients are also faced with the challenge of providing meaningful therapy. Safety and treatment efficacy of swallowing rehabilitation in patients with DOC is still debated (Brady et al., 2006; Mackay et al., 1999a; O'Neil-Pirozzi et al., 2003) (for a review see Maudoux et al., 2017). Some clinicians advocate providing patients with a level II (generalized responses/vegetative state) or III (localized responses/minimally conscious) in Ranchos Los Amigos Scale (RLAS, Hagen et al., 1987) with food/liquid presentations for taste stimulation (Mackay et al., 1999a). Other clinicians recommend no oral feedings until the patient's level of consciousness improves beyond level III in RLAS (Brady et al., 2006; De Tanti et al., 2015; Winstein, 1983). However, based on our observations, a few patients who do not show conscious behaviour according to the CRS-R can perform oral feeding even if the majority of DOC patients are fed with enteral feeding. Thus, we believe that the decision to introduce food or liquid should not rely uniquely on the observation of conscious behaviour but rather on performance observed during an objective swallowing assessment.

Several **limitations** of the study should be taken into account. First, we have considered only patients who were known to be fed at the moment of their admission for the one-week multimodal assessment. This introduces a bias in our data given that we might have missed patients who can potentially be fed orally but who are not (due for example to the lack of stimulation, fear of bronchoinhalation, etc.). However, we think that this number of missed patients is probably low. In our experience almost all families try to reintroduce oral feeding. Most of the time they are confronted to difficult situations making it impossible. This is namely the hypercontraction of masseter or bite reflex reducing considerably the chance of oral-feeding, the total absence of orofacial reaction when trying to put some food in the mouth, the absence of swallowing reflex, etc. When these difficulties are not present, further testing is usually undertaken and if judged safe, oral feeding is pursued. Therefore, the number of patients that were not fed at the moment of their admission but could have had full oral feeding is probably very low. Second, as we described before, it has been more informative if we had swallowing assessment with standardized otorhinolaryngological techniques for all UWS/VS patients. Further studies are needed to better estimate rate and characteristics of swallowing in these DOC patients. Finally, we cannot totally exclude that the absence of response on resting state fMRI in our two patients is not due to the administration of sedation during the scanning. However, this was a light sedation (0.8mg/mL) done mainly to improve the patients' comfort in the scanner. Moreover, a recent study demonstrated that connectivity decreases due to propofol sedation are relatively small compared to those already caused by structural brain injury (Kirsch et al., 2017). Another recent study also showed that administration of sedation did not prevent some patients with DOC to show fMRI responses during active imagery tasks (Bodien et al., 2017).

Conclusion

Oral feeding in UWS/VS patients is rare. We here presented the case of two patients who could achieve oral feeding. Although the diagnosis based on clinical behavioural assessment suggests an UWS/VS, we found some atypical neuroimaging results in the second patient who performed full oral feeding. Resuming full oral feeding may be related to recovery of some brain functions, which probably lead to a higher level of consciousness than UWS/VS. Full oral feeding could thus potentially be considered as a sign of consciousness. However, further studies will have to explore more precisely if functional swallowing is really a sign of consciousness and if this observation can be another key element to determine the diagnosis. We suggest that only the recovery of a full and complex oral phase (including solid food) should be considered as a sign of consciousness. Indeed, in some UWS/VS patients, the rare recovery of oral feeding with liquid and semi-liquid textures could be due to the presence of reflex swallowing rather than conscious swallowing.

A systematic swallowing assessment should be performed in all DOC patients regardless of their level of consciousness. This will allow to better tract residual swallowing function in DOC patients, and see if it can be related to the level of consciousness. Various therapeutic techniques should be assessed and therapeutical objectives/purposes should be developed. Finally, we would like to emphasize that in these two patients the presence of relatively preserved swallowing function does not seem to predict good prognostic in terms of functional outcomes given their long history of chronic UWS/VS condition.

The study was approved by the Ethics Committee of the Medical School of the University of Liège and written consents were obtained from the legal representative of each patient.

The authors declare that they have no conflict of interest.

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CHAPTER 03

SWALLOWING IN INDIVIDUALS WITH DISORDERS OF CONSCIOUSNESS: A COHORT STUDY

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ABSTRACT

Objective: After a period of coma, a proportion of patients with severe brain injury remain in an altered state of consciousness before regaining partial or complete recovery. Patients with disorders of consciousness (DOC) classically receive hydration and nutrition through an enteral feeding tube. However, the real impact of the level of consciousness on a patient's swallowing ability remains poorly investigated. The aims of this study were to document the incidence and characteristics of dysphagia in DOC patients, and to evaluate the link between different components of swallowing and the level of consciousness.

Methods: We analyzed clinical data on the respiratory status, oral feeding and otolaryngologic examination of swallowing in DOC patients. Univariate and multivariate logistic regressions were performed between patients' groups (i.e., unresponsive wakefulness syndrome – UWS and minimally conscious state – MCS) and each analyzed criterion.

Results: 92 DOC patients were included (26 UWS and 66 MCS patients). Deficits in the oral and/or pharyngeal phase of swallowing were present in 99% of the patients. Compared to MCS, UWS patients were more frequently tracheotomized (69% UWS vs 24% MCS) with diminished cough reflex (27% UWS vs 54% MCS) and no effective oral phase (0% UWS vs 21% MCS).

Conclusion: Almost all DOC patients have severe dysphagia. Results show that some components of swallowing (i.e., tracheostomy, cough reflex and efficacy of the oral phase of swallowing) were related to consciousness. In particular, none of the UWS patients had an efficient oral phase, suggesting that its presence may be a sign of consciousness. In addition, none of the UWS patients could be fed entirely orally while none of the MCS patients received ordinary oral food. Our study also confirms that objective swallowing assessment can be successfully completed and that specific care is needed to treat severe dysphagia in DOC.

Introduction

After a period of coma, individuals with severe brain injury may remain in an altered state of consciousness before regaining partial or complete recovery (Schnakers, 2017). Disorders of consciousness (DOC) consist of 3 states ranging from no awareness and no arousal to the preservation of arousal with fluctuating awareness (Gosseries et al., 2014): coma, vegetative state/unresponsive wakefulness syndrome (UWS) (Laureys et al., 2010) and minimally conscious state (MCS) (Giacino et al., 2002). UWS is characterized by the presence of eye-opening and reflexive movements, without conscious behaviours (Laureys et al., 2010). Individuals with MCS show reproducible but inconsistent signs of consciousness, such as command following, visual pursuit, and localization to noxious stimulation (Giacino et al., 2002). When they recover the ability to functionally communicate or to use objects adequately, they emerge from the MCS (Giacino et al., 2002).

Swallowing disorders are relatively frequent after an acquired brain injury from traumatic or anoxic causes, ranging from 25% to 61% depending on the studies (Mackay et al., 1999a; Winstein, 1983). Oral feeding has been suggested to be related to the level of consciousness in previous studies evaluating swallowing in severe brain-injured individuals (Brady et al., 2006; Bremare et al., 2016; Crary et al., 2013; Formisano et al., 2004; Godet et al., 2017; Hansen et al., 2008; Mackay et al., 1999a; Mandaville et al., 2014; Melotte et al., 2018; O'Neil-Pirozzi et al., 2003; Terré & Mearin, 2007,2009; Winstein, 1983). Individuals with DOC classically receive hydration and nutrition through an enteral feeding tube (Whyte et al., 1999). The real impact of the level of consciousness on individuals' swallowing ability remains poorly investigated. Indeed, previous studies that assessed swallowing in individuals with severe brain injury had small sample sizes (Bremare et al., 2016), focused on only one component such as the type of feeding (Mélotte et al., 2018; **Chapter 2**) or the possibility of extubation (Godet et al., 2017) and/or they mostly used clinical assessment of consciousness that was not based on established diagnostic criteria (Giacino et al., 2002) (see Brady et al., 2006; Crary et al., 2013; Formisano et al., 2004; Hansen et al., 2008; Mackay et al., 1999a; Mandaville et al., 2014; O'Neil-Pirozzi et al., 2003; Terré & Mearin, 2007,2009; Winstein, 1983). In line with this, previous literature showed that the Coma Recovery Scale-Revised (CRS-R) (Giacino et al., 2004) is the current gold standard to assess the level of consciousness in DOC individuals, and multiple evaluations should be performed to decrease misdiagnosis (Wannez et al., 2017). Accurate diagnosis is challenging because of confounding factors such as aphasia and motor deficits, but it has important implications for prognosis (Luaute et al., 2010), treatment management (Thibaut et al., 2014) and related ethical considerations (Demertzi et al., 2011).

Swallowing has not yet been studied systematically in DOC individuals, and to our knowledge, the link between the level of consciousness and swallowing components (e.g., lip prehension, lingual propulsion, pharyngo-laryngeal sensitivity, efficacy of the pharyngeal phase and ability to clear saliva) has never been investigated. We recently suggested that an effective oral phase of swallowing could be a determinant to consider swallowing as a conscious behavior (Mélotte et al., 2018, **Chapter 2**). However, in this previous study, we included only UWS participants and based our conclusion on only 2 components (i.e., presence or absence of oral feeding and type of oral feeding).

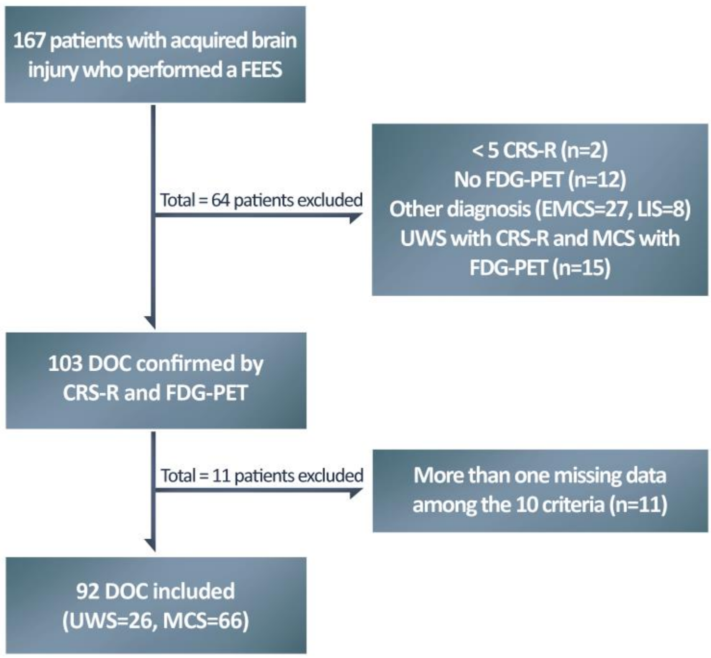
In the present work, we collected respiratory and nutritional status as well as the otolaryngological results of swallowing in a large cohort of individuals with prolonged DOC. We predicted that most individuals have severe alterations of the different components of swallowing and that some components of the swallowing process, such as the oral phase, may be linked to the level of consciousness.

Participants and methods

Participants

We retrospectively collected data for individuals admitted consecutively from January 2010 to August 2018 to the University Hospital of Liege (Belgium) for a 1-week multimodal assessment of consciousness for diagnostic and prognostic purposes. **Figure 7** illustrates the flow of participants in the study. Inclusion criteria were 1) recovered from coma caused by a severe acquired brain injury, 2) with a prolonged condition (> 1 month post-insult) (Giacino et al., 2018a, 2018b), 3) medically stable, 4) underwent fiberoptic endoscopic examination of swallowing (FEES), 5) a diagnosis of UWS or MCS based on a minimum of 5 CRS-R tests (to avoid diagnostic errors due to fluctuations in responsiveness and to obtain a stable clinical diagnosis) (Wannez et al., 2017), which was confirmed on fluorodeoxyglucose-positron emission tomography (FDG-PET) (see next sections concerning data acquisition and analyses) and 6) no more than 1 missing data item (i.e., at least 9 of 10 selected criteria regarding respiratory status, type of feeding and components of the oral and pharyngeal phases of swallowing).

Figure 7. Flowchart of the study



Note: FEES, fiberoptic endoscopic evaluation of swallowing; CRS-R, Coma Recovery Scale-Revised; FDG-PET, fluorodeoxyglucose-positron emission tomography; EMCS, emergence from minimally conscious state; LIS, locked-in syndrome; DOC, disorders of consciousness; UWS, unresponsive wakefulness syndrome; MCS, minimally conscious state.

We extracted demographic data (i.e., sex, age, etiology, time since insult) and DOC diagnosis from participants' medical records. Etiology was classified in terms of focal or global injury to distinguish between on one hand, ischemic, hemorrhagic and traumatic brain injury, and on the other, anoxic and metabolic encephalopathy.

The study was approved by the Ethics Committee of the Faculty of Medicine of the University Hospital of Liege, and written informed consent was obtained from all legal surrogates. We followed the principles of the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) (von Elm et al., 2007) (**see Appendix 3**).

Diagnosis of consciousness

The diagnosis was established after repeated behavioral assessments performed by trained and experienced clinician researchers using the CRS-R (Giacino et al., 2004) and FDG-PET. The CRS-R consists of 6 subscales (auditory, visual, motor, and oromotor functions as well as communication and arousal) of 23 items ordered by degree of complexity, ranging from reflexive to cognitively mediated behaviors (Naccache, 2018). All participants underwent at least 5 CRS-R tests over a maximum of 10 days and the best result was kept for the behavioral diagnosis (Wannez et al., 2017). To confirm the behavioral diagnosis, FDG-PET images were visually inspected by experts and classified as compatible with UWS (when the statistical tool detected no voxels with preserved metabolism in the associative fronto-parietal network bilaterally) or compatible with MCS (with incomplete hypometabolism or partial preservation of metabolic activity detected in the fronto-parietal network). The acquisition procedure and analyses of FDG-PET data were described previously (Bodart et al., 2017; Stender et al., 2014). The brain activity map was obtained with a threshold of uncorrected $p<0.05$ in all contrasts for single-subject analyses, as in previous studies (Bodart et al., 2017; Stender et al., 2014). We excluded individuals with a diagnosis of UWS based on the CRS-R but with FDG-PET results compatible with MCS because these individuals may present covert consciousness (referred to as MCS*) (Gosseries et al., 2014).

Respiratory status, type of feeding and swallowing assessments

We collected data on 10 specific criteria based on the results of the ear, nose and throat (ENT) examination (performed by SD, AM or AL) and from the questionnaires completed by the family (for the type of feeding).

For respiratory status, we reported the presence or absence of tracheostomy (criterion 1). The type of feeding (criterion 2) referred to the presence or absence of exclusive enteral-feeding. For participants who received oral feeding, we distinguished type of feeding based on the criteria of the Food Intake Level Scale (FILS) (Kunieda et al., 2013). The FILS is an observer-rating scale for assessing the severity of dysphagia, examining to what degree individuals take food orally on a daily basis, ranging from 0 (no oral intake, and no swallowing training) to 10 (normal oral food intake). Scores 1 to 3 correspond to no oral intake, 4 to 6 oral intake with alternative nutrition, and 7 to 10 oral intake exclusively.

The other 8 criteria were related to the otolaryngological examination performed by ENT experts. A FEES was performed with a flexible videorhinolaryngoscope (Olympus Visera OTP-S7, Tokyo) and color monitor. We excluded all criteria that required a response to a command (e.g., assessment of the nasopharyngeal or vocal fold closure with the production of sounds, apnea, volunteer saliva swallow, cough). The first 3 criteria of the otolaryngological examination were related to the oral phase of swallowing with the presence or absence of hypertonia of jaw muscles (criterion 3), the presence or absence of an oral phase of swallowing (lip prehension or lingual propulsion; criterion 4), and the observation or not of an effective oral phase (criterion 5). Practically, we moved a spoon to in front of the individual's mouth and observed the reaction. With absence of lip prehension, we placed a 2-ml bolus in the middle of the tongue and observed if lingual propulsion occurred. We considered the oral phase effective if we detected consecutively lip prehension, lingual propulsion and no post-swallowing oral stasis. The last 4 criteria were related to the pharyngeal phase of swallowing. The presence or absence of secretions in the pharyngo-laryngeal area (criterion 6) and the salivary aspiration (criterion 7) informed on participants' ability to manage secretions. The cough reflex (criterion 8) was evaluated by stimulating the laryngeal area, and if no cough was observed, the pharyngo-laryngeal sensitivity was considered absent. Finally, we noted the presence or absence of bolus aspiration during the swallowing of 2 ml of thick and liquid textures (criteria 9 and 10, respectively). Some participants did not undergo the functional swallowing test because of a severe bite reflex, an inefficacity of the oral phase, or because it was considered too dangerous regarding other parameters (e.g., too many saliva aspirations, absence of spontaneous saliva swallowing).

Statistical analysis

We performed a descriptive analysis for each diagnosis group (UWS and MCS) in terms of sex, age, etiology and time since insult. Normality was assessed with histograms, quantile plots and Shapiro-Wilk tests. Univariate comparisons between UWS and MCS groups involved chi-square or Fisher exact test for categorical variables and Kruskal-Wallis test for non-normally distributed continuous variables. The association between each of the 10 criteria and the diagnosis groups was assessed by univariate logistic regression. These associations were further investigated by multivariable logistic regression adjusted for etiology and time since insult. The results of logistic regressions are presented as odds ratios (ORs) and adjusted ORs together with their 95% confidence intervals (CIs). $P < 0.05$ was considered statistically significant. Individuals with missing values were excluded from the analysis for the considered criteria. Statistical analyses were performed with Stata v14.2 (Stata Corp. 2015, College Station, TX).

Results

We first present the descriptive analysis **(Table 8)** and then the percentage of participants for each of the 10 selected criteria, the univariate analysis for each criterion by diagnosis (p_{uni}), and the adjusted multivariate analysis ($p_{adjusted}$) for etiology and time since insult **(Table 9)**. We also illustrate the percentage of UWS and MCS participants for each criterion in **Figure 8**.

Table 8. Descriptive statistics of the whole sample

	UWS (n=26)	**MCS (n=66)**	**P-value**
Sex (F/M)	9/17	30/36	0.343
Age, years, mean (SD)	41 (12)	38 (12)	0.405
Etiology	Focal: 11 Global: 15	Focal: 49 Global: 17	0.004
Time since injury, months, mean (SD)	30 (22)	40 (34)	0.014

Note: UWS, unresponsive wakefulness syndrome; MCS, minimally conscious state

In total, 91 of 92 participants presented disorders in at least one criterion linked to the oral or pharyngeal phase of swallowing (i.e., criteria 3 to 10). Regarding respiratory status, 34 (37%) participants still had a tracheostomy at the time of assessment. As compared with MCS individuals, UWS individuals more frequently had a tracheostomy ($p_{adjusted}$=0.002). In total, 71 (77%) participants received enteral feeding exclusively, with no significant difference between UWS and MCS groups ($p_{adjusted}$=0.254). None of the MCS participants received exclusive ordinary solid food (FILS 10).

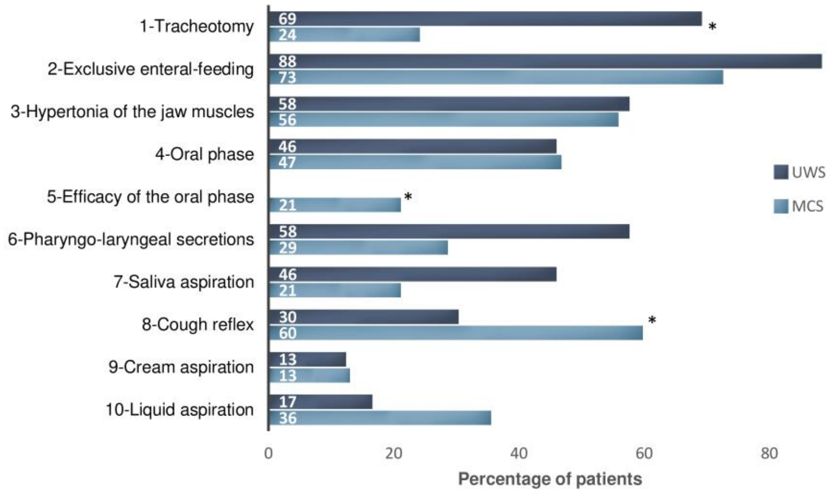
Regarding the ENT examination, for the oral phase, 52 (56%) participants presented hypertonia of the jaw muscles, with no difference between UWS and MCS groups ($p_{adjusted}$=0.881). In total, 43 (47%) participants showed at least one component of the oral phase of swallowing (lip prehension or lingual propulsion), with no difference between groups ($p_{adjusted}$=0.94). However, UWS and MCS groups differed in efficacy of the oral phase of swallowing ($p_{adjusted}$=0.011), characterized by the presence of lip prehension and lingual propulsion without post-swallowing oral stasis. For the pharyngeal phase, 34 (37%) participants had pharyngo-laryngeal secretions and 26 (28%) saliva aspiration. UWS and MCS groups differed on univariate analysis for the pharyngo-laryngeal secretions (p_{uni}=0.012) and saliva aspiration (p_{uni}=0.019) but not significantly on multivariable analysis (pharyngo-laryngeal secretions: $p_{adjusted}$=0.067; saliva aspiration: $p_{adjusted}$=0.062). For the test of the cough reflex, among the 63 participants assessed, 43 (52%) showed decreased pharyngo-laryngeal sensitivity, with significantly more MCS participants presenting a cough reflex than UWS participants ($p_{adjusted}$=0.027). Regarding the functional test with thick and liquid texture, 16 (61%) and 53 (80%) UWS and MCS participants, respectively, performed the swallowing test with a cream texture and 12 (46%) and 42 (63%) with a liquid texture. Nine (13%) participants showed aspiration with a thick texture and 17 (31%) with a liquid texture, with no difference between groups (thick texture: $p_{adjusted}$=0.798; liquid texture: $p_{adjusted}$=0.226).

Table 9. Descriptive and statistical analysis of the 10 criteria in the UWS and MCS groups

					UWS vs MCS	
Criteria	**UWS** n (%)	**MCS** n (%)	p_{uni}	$p_{adjusted}$	**OR**	**95% CI**
1. Tracheostomy still in place Tracheostomy removed Never had a tracheostomy	18/26 (69.2) 5 3	16/66 (24.2) 38 12	<0.001	0.002	5.67	1.86–17.27
2. Full enteral feeding Partial oral feeding (FILS 7) Full oral feeding (FILS 7) Full oral feeding (FILS 7) with gastrostomy for hydration	23/26 (88.5) 3 0 0	48/66 (72.7) 13 3 2	0.117	0.254	2.45	0.53–11.39
ORAL PHASE						
3. Hypertonia of the jaw muscles	15/26 (57.7)	37/66 (56.1)	0.887	0.881	1.08	0.41–2.87
4. Oral phase	12/26 (46.2)	31/66 (47.0)	0.844	0.94	0.96	0.37–2.53
5. Efficacy of the oral phase	0/26 (0)	14/66 (21.2)	0.007	0.011	0.09	0–0.63
PHARYNGEAL PHASE						
6. Pharyngo-laryngeal secretions	15/26 (57.7)	19/66 (28.8)	0.012	0.067	2.53	0.94–6.82
7. Saliva aspiration	12/26 (46.2)	14/66 (21.2)	0.019	0.062	2.65	0.95–7.38
8. Cough reflex	7/23 (30.4)	36/60 (60)	0.019	0.027	0.30	0.10–0.87
9. Cream aspiration Not performed[a]	2/16 (12.5) 10	7/53 (13.2) 13	0.941	0.798	1.26	0.21–7.44
10. Liquid aspiration Not performed[a]	2/12 (16.7) 14	15/42 (35.7) 24	0.223	0.226	0.35	0.07–1.90

Note: p_{uni}, univariate analysis between UWS and MCS; $p_{adjusted}$, multivariable analysis between UWS and MCS adjusted for etiology and time since insult; PL, pharyngo-laryngeal; OR, odds ratio; CI, confidence interval; FILS, Food Intake Level Scale. [a]Not performed because it was considered too risky by examiners or because of troubles in the oral phase (e.g., bite reflex, no lingual propulsion).

Figure 8. Percentage of UWS and MCS patients for the 10 criteria. UWS



Note: UWS, unresponsive wakefulness syndrome; MCS, minimally conscious state.

Discussion

The main aims of this study were to document the proportion and characteristics of dysphagia in individuals with DOC, and to evaluate the link between different criteria of swallowing and level of consciousness. To our knowledge, this is the first study of respiratory status, oral feeding and FEES in a large cohort of individuals with DOC. In our study, all but one DOC individual (MCS) presented at least one swallowing dysfunction of the oral and/or pharyngeal phase. Also, tracheostomy, cough reflex and the efficacy of the oral phase were the 3 criteria related to consciousness. Finally, none of the UWS individuals could be fed entirely orally, whereas none of the MCS individuals received ordinary oral food.

Regarding type of feeding, none of the UWS participants could achieve a full oral feeding, most probably linked to the absence of an effective swallowing oral phase and less effective pharyngeal phase, as shown by the proportion of participants with tracheostomy. Only a small proportion (7%) of MCS participants could safely resume full oral feeding with easy-to-swallow food (i.e., FILS 7). Despite the ability of some MCS participants to resume oral feeding, a higher level of consciousness (i.e., EMCS) is probably necessary to enable a full ordinary oral food (FILS 10).

Some swallowing criteria were notably related to the level of consciousness. First, UWS and MCS participants differed in spontaneous saliva management because more UWS participants still had a tracheostomy at the time of the evaluation than MCS participants. None of the participants were respirator-dependent. The need for the tracheostomy in about one third of the participants can probably be explained by insufficient saliva swallowing reflexes and ineffective pharyngeal phase of swallowing. Also, we observed more pharyngo-laryngeal secretions and saliva aspiration in UWS than MCS participants although not significantly after controlling for time since injury and etiology. These findings suggest that the level of consciousness may affect the ability to correctly manage saliva.

Second, both UWS and MCS participants showed a partial oral phase of swallowing (e.g., tongue and masticatory-like movements). However, no UWS participants and only a small number of MCS participants showed an effective oral phase of swallowing (lip prehension, lingual propulsion and no post-swallowing oral stasis). From this result and as already suggested in our previous study (Mélotte et al., 2018, **Chapter 2**), an effective oral phase should be considered a sign of consciousness and thus should be taken into account in DOC diagnosis. The oral phase of swallowing is usually described as the voluntary (conscious) part of swallowing, controlled by multiple cortical regions such as the primary sensori-motor cortex, supplementary motor area, premotor cortex (also called "cortical masticatory area"), thalamus, cingulate, putamen and insulo-opercular cortex that interact with regions in the brainstem (Avivi-Arber et al., 2011; Sessle et al., 2005; Shaker, 2013). Some authors showed that masticatory-like movements and rhythmic tongue activity can be produced by the recruitment of the brainstem alone (Dellow & Lund, 1971; Yamada et al., 2005). However, although the brainstem controls basic activity patterns of the cranial motoneuron groups involved in the oral phase of swallowing (hypoglossal, trigeminal, facial, vagal), descending inputs from the central nervous system also play an important role. Indeed, for some authors (Yamada et al., 2005), the activity pattern of each motoneuron is modulated by higher brain and peripheral inputs. This cortical and peripheral recruitment allows that the final motor outputs fit the environmental demand. If the components of the oral phase of swallowing (e.g., mastication) were based on only a central pattern generator in the brainstem, it would be stereotyped (Moore et al., 2014). Thus, the presence of an effective oral phase of swallowing seems highly dependent on cortical recruitment, which would explain why UWS individuals who show severe alterations of supratentorial cerebral metabolism do not present an effective oral phase of swallowing.

Finally, the presence of a cough reflex was a criterion more present in MCS than UWS participants. As shown in neuroimaging studies (Mazzone et al., 2011), the cough reflex is probably not a simple pontomedullary reflex arc. Indeed, in these previous studies, the cough reflex was facilitated by cortical activations (mainly the primary motor cortex, posterior insula, paracentral lobule, posterior mid-cingulate cortex, premotor cortex). Thus, the impact of the level of consciousness highlighted in the present study might probably be linked to the importance of the underlying cortical damage. Moreover, it is now generally accepted in stroke literature that the cortex plays an important role in the control of swallowing and that damages to swallowing motor areas and/or their connection to the brainstem usually result in dysphagia (Hamdy et al., 2001; Martin & Sessle, 1993).

Besides these main findings, hypertonia of the jaw muscles and the number of aspirations on cream/liquid texture did not differ between UWS and MCS groups. However, more MCS participants performed the functional test with thick and liquid texture than did UWS participants, which highlights that UWS participants seem to be generally considered more at risk of aspiration by the examiners or had more troubles in the oral phase (e.g., hypertonicity, absence of lip prehension or lingual propulsion) than MCS participants.

Our findings also agree with previous studies showing that objective swallowing assessment such as the FEES can be successfully completed in DOC individuals (Brady et al., 2006; Bremare et al., 2016; O'Neil-Pirozzi et al., 2003). The ENT examination gives precious information on 2 main points, first regarding tracheostomy and second regarding the possibility of oral feeding. After the FEES, the ENT specialist suggested removing the tracheostomy for several DOC participants (8 MCS participants and 6 UWS participants) because of good saliva management and the absence of stenosis or laryngeal paralysis. In these cases, the tracheostomy was probably maintained to prevent any respiratory complications because of the lack of adequate information regarding the management of the tracheostomy or because no one tested the possibility to begin a tracheostomy weaning. A previous study reported that individuals with a tracheostomy are more likely to develop pneumonia than patients without a tracheostomy (Matthews & Coyle, 2010). This should be kept in mind when making decisions on the need to maintain a tracheostomy in this fragile population. In this regard, the FEES can help in deciding on possible decannulation, but given the complexities of saliva management in the DOC population, the decision for tracheostomy weaning should be discussed in a multidisciplinary team. Besides tracheotomy management, the ENT examination is crucial for patients in whom we would like to start or continue oral feeding. Indeed, with the high proportion of patients with absence of cough reflex (about 54% in the whole sample), there is a high risk of silent aspiration. In this study, the ENT examination also advised starting partial oral feeding in 3 more UWS participants and 13 MCS participants and to stop full or partial oral feeding in 3 MCS participants. A functional swallowing test can be difficult to implement in individuals with severe trismus or total absence of an oral phase of swallowing, but as long as partial oral phase is present (e.g., partial lip prehension and lingual propulsion), thick or liquid swallowing can be tested by a qualified clinician.

Regarding the severity of dysphagia in DOC individuals, specific care such as nursing, chest physiotherapy, and speech therapy are recommended (Roberts & Greenwood, 2019). Management of swallowing should be integrated into a global approach taking into account respiration, mobility and tonicity of the face and considering emotional reactions, spasticity, and potential hypersensitivity. Clinically, we noticed that therapeutic feeding (i.e., swallowing small amounts of tasty easy-to-swallow food) can sometimes help clear excess saliva secretions in the pharyngo-laryngeal area. In addition, taste stimulation (involving only a very small amount of food or liquid that is delivered via a cotton swab in particular zones of the oral cavity) is also a good option for individuals who are at risk of aspiration. Nevertheless, the decision to introduce oral food or liquid in DOC individuals as therapeutic feeding or as a real part of the feeding should only be made after the completion of an objective swallowing evaluation (Brady et al., 2006).

There are several limitations of the study related to its retrospective, observational and single-centre design, which suggests that our data are moderately representative of the general DOC population. The presence of missing data for one criterion (cough reflex) should be acknowledged. We were also limited in the number of available criteria that could be studied. A prospective analysis, given a prescribed test protocol for DOC individuals with more detailed criteria, may yield additional information that were not covered in the current study, such as the duration of the oral phase before the swallowing reflex, the frequency of spontaneous saliva swallowing reflex (Crary et al., 2013) or the importance of secretions post-swallowing with a valid protocol such as the New Zealand secretion scale (Miles et al., 2018). Future longitudinal studies should also investigate the recovery of dysphagia along with consciousness recovery within the same individuals.

In conclusion, this study provides promising results linking swallowing and consciousness, notably regarding the ability of (minimally) “conscious” individuals to better manage spontaneous swallowing of saliva (reflected here by the presence or absence of tracheostomy), the cough reflex and the efficiency of the oral phase of swallowing. We should continue our efforts in the assessment of the orofacial area in DOC individuals to be able to propose appropriate and sensible care management.

Conflict of interest. None declared.

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CHAPTER 04

THE DEVELOPMENT AND VALIDATION OF THE SWADOC: A STUDY PROTOCOL FOR A MULTICENTER PROSPECTIVE COHORT STUDY

Submitted

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ABSTRACT

Background: After a coma, patients with severe brain injury may present disorders of consciousness (DOC). A substantial proportion of these patients also suffer from severe dysphagia. Assessment of and therapy for swallowing disabilities of patients with DOC are essential because dysphagia has major functional consequences and comorbidities. Dysphagia evaluation in patients with DOC is impeded by the lack of adapted tools. The first aim of this study was to create a new tool, the SWallowing Assessment in Disorders Of Consciousness (SWADOC), and propose a validation protocol. The SWADOC was developed to help therapists assess factors related to swallowing in patients with DOC. The second aim was to investigate the relationship between patients' level of consciousness and SWADOC items and scores.

Method/design: In this multicenter prospective cohort, 104 patients with DOC will be tested three times over five consecutive days with the SWADOC. Statistical analyses will focus on the reliability and validity of the SWADOC, especially the intra- and interrater reliability, internal consistency, measures of dispersion and concurrent validity with the Facial Oral Tract Therapy Swallowing Assessment of Saliva (FOTT-SAS). The level of consciousness will be assessed with the Simplified Evaluation of CONsciousness Disorders (SECONDs) and the Coma Recovery Scale-Revised (CRS-R).

Discussion: The assessment of swallowing abilities among patients with DOC is the first necessary step toward the development of a customized dysphagia care plan. A validated scoring tool will be essential for clinicians to better assess dysphagia in patients with DOC and document the evolution of their disorders.

Trial Registration: NCT04706689

1 Introduction

After a coma, some patients with severe brain injury will develop an altered state of consciousness before recovering partial or complete consciousness. Disorders of consciousness (DOC) consist of three states ranging from no awareness and no arousal to the preservation of arousal with fluctuating awareness (Gosseries et al., 2014): coma (Posner et al., 2007), vegetative state/unresponsive wakefulness syndrome (UWS) (Jennett & Plum, 1972; Laureys et al., 2010) and minimally conscious state (MCS) (Giacino et al., 2002). Patients with UWS typically exhibit only oromotor reflexes, blinks and startle responses, as well as withdrawal from noxious stimuli (Laureys et al., 2010). These patients do not respond to command and do not show visual pursuit or fixation. Individuals with MCS show reproducible but inconsistent signs of consciousness, such as following commands, visual pursuit or fixation, and localization of noxious stimuli (Giacino et al., 2002). MCS has been subcategorized into MCS PLUS (MCS+) and MINUS (MCS–) based on the complexity of the observed responses: MCS+ describes high-level behavioral responses (i.e., following commands, intelligible verbalizations, intentional communication using a gestural or verbal yes/no code) and MCS– describes low-level behavioral responses (i.e., automatic motor behaviors, object manipulation, localizing objects in space, localizing noxious stimuli, visual pursuit or fixation) (Bruno et al., 2011; Thibaut et al., 2020). When patients recover the ability to functionally communicate or to use objects appropriately, we consider that they have emerged from MCS (EMCS) (Giacino et al., 2002). The currently recommended scale for behavioral assessment of consciousness is the Coma Recovery Scale – Revised (CRS-R) (Giacino et al., 2004) as it fulfills all the Aspen Neurobehavioral Workgroup criteria (Seel et al., 2010). The CRS-R has an oromotor subscale that includes the assessment of basic oromotor reflexes and vocalizations or verbalizations, but no swallowing components are integrated in this scale. Recently, the Simplified Evaluation of CONsciousness Disorders (SECONDs) scale (Aubinet et al., 2020; Sanz et al., 2020) was developed based on the most prevalent signs of consciousness observed using the CRS-R (Wannez et al., 2018). This tool is quick and easy to administer (Sanz et al., 2020).

Almost all patients with DOC have severe dysphagia (Mélotte et al., 2020, **Chapter 3**) requiring the use of ventilation and nutritional support (i.e., tracheostomy, gastrostomy) to limit the occurrence of comorbidities (e.g., bronchopulmonary infection, undernutrition). Individuals with DOC classically receive hydration and nutrition through an enteral feeding tube (Whyte et al., 1999) and a large majority will not be able to return to exclusively oral feeding (Mélotte et al., 2020, **Chapter 3**). An objective swallowing assessment using fiber-optic endoscopic or videofluoroscopic swallowing evaluations is required in patients with DOC, for whom the possibility of partial or total oral feeding is being considered. These examinations, performed by experienced clinicians, constitute the gold standard tool for assessing dysphagia in this population. Indeed, these examinations allow clinicians to precisely analyze the mechanisms at play during swallowing and to detect possible silent aspirations, which are very prevalent in patients with DOC (Mélotte et al., 2020, **Chapter 3**). As Mélotte et al. (2020) showed in a cohort of 92 patients, the risk of silent aspiration is high for these patients, as 52% of patients with DOC do not have a cough reflex. Moreover, 28% presented saliva aspiration, 13% aspiration with thick texture and 32% aspiration with liquid texture. A lack of knowledge of the specific features of DOC prevents some clinicians from performing these exams. Moreover, performing a functional swallowing test (liquid and food test) can be difficult in patients with severe trismus (lockjaw) or total absence of the oral phase of swallowing, but as long as a partial oral phase with initiation of swallowing exists, thick or liquid swallowing can be tested (Brady et al., 2006; Bremare et al., 2016; Mélotte et al., 2020, **Chapter 3**; O'Neil-Pirozzi et al., 2003).

In daily practice, speech therapists help to document the presence or absence of a range of components required for swallowing in order to guide therapy and monitor its effectiveness by repeated assessment over time. The clinical reality of patients with DOC, mainly the lack of response to simple motor commands (in UWS and MCS–) and functional communication, makes it difficult to fully understand and appropriately treat their swallowing disorders. For these reasons, classical swallowing assessment at the bedside can be unsuitable for this population. There is a lack of appropriate bedside tools to appraise and monitor swallowing disorders in patients with DOC. The impossibility of orienting interventions based on determined quantitative and qualitative swallowing components makes it more difficult to develop a treatment plan and assess the patient's progress.

Our recent DOC cohort study (Mélotte et al., 2020, **Chapter 3**) found some links between swallowing and level of consciousness. In particular, none of the patients with UWS and only a minority of the patients with MCS exhibited an effective oral phase of swallowing (adequate lip prehension, tongue propulsion and no post-swallowing oral stasis). However, these links are not yet completely understood and further studies are necessary to increase our knowledge of which components of swallowing are linked to consciousness and to what extent. In this context, the validation of a tool that focuses on qualitative and quantitative swallowing components will help us to identify swallowing behaviors which may be considered as unequivocal signs of consciousness in patients with DOC. These results may eventually contribute to the development of new diagnostic guidelines for DOC that would include swallowing behaviors in their criteria.

The aim of this article is to present a protocol, which develops and validates the SWallowing Assessment in Disorders Of Consciousness

(SWADOC). This tool will be administered repeatedly to a population of patients with DOC by different examiners and intrinsic test characteristics will be calculated. The relationship between patients' level of consciousness and SWADOC scores will also be studied.

2 Method and analysis

2.1. Development of the SWADOC

2.1.1. Identification of domain(s) and item generation

The SWADOC was developed to overcome the lack of a suitable tool that would allow clinicians to assess and measure swallowing-related components in patients with DOC. It explores some of the oral and pharyngeal components of swallowing as well as a range of prerequisites and related components of swallowing. Our first aim was to develop a rapid, reliable quantitative tool. However, although quantitative items present advantages, many qualitative elements are also meaningful in fully understanding a patient's profile. Thus, we decided to include both quantitative and qualitative items.

This tool was developed by three speech therapists and then submitted to ten experts (otorhinolaryngologists and speech therapists) who work with patients with DOC for evaluation. Their comments contributed to the final version. The development period lasted approximately 10 months.

The tool was developed based on both deductive and inductive methods (Boateng et al., 2018). First, we examined literature in the field of consciousness and swallowing and looked for existing scales (deductive method). The construction of the tool was inspired by current knowledge of dysphagia in patients with DOC based on the few studies dedicated to swallowing in this population (Bremare et al., 2016; Mélotte et al., 2018, 2020; Wang et al., 2019). The SWADOC was based upon several existing tools: the Facial Oral Tract Therapy (FOTT) (Bicego et al., 2014; Hansen & Jakobsen, 2010), the SECONDs (Aubinet et al., 2020; Sanz et al., 2020), the New Zealand Secretions Scale (NZSS) (Miles & Hunting, 2019), the Oral/Facial Sensitivity subtest of the Comprehensive Assessment Measure for Minimally Responsive Individuals (CAMMRI) (Gollega et al., 2015), the stimulation method for sensory processing disorder (sensory dysorality) proposed by Senez (2015), and the arousal protocol of the CRS-R (Giacino et al., 2004). It includes some medical history information from the Food Intake LEVEL Scale (FILS) (Kunieda et al., 2013) and the IDDSI (International Dysphagia Diet Standardisation Initiative) (Cichero et al., 2017).

The SWADOC was inspired by the FOTT (Hansen & Jakobsen, 2010), as adapted for patients with DOC in French by Bicego et al. (2014), and modified based on our day-to-day clinical experience with patients with DOC. The items assessing command following are based on the SECONDs principles (Aubinet et al., 2020; Sanz et al., 2020), insofar as response to verbal command is considered intact if the patient passes a minimum of two out of three trials. The item on quantitative saliva secretions is based on the NZSS (Miles & Hunting, 2019), which assesses secretion severity during endoscopy by location, amount (as a percentage) and response. We used the percentages proposed in that scale and adapted them to the oral cavity. Since the oral area is larger than the laryngeal area, the percentages are more difficult to evaluate, but to our knowledge there is no validated scale for the evaluation of accumulated secretions in the mouth. Tactile stimulation is inspired by Senez's stimulation method for sensory processing disorder (2015). Finally, the SWADOC requires the examiner to perform an arousal protocol similar to the CRS-R (Giacino et al., 2004) if the patient falls asleep during the procedure. The medical history taking subsection also features the IDDSI (International Dysphagia Diet Standardisation Initiative) (Cichero et al., 2017) score and the Food Intake LEVEL Scale (FILS) (Kunieda et al., 2013) score.

We then applied the tool in routine clinical practice with patients with different levels of consciousness and adjusted some items as a result (inductive method).

2.1.2. Content validity

Ten experts were asked to judge the SWADOC overall and per item with a Likert scale, to solicit their opinion of its relevance in their clinical practice, its suitability for patients with DOC, and the clarity of the administration guidelines. The experts' responses focused on the clarity of certain instructions and suggested that some qualitative items be added and some quantitative items modified (levels that were too subjective or dependent on hospital functioning and not on patients themselves). These suggestions were analyzed and taken into account to improve the

SWADOC by clarifying instructions, adding qualitative items and modifying quantitative items.

2.2. Presentation of the tool

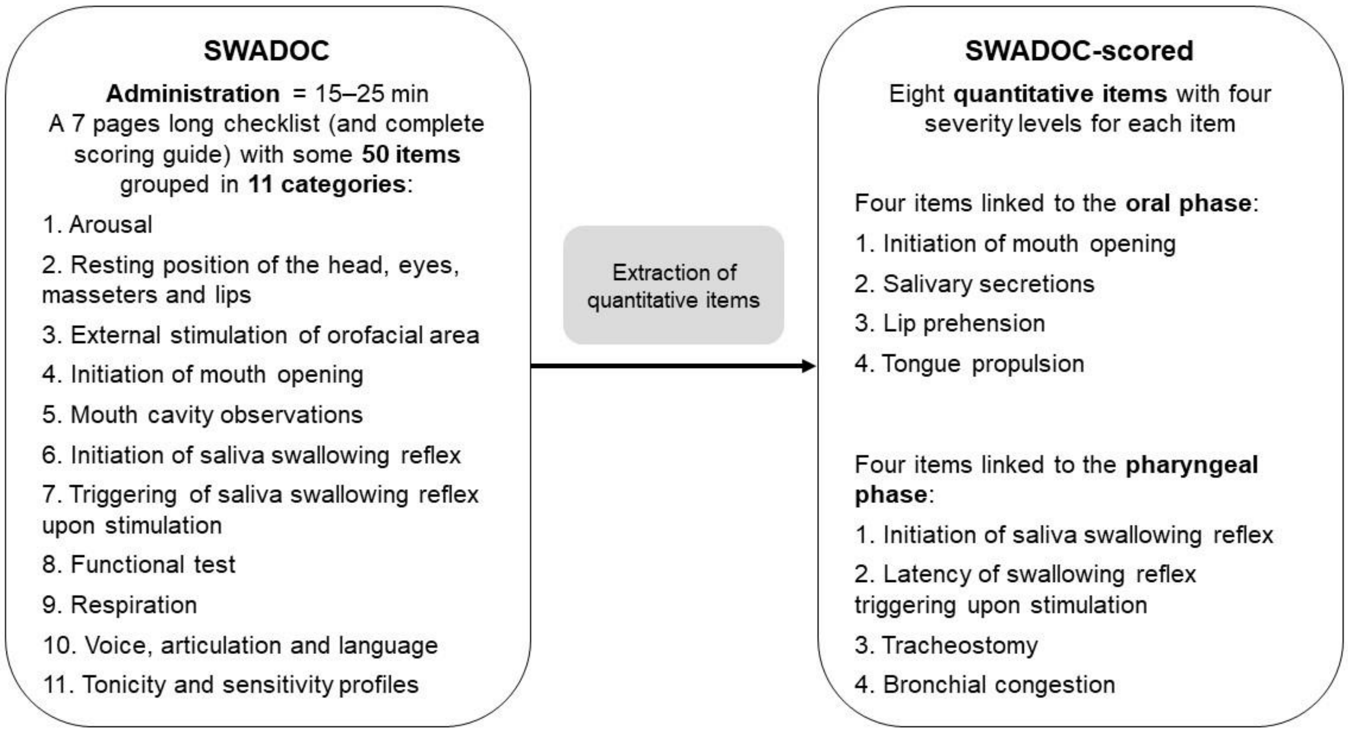
The tool is composed of some 50 qualitative items and a subsection called the “SWADOC-scored” comprising 8 quantitative items. The instruction guide comprises (1) one page with general recommendations; (2) a list of required materials; (3) explanations of the quantitative items; (4) a detailed medical history; (5) the SWADOC-scored grid; and (6) a checklist and 7 pages of instructions covering all the quantitative and qualitative items (see **figure 9** and **Appendix 4.1 & 4.2**). The tool was translated into English for the convenience of readers of this paper. However, if an English validation is carried out, a back-translation method will be applied.

The “SWADOC-scored” subsection includes 8 quantitative items (see **figure 10 and Appendix 4.3**). Four items are linked to the oral phase and four to the pharyngeal phase. For each quantitative item, patient’s abilities are rated on a four-level scale ranging from 0 to 3. These levels correspond to item scores that can be added together to calculate three performance scores: the oral phase subscore (sum of the 4 oral item scores), the pharyngeal phase subscore (sum of the 4 pharyngeal item scores) and the total swallowing score (sum of the 8 item scores).

The administration procedure for the test and the sequencing of items were designed to put patients in optimal conditions for the exam. For example, the therapist first introduces himself/herself, describes the assessment procedure and then begins with external facial stimulation before doing the mouth cavity stimulation. The therapist assesses the patient at the bedside or in their usual chair and only if the patient is awake and shows no signs of pain or medical problem (e.g., fever, hypoxemia, arrhythmia). In addition, during the assessment, some parameters for stopping are provided to avoid presenting stimulations that are inappropriate for the patient’s abilities (e.g., swallowing a minimal amount of thickened liquid). All these recommendations are described in the administration guide.

The objectives of the SWADOC are to address all the goals of an assessment tool: (1) document the prerequisites for swallowing; (2) determine the active ingredients of the therapy; (3) track changes in a patient’s swallowing abilities; and (4) monitor the effectiveness of a therapy. In a scientific research context, the SWADOC will help us to better understand the links between level of consciousness and swallowing components.

Figure 9. Description of the SWADOC



Note: ENT=Ear, Nose and Throat

Figure 10. SWADOC-scored (English version)

	Items	Level 0	Level 1	Level 2	Level 3
Oral phase	**1. Initiation of mouth opening**	□ Mouth opening impossible or only with the therapist's active assistance	□ Mouth opening upon lip stimulation	□ Mouth opening upon presentation of spoon	□ Mouth opening upon command (min 2/3)
	2. Endo-buccal secretions	□ Substantial amount of secretions (80%–100%)	□ Moderate amount of secretions (20%–80%)	□ Few secretions (0%–20%)	□ Moist mouth but without significant secretions
	3. Lip prehension	□ No lip prehension (no reaction or tightening of lips)	□ Incomplete lip prehension spontaneously or upon verbal stimulation	□ Appropriate lip prehension but not consistently or only upon verbal stimulation	□ Consistently correct, spontaneous lip prehension
	4. Tongue propulsion	□ No tongue movement: passive movement of the bolus to the pharyngeal level, stagnation in mouth or expulsion when drooling	□ A few tongue movements but not sufficient to propel the bolus	□ Pathological tongue propulsion, possibly with post-swallowing stasis	□ Appropriate tongue propulsion
Pharyngeal phase	**1. Initiation of saliva swallowing reflex**	□ No saliva swallowing spontaneously or upon stimulation	□ Saliva swallowing only upon stimulation	□ Saliva swallowing spontaneously and upon stimulation	□ Saliva swallowing upon command (min 2/3)
	2. Latency of swallowing reflex triggering upon stimulation	□ No triggering or cannot be completed	□ > 10 seconds	□ 5 to 10 seconds	□ 0 to 5 seconds
	3. Tracheostomy	□ Tracheostomy with inflated cuff	□ Tracheostomy with cuff, ongoing deflation	□ Tracheostomy without cuff or with permanently deflated cuff	□ Tracheostomy with ongoing weaning, or no tracheostomy
	4. Bronchial congestion	□ Frequent bronchopneumonia or heavy congestion	□ Moderate congestion	□ Little congestion	□ No congestion
SWADOC-scored – oral phase: /12		**SWADOC-scored – pharyngeal phase: /12**		**SWADOC-scored – total: /24**	

Note: DOC=disorders of consciousness

2.3 Study design

This project is a multicenter prospective cohort study that will take place in several hospitals and clinics in Belgium and France. The SWADOC was created in French.

2.4 Population and recruitment

This study will be carried out in patients with DOC or emerging from DOC following severe acquired brain injury. Patients will be divided into four groups according to their clinical diagnosis, as assessed with the SECONDs and the CRS-R: UWS, MCS–, MCS+ and EMCS. Participants will be recruited from inpatient neurological rehabilitation programs in post-coma units and rehabilitation services, or among patients hospitalized for a multimodal assessment of consciousness for diagnostic and prognostic purposes.

Only patients who meet all of the following inclusion criteria will be considered for enrolment: (1) age above 18 years; (2) perfect knowledge of French language before the injury; (3) previous coma phase caused by a severe acquired brain injury; (4) medical stability (no mechanical ventilation or sedation, no acute medical pathology such as infection or respiratory distress); (5) no neurological or otorhinolaryngological disease that can impact swallowing prior to the brain injury; (6) minimum of 28 days since the acquired brain injury at inclusion (Giacino et al., 2018a, 2018b); (7) diagnosis of UWS, MCS–, MCS+ or EMCS based on the SECONDs and the CRS-R; (8) informed consent from the patient's legal representative; and (9) affiliated patient or beneficiary of a health insurance plan (for participants in France only).

2.5 Validation study procedure

Each patient enrolled in the validation study will have their level of consciousness assessed at baseline with a single administration of the CRS-R. Next, the level of consciousness and swallowing abilities will be assessed with three tools during three separate sessions (only one administration of the FOTT-SAS) in the morning or the afternoon in order to assess the tool's intra- and interrater reliability. The baseline assessment and sessions will be spread over five consecutive days.

1. **CRS-R**: This is a standardized neurobehavioral assessment of consciousness composed of six subscales (auditory, visual, motor, oromotor/verbal, communication and arousal), which assess different functions with various numbers of hierarchically arranged items that distinguish UWS, MCS and EMCS patients. The total score is composed of the sum of the maximum scores obtained in each subscale.

2. **SECONDs:** It is shorter to administer (median of 7 minutes) and requires only a mirror as material. It consists of 8 items: observation and reporting spontaneous of behaviors, response to command, communication, visual pursuit and fixation, pain localization, oriented behaviors and arousal. We have chosen this consciousness tool during sessions rather than the CRS-R because of its short duration so that the SWADOC can be administered immediately before or after, given that attentional abilities are often reduced in patients with DOC. The SECONDs provides a total score directly reflecting one diagnosis (0 = coma, 1 = UWS, 2–5 = MCS–, 6–7 = MCS+, 8 = EMCS).

3. **SWADOC:** This tool includes a battery of about 50 quantitative and qualitative items. Quantitative items are grouped in the SWADOC-scored, with oral and pharyngeal subscores and a total score. Running the whole SWADOC lasts between 15 and 25 minutes based on preliminary tests.

4. **FOTT-SAS:** The results of the SWADOC-scored in one session will be compared to the FOTT Swallowing Assessment of Saliva (FOTT-SAS) (Mortensen et al., 2016). The test comprises 7 questions; if items 1 to 4 are answered "Yes" and items 5 to 7 are answered "No," oral intake should be initiated (see **Appendix 4.4**). The FOTT-SAS includes items that can be scored based on the administration of the SWADOC. In that respect, no additional administration will be required.

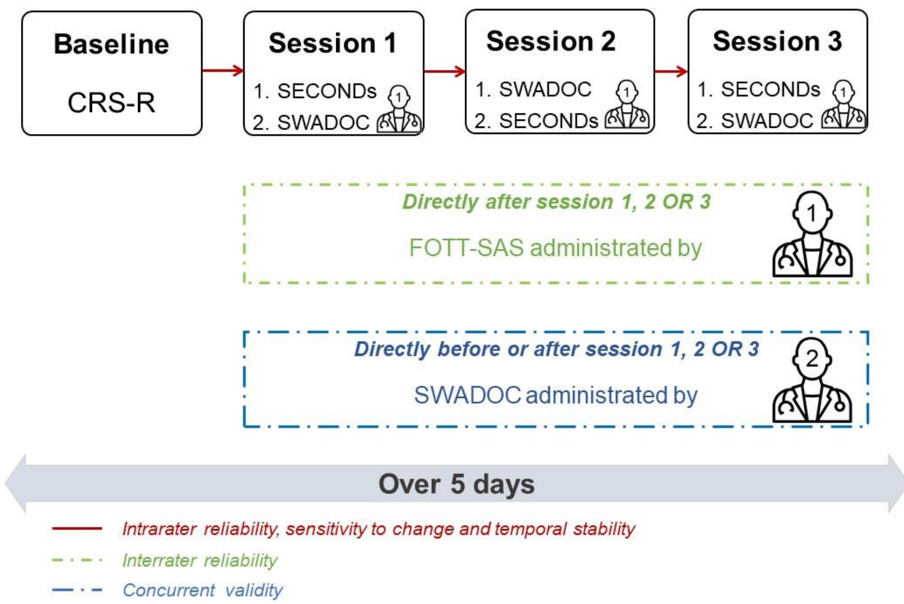
The clinical protocol procedure is illustrated in **Figure 11**.

Because of clinical realities, no attempt will be made beforehand to standardize the order (SECONDs before or after SWADOC and examiner 2 before or after examiner 1) or time of day (morning or afternoon) of evaluations. However, during data collection, efforts will progressively be made to balance the order and time of day and the time of evaluation of examiner 2 (before or after examiner 1).

The administration of the SWADOC at each session will allow us to assess the tool's intrarater reliability (temporal stability). Directly before or after one of the three sessions, a second examiner will administer the SWADOC a second time to test its interrater reliability. The second assessment will be blinded to the results of the first. To be able to take into account potential mismatches between the ratings of the two examiners, each scoring protocol will be analyzed directly after the inter-rater session and a discussion will follow to try to understand the reasons for any discrepancies. This information will be noted in the protocol. After the recruitment procedure and depending on the degree of agreement based on the statistical analysis, modifications of the instructions and/or items will be considered based on the qualitative information collected from the examiners.

Sensitivity to change will determine whether changes in the level of consciousness (variations in SECONDs scores) result in changes in the SWADOC-scored across the three assessments of the same patient. Repeating the SECONDs assessment will also allow for a reliable assessment of the patient's level of consciousness (UWS, MCS–, MCS+ or EMCS) and decrease the risk of misdiagnosis (Wannez et al., 2017).

Figure 11. Study protocol



Note: Example of the assessment program for a patient. The program for each patient is organized such that the three sessions take place over two days. The first two sessions will be administered on day 1 (morning or afternoon) or on two different days (session 1 on day 1 in the morning or afternoon and session 2 on day 2 in the morning), and session 3 always on day 2 (morning or afternoon depending on session 2). The SECONDs is administered before or after the SWADOC. Examiner 2 will administer the SWADOC before or after examiner 1 in one of the three sessions. Examiner 1 will score the FOTT-SAS after one of the three sessions. SECONDs = Simplified Evaluation of CONsciousness Disorders; SWADOC = Swallowing in Disorders Of Consciousness; FOTT-SAS = Facial Oral Tract Therapy Swallowing Assessment of Saliva.

2.6 Study hypotheses

Our main hypothesis is that the SWADOC is reliable and valid.

Our second hypothesis is that the subscores (oral phase and pharyngeal phase) and the total score are related to the patient's level of consciousness. Moreover, based on previous studies (Mélotte et al., 2018, **Chapter 2**; Mélotte et al., 2020, **Chapter 3**), we expect that UWS patients will be at level 0 for oral phase items 1, 3, and 4 of the SWADOC-scored: no mouth opening at spoon approach, no spontaneous lip prehension and no appropriate tongue propulsion.

2.7 Data analysis

The statistical significance will be set at $p < 0.05$.

2.7.1 Power of the study

The sample size was calculated using a power calculation (G ∗ Power, Universities of Kiel, Mannheim and Düsseldorf) in a one-way analysis of variance (ANOVA) with a significance level of 0.05 and a power of 0.8. Effect size is based on previous published data on swallowing performance in patients with DOC (Mélotte et al., 2020, **Chapter 3**). Cohen's *d* was used to estimate the effect size; the result was .659, corresponding to an eta-squared of .0979. We round up and base our calculation on an effect size of 0.1, corresponding to an intermediate effect. In this context, a total sample size of 104 participants (26 per group) is needed to demonstrate a difference in SWADOC subscores and total score between the four consciousness groups. If, by the end of June 2025, the sample size is not reached, we will discuss extending the data collection period if necessary.

2.7.2 Descriptive analysis

First, descriptive statistics will be performed to describe the entire group and each diagnostic group (UWS, MCS–, MCS+ and EMCS) for age, gender, etiology and time since insult. To test gender independence between groups, we will use chi-square tests. For the other variables, we will perform a one-way ANOVA with group as independent variable. Homogeneity of variance will be assessed using Levene's test. In case of violation, we will use Welch's approximation instead.

2.7.3 Reliability

The intrarater (i.e., SWADOC-scored vs. SWADOC-scored by the same examiner on the same day and on two different days) and interrater reliability (i.e., SWADOC-scored vs. SWADOC-scored on the same day by two different examiners) will be calculated in two separate analyses using weighted Fleiss's kappa coefficients (K_W). A value below 0 will be considered to indicate poor agreement, between 0 and 0.2 slight agreement, between 0.21 and 0.4 fair agreement, between 0.41 and 0.6 moderate agreement, between 0.61 and 0.8 substantial agreement, and between 0.81 and 1 almost perfect to perfect agreement (Landis & Koch, 1977). We will also determine the internal consistency of the SWADOC-scored with Cronbach and Spearman intercorrelations to determine the interrelatedness of the constituent items.

2.7.4 Validity

2.7.4.1 Concurrent validity

The results of the SWADOC-scored will be compared to the FOTT-SAS score for the same time and with the best score using Pearson's correlation (parametric test) or Kendall's correlations (nonparametric test) after examination of the data distributions.

2.7.4.2 Measures of dispersion

The distribution of total SWADOC-scored scores will be examined to determine whether performance on the scale is evenly distributed across the range of possible scores and each item will be analyzed to identify possible floor or ceiling effects. Based on these results, we will consider the need to modify the scale accordingly.

2.7.5 Relationship between swallowing components and levels of consciousness

The differences in SWADOC-scored items, oral and pharyngeal subscores for the SWADOC-scored and total score for the SWADOC-scored for the consciousness diagnostic groups will be assessed using a comparison of means with a one-way ANOVA. Violation of the homogeneity of variance will be checked using Levene's test. If this is the case, we will use Welch's approximation instead of an ANOVA. If there is a significant main effect, we will perform Tukey's HSD test to compare all pairwise differences. If there is a severe violation of the normality, we will perform a Kruskal-Wallis test with the Dwass-Steel-Critchlow-Fligner (DSCF) multiple comparison analysis. Partial eta-squared will be used as a measure of effect size. Post hoc multiple comparisons will be conducted to identify between where significant differences between consciousness groups exist. SWADOC scores will be the dependent variable while consciousness group will be the independent variable. Statistical analysis will be performed by a researcher blind to the consciousness category.

3 Discussion

It is challenging to assess swallowing in patients with DOC because of the clinical reality of this population. This protocol describes a clinical study that will seek to validate the SWADOC, a tool adapted for bedside swallowing assessments in patients with DOC. The link between patients' level of consciousness and SWADOC scores will also be studied. To achieve these goals, a multicenter prospective cohort study design will be adopted.

3.1 Strengths and opportunities

To our knowledge, this is the only published study protocol that seeks to validate a swallowing assessment tool for patients with DOC. To meet all the criteria for an optimal assessment tool (i.e., appraise patients' abilities, monitor their progress, measure the effect of a given therapy, allow comparison with other patients), the SWADOC is composed of both quantitative and qualitative items.

The quantitative items will help to measure any changes and treatment effects, while the qualitative items will help clinicians to provide a clear and accurate summary of the patient's strengths and weaknesses and thus orient their therapy in the best possible way. Depending on the treatment plan, the dysphagia therapy may be oriented more toward active stimulation to improve salivary control and efficiency of the oral and pharyngeal phases or toward maximizing the patient's comfort.

In a second phase, it would be interesting to compare the results of the SWADOC with an objective assessment (fiber-optic endoscopic evaluation of swallowing or videofluoroscopic swallowing study) to determine its predictive validity and investigate its construct validity. However, the SWADOC is not intended to be the only tool used to determine the possibility of reintroducing oral nutrition for the patient: we acknowledge the need to objectively evaluate patients with DOC before reintroducing oral feeding, as the risk of inhalations and silent aspirations is very high. The SWADOC will complement the therapeutic framework for dysphagia among patients with DOC in order to set up the active components of therapy (Ratner, 2006), measure the efficacy of the therapy, and orient therapists toward an objective examination when the patient's recovery seems to allow it.

3.2 Limitations and pitfalls

There are a number of limitations on this study, especially because of the clinical challenges of dealing with patients with DOC. The main limitation is the feasibility of having each patient undergo a baseline administration of the CRS-R and three assessments. This group's arousal fluctuates considerably as they are highly sensitive to stress and fatigue, and often subject to medical complications (e.g., vomiting, pain, respiratory infections, etc.) that may limit their availability to participate in the study. To take into account this pitfall of the application of the methodology to patients with DOC, we chose to extend the evaluation period to five days rather than two days as initially planned.

Although we have developed the most accurate levels possible for each item, and a complete scoring guide, the SWADOC is based on subjective observations of swallowing components. The interrater reliability will help us to determine the consistency of the rating system between examiners. Depending on these results, the scale may be adapted.

Furthermore, the decision to assess the level of consciousness using the SECONDs may seem questionable because this scale is recent, but it is derived from the CRS-R, which is known to be the gold standard scale for behavioral assessment of consciousness. Nevertheless, the SECONDs is much quicker to administer and includes the five CRS-R items that detect 99% of MCS patients (Wannez, 2018). Moreover, this scale has good intra- and inter-rater reliability (kappas ranging from 0.85 to 0.91 and 0.82 to 0.85, respectively). However, we considered adding one administration of the CRS-R at baseline before the three sessions because the CRS-R gives more details and precision on the patient's overall state, including reflexes.

4 Ethics and dissemination

Information documents and explanations of the study will be given to the patients' legal representatives, to provide them with all the necessary information to make an informed decision about participation to the study. Written informed consent, including the name and contact information of the investigators in charge of the study, will be obtained from all patients' legal representatives prior to participation. The information form will also contain a paragraph indicating that the investigators in charge of the study have insurance that will cover accidental damages. The legal representatives will be informed that they can choose not to participate in the study without any consequences for the patients' quality of care, and may, at any time and without giving a reason, withdraw from the study. All information collected during this study will be kept confidential. The data will be pseudo-anonymized and listed under an ID code accessible only to the researchers in charge of the study and protected by a firewall. The principal investigators of the study (EM, MB, OG) are responsible for these data. Data management will comply with the General Data Protection Regulation (EU 2016/679) including the fact that data will be used during scientific presentations and publications without mentioning the participants' identity.

This research protocol was reviewed and approved by the two central ethics committees (Ethics Committee of the Faculty of Medicine of the University Hospital of Liège (2020-79) and Ethics Committee of Île de France XI (20.05.26.70621), as well as by the Ethics Committees of the participating hospitals and clinics.

5 Authors' contribution

E.M., M.B., and R.H. developed the SWADOC. E.M., M.B., R.H. and O.G. contributed to conception and design of the study. E.M., M.B., R.H. and O.G. drafted the manuscript. J.S., J.-F.K., A.L., D.M., L.R.D.S., S.L., and F.P. made major revisions of significant portions of the manuscript. F.P. and O.G. contributed equally.

6 List of nonstandard abbreviations

CAMMRI = Comprehensive Assessment Measure for Minimally Responsive Individuals
CRS-R = Coma Recovery Scale -– Revised
DOC = Disorders Of Consciousness

EMCS = Emergence from the Minimally Conscious State
FILS = Food Intake LEVEL Scale
FOTT = Facial Oral Tract Therapy
FOTT-SAS = FOTT Swallowing Assessment of Saliva
IDDSI = International Dysphagia Diet Standardisation Initiative
MCS = Minimally Conscious State
NZSS = New Zealand Secretions Scale (NZSS)
SECONDs = Simplified Evaluation of CONsciousness Disorders
SWADOC = SWallowing Assessment in Disorders Of Consciousness
UWS = Unresponsive Wakefulness Syndrome

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GENERAL DISCUSSION AND PROSPECTS

The study of swallowing reveals that the most commonplace phenomenon can be more complex than it appears at first sight. The transition of a bolus of saliva or food from the mouth to the stomach requires the sequencing of a range of mechanisms that usually take place beyond our awareness. We might think that swallowing occurs only when we are awake and conscious but the reality is more complicated.

Consciousness is classically defined as awareness of the self and the environment (Laureys, 2005). This conception leads us to define **three entities on a continuum ranging from no awareness** (UWS) to **partial preservation of conscious awareness** (MCS) **and the emergence of functionally useful behaviors** (EMCS). In UWS, the patient is awake but unaware of the self or the environment, while patients with MCS are awake and show some reproducible but inconsistent awareness of themselves and their surroundings (Giacino et al., 2002). An expert group of researchers and clinicians working with patients with DOC defined specific behavioral criteria of consciousness that led to the current standard behavioral assessment of consciousness: the CRS-R. In the case of MCS, we talk about "minimally conscious" because of the manifestation of **partial preservation of conscious awareness** (minimally conscious MINUS (MCS–) or PLUS (MCS+) based on the presence (MCS+) or absence (MCS–) of behaviors indicating at least partial preservation of language abilities). Patients with MCS show heterogeneous manifestations of consciousness. Indeed, motor disease, aphasia and sensory disturbances lead to a wide range of clinical pictures. The upper boundary of the continuum defining the emergence from MCS was arbitrarily defined based on the presence of **functionally useful behaviors** (i.e., functional interactive communication and/or functional use of two different objects).

In addition to the signs of consciousness presented in the CRS-R, **other serious proposals of clinical manifestations of consciousness have recently emerged,** such as the learning test procedure (Lancioni et al., 2014), olfactory sniffing signals (Arzi et al., 2020) and habituation to the auditory startle reflex (Hermann et al., 2020).

By definition, behavioral signs of consciousness are criteria that are present in patients with MCS or EMCS (but not in those with UWS; Giacino et al., 2002) or in patients behaviorally classified as having UWS but who show MCS-like patterns of brain activity (MCS*) (Coleman et al., 2009;

Gosseries et al., 2016). Naccache (2018) drew our attention to the fact that all the CRS-R items defining MCS/EMCS refer to cortically mediated behaviors, whereas all the items defining UWS refer to subcortically mediated behaviors. However, **we cannot reduce "conscious behavior" to all types of cognitive processes that require cortical networks** because many types of unconscious cognitive operations have been associated with the activity of various cortical networks (Naccache, 2018). Moreover, the patterns of brain activity in patients with UWS are not strictly reduced to the subcortical or brainstem nervous system (Laureys, 2005; Schiff et al., 2002). For that reason, future studies should continue to identify brain markers enabling the detection of a conscious state. Moreover, the combination of behavioral and brain-imaging techniques is essential to decrease the risk of misdiagnosis.

Hitherto, the diagnostic criteria of consciousness have not included components related to swallowing[3]. Moreover, the pathophysiology of swallowing of patients with DOC is not well described in the literature.

The aim of this thesis was to contribute to the study of the links between consciousness and swallowing. Our hypotheses were that there is a relationship between swallowing capacities and level of consciousness, and that specific components of swallowing constitute possible signs of consciousness.

What did our studies tell us about that?

In **Chapter 1**, to provide a theoretical introduction, we presented our literature review on the links between swallowing and consciousness (Mélotte et al., submitted). In that section, we identified several thematic areas that address the relationships between swallowing and consciousness.

We dissected the **different components of swallowing from the perspective of volition**.

[3] The CRS-R propose a mouth-opening test for patients in the motor function scale ("automatic motor response" item) if the patient does not show episodes of automatic motor behaviors. However, this item is applied only if the examiner judges that the patient presents some inability to move their limbs and is not able to perform a wave sign. Moreover, the item tests the ability to inhibit the automatic motor behavior of opening the mouth when a spoon is presented because we ask the patient not to move at all.

As we described in the introduction, identifying signs of consciousness is essential regarding functional and survival prognosis (Giacino & Kalmar, 1997; Luaute et al., 2010; Noé et al., 2012), pain management (Demertzi et al., 2009) and end-of-life decisions (Demertzi et al., 2011). The identification of behavioral signs of consciousness is historically based on the principle of differentiating reflexive from volitional behaviors, with the idea that unconscious patients show only purely reflexive behaviors while conscious patients show volitional behaviors (Giacino et al., 2002). However, some ambiguity still exists between conscious and reflexive behaviors (Fischer & Truog, 2015). In fact, there are no empirical characteristics that allow one to reliably distinguish reflexive behaviors from conscious behaviors (Fischer & Truog, 2015).

Based on the characteristics of swallowing components in each phase of swallowing, we tried to distinguish voluntary from reflexive components of swallowing. Our classification is based on the characteristics of voluntary behavior and somatic and autonomic reflexes **(see Chapter 1, table 1)**. We postulated that the triggering of the swallowing reflex constitutes the borderline between voluntary and reflexive behaviors. Components that occur before the initiation of the swallowing reflex (oral phase components) can be considered as voluntary while components that happen afterward (pharyngeal and esophageal components) can be considered reflexive. The opening of the UES constitutes the border between somatic reflexes (pharyngeal phase) and autonomic reflexes (esophageal phase). In light of this information and based on the results of experimental studies, we will discuss the conscious or unconscious nature of each phase of swallowing.

In addition, we put this in the context of **volitional (VOST) versus non-volitional swallowing tasks (NVOST)** in neuroimaging studies. Many neuroimaging studies have explored cortical activation during swallowing in healthy subjects using voluntary tasks but very few have used spontaneous/reflex tasks; consequently, comparisons between VOST and NVOST tasks are unreliable. Some cortical areas activated during swallowing tasks are not specific to the swallowing function but are also activated during related motor tasks (e.g., lip pursing, mastication, tongue movement) (Birn et al., 1999; Kern et al., 2001; Komisaruk et al., 2002; Malandraki et al., 2009, 2010; Martin et al., 2004; Zald & Pardo, 1999). We showed that the sensorimotor network (primary sensorimotor cortex, premotor cortex and supplementary motor area), cerebellum, anterior part of the cingulate cortex and insula are involved in both VOST and NVOST swallowing tasks. These findings support the idea that swallowing is a cortically mediated behavior.

Moreover, VOST seem to activate some brain areas shared with consciousness networks, including the posterior cingulate cortex, inferior parietal lobule, precuneus and superior frontal gyrus.

We analyzed **studies describing a link between the level of consciousness of patients with brain injuries and swallowing-related abilities**. In severe brain-injured patients, the level of consciousness is associated with several components related to swallowing, such as the possibility of extubation, risk of pneumonia, type of feeding or components directly related to swallowing like oral or pharyngeal abnormalities. In contrast, our two retrospective studies are the only ones that have analyzed the pathophysiology of swallowing specifically in patients with DOC diagnosed further to repeated behavioral assessments and neuroimaging exams. Below, we present the main findings of these two studies.

Finally, we reviewed current knowledge of the assessment and treatment of dysphagia in patients with DOC. In day-to-day practice, clinicians need to appraise and measure swallowing-related capacities in patients with DOC. However, the majority of existing tools are not adapted to these patients. Indeed, they require active participation by the patient or involve a functional test with a significant amount of liquid or solid food, exposing the patient to a high risk of aspiration. To address this problem, we developed a new tool – the SWADOC – and proposed a validation study.

Moreover, an objective swallowing examination performed by an otorhinolaryngologist is feasible and relevant for patients with DOC regardless of their level of consciousness and whether it is done to discuss the utility of maintaining a tracheostomy, document the utility of botulinum toxin to improve saliva management, or assess the feasibility of therapeutic feeding (Brady et al., 2006; Bremare et al., 2016; Mélotte et al., 2020; O’Neil-Pirozzi et al., 2003).

There is an urgent need for clinical guidelines focusing on treatment of dysphagia in patients with DOC.

Chapter 2 presented our retrospective study of the possibility of oral feeding in patients without behavioral signs of consciousness (Mélotte et al., 2018). This study revealed that oral feeding of patients with UWS is rare. Out of the 68 patients with UWS, only two were able to resume oral feeding (3%). The first patient received oral feeding (only liquids and semi-liquids) in addition to gastrostomy feeding, and the second one was able to engage in full oral feeding (liquid and mixed solid food). Repeated clinical behavioral assessments with the CRS-R concluded that both patients fulfilled the criteria for a diagnosis of UWS. However, the neuroimaging and neurophysiology results were typical for the first patient with regard to the diagnosis of UWS, but atypical for the second patient. In fact, the neuroimaging findings for the second patient were closer to MCS-like patterns of brain activity. Other studies have shown that some patients with clinical UWS show patterns of brain activity suggestive of MCS or a conscious state (Claassen et al., 2019; Edlow et al., 2017; Kondziella et al., 2016; Owen et al., 2006; Sitt et al., 2014). These findings highlight the importance of combining behavioral and brain-imaging techniques. Given the dissociation between the behavioral and neuroimaging findings, patient 2 could be considered as being in a functional locked-in state (Bruno et al., 2011; Formisano et al., 2013), in MCS* (Bodart et al., 2017; Gosseries et al., 2014) or in a state of cognitive motor dissociation (Schiff, 2015).[4]

These results suggest that **the possibility of full oral feeding is associated with the recovery of cortical activation**. Furthermore, we can point out that, in patient 2, full oral feeding was also associated with the recovery of some oral functions. In fact, patient 2 received mixed solid food, suggesting that he presented some degree of bolus manipulation and tongue propulsion.

Based on these findings, **the presence of oral components of swallowing** (lip prehension, bolus manipulation and/or tongue propulsion)

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[4] A ***functional locked-in state*** characterizes patients who unambiguously demonstrate a dissociation between preserved higher cognitive functions, only measurable by functional imaging techniques, and extremely limited motor responsiveness during bedside clinical testing. This designation should be reserved, however, for patients who show consistent and reliable communication using non-speech and non-gestural communication through direct brain signaling (Steven Laureys & Schiff, 2012).
MCS* refers to patients who show a MCS-like patterns of brain activity (passive or active stimulation or other patterns in a brain-imaging technique).
Patients **with *cognitive motor dissociation*** demonstrate a behavioral profile characteristic of UWS or a low-level, minimally conscious state (restricted to nonreflexive behaviors, such as tracking, but unable to follow commands) and fMRI or electrophysiological evidence of command following (Schiff, 2015).

and, consequently, the possibility of full oral feeding **is a cortically mediated behavior and probably a sign of consciousness**.

Our second behavioral retrospective study, presented in **Chapter 3**, provided more data on patients with MCS, and retrospectively explored several components related to swallowing, rather than only the possibility of oral feeding (Mélotte et al., 2020). The results showed that deficits in the oral and/or pharyngeal phase of swallowing were present in 99% of patients with DOC independently of their level of consciousness. We found some differences in the swallowing capacities of patients with UWS and MCS, suggesting that some components of swallowing are linked to level of consciousness.

First, this study allowed us to identify a strong link between the oral phase of swallowing and level of consciousness. Indeed, we did not detect an effective oral phase of swallowing (lip prehension, tongue propulsion and no post-swallowing oral stasis) in any of the patients with UWS, and in only a small minority of those with MCS. This also helped to explain why no patients with UWS were able to achieve full oral feeding and why only a small proportion of the patients with MCS could safely resume full oral feeding with easy-to-swallow food. Despite the ability of some patients with MCS to resume oral feeding, a higher level of consciousness (i.e., EMCS) is probably necessary to allow a full return to ordinary oral feeding. As suggested by our first study (Mélotte et al., 2018, **Chapter 2**) and based on this result, **an effective oral phase** (present in 21% of patients with MCS in our cohort) **should be considered as a sign of consciousness** and, consequently, it should be taken into account in diagnosing DOC.

Secondly, patients with UWS and MCS differed in their **spontaneous saliva management**. Indeed, patients with UWS had more pharyngo-laryngeal secretions (UWS=57.7%; MCS=28.8%) and saliva aspiration (UWS=46.2%; MCS=21.2%) and a larger proportion still had a tracheostomy (UWS=69.2%; MCS=24.2%) in place at the time of the evaluation. These results suggest that **there is a link between the pharyngeal phase of swallowing and level of consciousness** in this cohort. However, at this point, we are not able to identify whether the mechanism involved is a decrease in the frequency of spontaneous swallowing or a lack of efficacy of the pharyngeal phase as such, especially pharyngeal propulsion.

Thirdly, the **cough reflex** was another component that was more evident in MCS than in UWS (UWS=30.4%; MCS=60%). Despite the term “reflex,” this result shows that the cough reflex is not solely a brainstem-mediated reflex response but seems to be facilitated by cortical activations (Mazzone et al., 2011). Indeed, the impact of level of consciousness on the existence of the cough reflex may be linked to the scope of the underlying cortical damage. Moreover, we can postulate that the cough reflex is a somatic reflex, rather than an autonomic reflex, given the ability of healthy patients to suppress a cough to some extent.

The other components analyzed (hypertonia of the jaw muscles, type of feeding, cream or liquid aspiration) were not significantly linked to level of consciousness when we compare patients with UWS and MCS.

Based on theoretical and behavioral analyses, can we consider oral phase components to be conscious and pharyngeal and esophageal phase components to be unconscious?

The response seems to be relatively clear for oral phase components. Although they contain automatic processes, oral phase components can be interrupted, influenced and suppressed, placing them in the category of “voluntary behaviors.” Based on our two retrospective studies in patients with DOC, the efficacy of the oral phase seems to be the most robust sign of consciousness. Indeed, until now, no typical patients with UWS are described in the literature as having a complex oral phase of swallowing enabling the preparation and mastication of solid food. Therefore, **oral phase components can be considered conscious components**.

The triggering of the swallowing reflex can be initiated voluntarily but usually occurs below conscious control. Nonpathological consciousness studies have taught us that sleep and anesthesia tend to decrease the frequency of spontaneous saliva swallowing. Until now, there have been no data about the frequency of saliva swallowing in patients with DOC. However, we highlighted the link between spontaneous saliva swallowing and level of consciousness by highlighting the higher proportion of tracheostomies, pharyngo-laryngeal secretions and saliva aspiration in patients with UWS than with MCS (Mélotte et al., 2020, **Chapter 3**). To identify which mechanism (the frequency of triggering of the swallowing reflex or the efficacy of the pharyngeal phase) is more influenced by consciousness, it would be interesting to explore the frequency of spontaneous swallowing in patients with different levels of consciousness.

A pretest in our research group with 8 patients with DOC identified the difficulty of reliably assessing awake patients with DOC given that many patients fall asleep during assessment and that the arousal protocol stimulation itself seems to influence the initiation of the swallowing reflex. To address this issue, it would be interesting, as a first step, to take measurements over 24 hours with “classical” sleep and wakening periods. We hypothesize that the frequency of saliva swallowing is lower in patients with DOC than in subjects without DOC during both wakefulness and sleep. Based on existing data, we can postulate that **the frequency of the swallowing reflex may be influenced by consciousness**.

Previously, there were no data about the esophageal phase of swallowing in patients with DOC. Based on our theoretical assumptions, we postulate that the esophageal components of swallowing are unconscious.

According to the literature and the main findings of our studies, the presence of oral phase components (mainly mouth opening, lip prehension and lingual propulsion) and the ability to receive exclusive oral feeding can be considered as signs of consciousness. Indeed, these components seem to be present only in patients with (E)MCS or in patients with MCS-like patterns of brain activity on neuroimaging tools. Several other components related to swallowing (**see table 10**) can be considered to be linked to the level of consciousness (cortically mediated state) without constituting signs of consciousness as such, based on current data.

Table 10: Hypotheses concerning which components of swallowing can be considered to be linked to level of consciousness according to the literature and the main findings of our studies

Components related to swallowing	**Degree of evidence suggesting a link with level of consciousness** → MCS > UWS but also present in some patients with UWS = cortically mediated behaviors
Oral feeding	
Exclusive oral feeding	++
Exclusive oral feeding with solid food	+++
Components of the oral phase	
Initiation of mouth opening	++
Some lip prehension or tongue propulsion	++
Efficient oral phase (lip prehension AND tongue propulsion without oral stasis post-swallowing)	+++
Hypertonia of the jaw muscles or lip injury	-
Components of the pharyngeal phase	
Frequency of saliva swallowing	?
Ability to manage saliva (tracheostomy, pharyngo-laryngeal secretions or saliva aspiration)	++
Pharyngeal propulsion	?
Components of the esophageal phase	-
Cough reflex	++

Related to

Note: + = weak evidence; ++ = moderate evidence; +++ =strong evidence; - = absence of evidence; ? = evidence not clearly determined hitherto

A proposal to enhance our understanding of the relationship between swallowing and consciousness: the SWADOC (Chapter 4)

At first sight, it may seem unnecessary or impossible to try to appraise or treat orofacial area and swallowing disabilities in patients with DOC.

Unnecessary, because the majority of patients with DOC receive enteral feeding? However, in addition to feeding, swallowing plays a crucial role in managing secretions and saliva.

Impossible, because of the lack of response to commands (UWS and MCS–), attentional disorders, and fluctuating responses? Appropriate tools and repeated observations can help us to achieve this goal.

With the development and future validation of the SWADOC, we aim to give clinicians a tool to appraise swallowing disabilities in patients with DOC (Mélotte et al., accepted). This tool will also be applicable to other populations of patients who do not respond to commands, such as patients with severe dementia, pervasive developmental disorder, psychiatric disorders, etc.

The tool is composed of approximately 50 qualitative items and a subsection called the "SWADOC-scored" comprising 8 quantitative items. The quantitative items will help to measure the patient's progress and treatment effects, while the qualitative items will help clinicians to provide a clear and accurate summary of the patient's strengths and weaknesses and thus orient therapy in the best possible way. Moreover, in a scientific context, the protocol study was designed to compare groups of patients with different levels of consciousness and thereby enhance our knowledge of the relationships between different components of swallowing and level of consciousness. Finally, this protocol study will address the retrospective limitations of our experimental studies.

Implications and prospects for further research and clinical practice

As a clinician in contact with patients who have severe brain injuries, our first ambition was to find ways to manage dysphagia despite the inability of some patients to actively participate. However, we realized that knowledge of the pathophysiology of swallowing in patients with DOC and of the impact of consciousness on swallowing was very limited. For this reason, we chose to devote this work to establishing the links between swallowing and consciousness.

For over 10 years, more than a hundred patients with DOC have benefited from a multimodal assessment during a one-week hospitalization at the University Hospital of Liège. We started our work by analyzing existing but untapped data on patients with DOC collected by several brilliant otorhinolaryngologists during this period. In a second step, we worked with otorhinolaryngologists to standardize the assessment protocol and make sure the same clinical information was collected from all patients with DOC. Simultaneously, we added a speech therapist's assessment of swallowing to the multimodal assessment week and started developing the SWADOC.

a) Continue prospective data collection

The next goal is to continue prospective data collection both during clinical bedside evaluation with the validation of the SWADOC and with otorhinolaryngological exams.

Following the validation period and potential adjustments of the tool, it would be interesting to suggest that all clinicians who specialize in dysphagia **integrate the administration of the tool into their clinical practice**.

It would be particularly interesting not only to compare patients with UWS and MCS but also to distinguish between those with MCS– and MCS+, as well as **adding results for patients with EMCS**. This will help us refine our hypotheses and the knowledge provided by this thesis work. In contrast, comparing patients with DOC and LIS patients seem less relevant because dysphagia in LIS patients is mainly attributable to brainstem lesions.

Administration of the SWADOC will give us information about possible links between consciousness and **other components related to swallowing** that were not previously explored. Specifically, it would be interesting to observe the presence or absence of a gag reflex in patients with DOC to see if level of consciousness has an impact on this reflex. However, given that approximately half of DOC patients present hypertonia of the jaw muscles, it might not be possible to obtain this information for all DOC patients. It will be also necessary to take into account the impact of pharmacological substances (Moulton et al., 1991).

Moreover, future data collection will help us to specify some mechanisms such as the reason for and implications of the presence of a tracheotomy over a prolonged period of time. Among other things, we know that the presence of an inflated cuff inflated for a long period has a negative impact on swallowing function.

b) Implement new techniques and measures

Two other techniques deserve our attention in the assessment of swallowing-related components. First, as described before, **measuring the frequency of spontaneous saliva swallowing** seems to be a simple, non-invasive technique that can give us additional information about saliva management. In future, robust, reliable measures of the frequency of swallowing may help us to take decisions about the process of tracheostomy weaning (together with other clinical information). This information may also allow for a quantitative measure of the patient's progress and a way to appraise the effect of a therapy that targets the triggering of the swallowing reflex.

Secondly, we think that **citric acid cough reflex testing** is a promising technique for patients with DOC. This test consists in administering a solution of citric acid via an aerosol and measuring the time between the start of the administration and the triggering of the cough reflex. This is a simple, non-invasive method of cough testing that does not require the patient's active participation. Some studies have shown a link between cough reflex testing and the presence of aspiration in an objective swallowing assessment (Miles et al., 2013; Sato et al., 2012; Wakasugi et al., 2008). Moreover, this technique can help clinicians to manage pharyngo-laryngeal and pulmonary congestion by expectoration of secretions.

c) Conduct longitudinal studies

Future longitudinal studies should also investigate recovery from dysphagia and recovery of consciousness within the same individuals. This type of analysis will give us information about potential good prognostic factors in terms of recovery of consciousness and/or possibility of return to oral feeding.

d) Explore the neurophysiological basis of swallowing components

To confirm that components of the oral phase reliably constitute signs of consciousness, it would be interesting to **correlate specific swallowing components** (i.e., initiation of mouth opening, lip prehension, tongue propulsion) **with brain activity** shown by neuroimaging tools to confirm if the presence of one or more of these components is associated with MCS-like patterns. In this respect, it could be considered to analyze the metabolic index of each hemisphere with FDG-PET as a diagnostic marker of MCS (Hermann et al., 2020).

e) Enrich bedside behavioral assessments of consciousness with swallowing components

Until now, the diagnostic criteria of consciousness have not included components related to swallowing.

Although our assumptions about the links between specific components of swallowing and level of consciousness must still be confirmed with prospective studies, it would be interesting to consider the **inclusion of swallowing components in behavioral assessments of consciousness** in the future.

Based on existing knowledge, **figure 12** presents an example of a quick test that can be added to enrich the bedside clinical toolbox of clinicians who need to examine patients. In this context, if one or more components identified as possible signs of consciousness are present, the test will support the decision to continue behavioral and neuroimaging investigations in search of other signs. In the future, this short version of the SWADOC could be integrated into the multimodal assessment of consciousness and administered by clinicians regardless of their knowledge of swallowing.

Figure 12. SWADOC-short (English Version)

Patient : .... Examiner : .... Date : .... Time : ....

SWADOC-short (English version)

Items	Instructions	Levels
Type of feeding	Request information from care team or the family.	□ **Level 3***: Exclusive oral-feeding (FILS 7-10) □ Level 2: Enteral and oral feeding (FILS 5-6) □ Level 1: Exclusive enteral feeding and therapeutic or pleasure feeding (FILS 3-4) □ Level 0: Exclusive enteral feeding (gastrostomy or jejunostomy) (FILS 1-2) * Solid food: *FILS level:……. IDDSI level:……..* * Are some liquids given orally? □ Yes □ No * If yes, are they thickened? □ Yes □ No (if yes, IDDSI level:…….)
Tracheostomy	In case of the presence of a tracheostomy, request information from care team about the presence or not of a cuff and its use.	□ **Level 3***: Tracheostomy with ongoing weaning, or no tracheostomy □ Level 2: Tracheostomy without cuff or with permanently deflated cuff □ Level 1: Tracheostomy with cuff, ongoing deflation □ Level 0: Tracheostomy with inflated cuff
Initiation of mouth opening	1. Ask the patient **"Open your mouth"** 3 times, leaving a minimum of 10 seconds between requests. Level 3 is achieved if the patient opens his/her mouth a minimum of twice. 2. If there is no reaction to the request to open the mouth, **bring a teaspoon (5 mL) of cold water up to the patient's mouth** – repeat 3 times if the patient does not react within 10 seconds. 3. If there is no reaction 10 seconds after the third presentation of the spoon, **rub the spoon, and then your index finger, back and forth on the lower lip.** 4. If there is no reaction 10 seconds after the lip stimulation, press your thumb against the lower jaw (active assistance). If the patient opens his/her mouth constantly, a greater mouth opening reaction to the approach of the spoon is expected. If there is not this reaction, score 0.	□ **Level 3****: Mouth opening upon command (min 2/3) □ **Level 2***: Mouth opening upon presentation of spoon (min 1/3) □ Level 1: Mouth opening upon lip stimulation (with the spoon or the finger) □ Level 0: Mouth opening impossible or only with the therapist's active assistance
Lip prehension	Observe the lip prehension of the spoon. If the patient does not react, stimulate him/her verbally by saying **"Take the spoon."** If the patient presents complete lip prehension, do two more trials with an empty spoon to verify the stability of prehension. If the patient continues to succeed at this item, score level 3; if the patient fails the second or third time, score level 2. If the patient does not present any lip or tongue reaction **after 10 seconds**, score 0.	□ **Level 3***: Consistently correct, spontaneous lip prehension □ Level 2: Appropriate lip prehension but not consistently or only upon verbal stimulation □ Level 1: Incomplete lip prehension spontaneously or upon verbal stimulation □ Level 0: No lip prehension (no reaction or tightening of lips)

*** Possible sign of consciousness**
**** Sign MCS+**

1

Patient : …………………………… Examiner : …………………………… Date : …………………………… Time : ……………………………

Appendix 1: Items of the *Food Intake Level Scale* (FILS)

No oral intake
Level 1: No swallowing training is performed except for oral care.
Level 2: Swallowing training not using food is performed.
Level 3: Swallowing training using a small quantity of food is performed.
Oral intake and alternative nutrition
Level 4: Easy-to-swallow food less than the quantity of a meal (enjoyment level) is ingested orally.
Level 5: Easy-to-swallow food is orally ingested in one to two meals, but alternative nutrition is also given.
Level 6: The patient is supported primarily by ingestion of easy-to-swallow food in three meals, but alternative nutrition is used as a complement.
Oral intake alone
Level 7: Easy-to-swallow food is orally ingested in three meals. No alternative nutrition is given.
Level 8: The patient eats three meals by excluding food that is particularly difficult to swallow.
Level 9: There is no dietary restriction, and the patient ingests three meals orally, but medical considerations are given.
Level 10: There is no dietary restriction, and the patient ingests three meals orally (normal).

Comments:

- Swallowing training: Training conducted by an expert, well-instructed caregiver, or the patient himself/herself to improve the swallowing function.
- Easy-to-swallow food: Food that is prepared so that it is easy to swallow even without mastication, for example, meat and vegetables are gelatinized or homogenized in a mixer.
- Alternative nutrition: Non-oral nutrition such as tube feeding and drip infusion.
- Food that is particularly difficult to eat: dry and brittle food, hard food, water, and so on.
- Medical considerations: guidance, tests, examinations, and so on, for symptoms suggestive of swallowing disorders such as choking and the feeling of food remaining in the pharynx.

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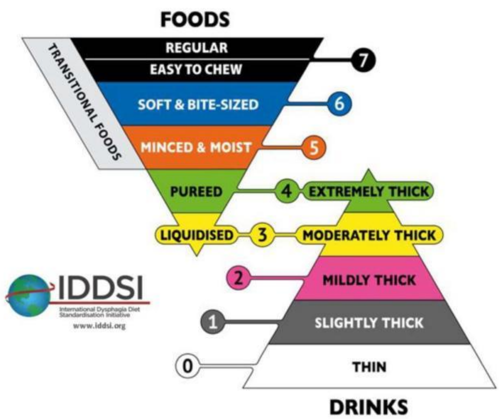
Appendix 2: International Dysphagia Diet Standardisation Initiative (IDDSI)[1]

For the corresponding FILS scores, note the textures of food and drinks offered to patients using the IDDSI terminology.



Cichero JAY, Lam P, Steele CM, et al. Development of international terminology and definitions for texture-modified foods and thickened fluids used in dysphagia management: The IDDSI framework. Dysphagia. 2017;32(2):293-314. doi:10.1007/s00455-016-9758-y

f) Suggest new guidelines for speech therapy

Based on a detailed analysis of swallowing-related components, clinicians can formulate active ingredients for the therapy. We suggest several possible clinical approaches to the management of orofacial and swallowing disabilities in patients with DOC that should be developed more in detail in the future.

- *Treating hypertonicity/hypersensitivity of the orofacial area*

In a high proportion of patients with DOC, we are not able to obtain a good mouth opening, as the patient shows permanent spasticity of the jaw muscles or resistance to mouth opening. Signs of discomfort or grimacing when the face, lips or tongue are touched are also frequent.

Based on the administration of the SWADOC, clinicians will be able to differentiate between hypertonicity/spasticity and hypersensitivity profiles.

When hypertonicity of the jaw muscles is present, clinicians can propose massage, inspired by the treatment of peripheral facial palsy with pressed stimulations in the direction of the fibers and from the center to the periphery of the face (Gatignol, 2007). In the case of severe spasticity, botulinum toxin injection can be discussed with the ENT or the neurologist.

In the case of hypersensitivity, it seems more appropriate to propose firm pressure rather than light touch. A specific desensitization protocol was proposed by Senez (2015).

In both cases, mouth opening should not be forced to avoid reinforcing bad feelings related to the orofacial area.

- *Manual therapy techniques*

Manual therapy techniques applied to the orofacial area, pharynx, larynx, neck and shoulder can help to normalize muscle tension and obtain a better amplitude of movement (Piron, 2007).

- *Passive and semi-active orofacial movement*

In the absence of hypertonicity/hypersensitivity, clinicians can passively or semi-actively encourage the execution of orofacial movements such as mouth opening, stretching and projection of the lips, etc.

- *Intrabuccal stimulation*

If mouth opening can be achieved without any difficulty, we can propose intrabuccal and taste stimulations with a cotton swab and various types of tastes and sensations (sweet, salty, soure, cold, hot, etc). Taste stimulation is an important first step in evaluating the patient's ability to accept food or liquid by mouth and to stimulate the triggering of the swallowing reflex (Brady, 2011).

- *Therapeutic feeding*

Unlike taste stimulation, therapeutic oral feeding provides the patient with small, controlled amounts of food or liquid in a bolus size ranging from 1 to 5 mL. Although therapeutic feeding is not sufficient to meet nutritional needs, it constitutes an entry route to stimulate the patient.

The potential mid- and long-term impact of taste stimulation and therapeutic feeding on the improvement of awareness should be evaluated.

- *Multisensory stimulation*

Olfactory, gustatory, tactile and visual stimulations constitute cues that can help patients to expand the range of feelings registered and modulated.

Stimulations have to be slow, repeated, brief, contrasted and significant for the patient in light of his or her history. Clinicians have to find the right balance between too little or too much stimulation. It is also important to ensure continuity in the stimulations.

- *Observation grid for reactions and behaviors*

Regardless of the type of stimulation, it is important to pay careful attention to each reaction and to compile them in order to be able to identify even minor changes in the observed behaviors.

This work contributes to our understanding of the relationship between swallowing and consciousness. However, a lot of work must still be done to increase our knowledge of swallowing disabilities in patients with DOC and of ways to treat them appropriately.

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APPENDICES

Appendix 1: Additional information related to General Introduction

Appendix 1.1. CRS-R administration and scoring guidelines

CRS-R
COMA RECOVERY SCALE-REVISED ©2004

Administration and Scoring Guidelines

Joseph T. Giacino, Ph.D.

Update by: Yelena G. Bodien. Ph. D, Camille Chatelle, Ph.D and Joseph T. Giacino, Ph.D.

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Rehabilitation Institute

1 Updated 2020

JFK COMA RECOVERY SCALE ©2004 Record Form This form should only be used in association with the "CRS-R ADMINISTRATION AND SCORING GUIDELINES" which provide instructions for standardized administration of the scale.										
Patient:	**Diagnosis:**									
Date of onset:	**Date of Admission:**									
Date										
Assessment	1		2		3		4		5	
AUDITORY FUNCTION SCALE	#	TCC	#	TCC	#	TCC	#	TCC	#	TCC
4 – Consistent Movement to Command▪										
3 – Reproducible Movement to Command▪										
2 – Localization to Sound										
1 – Auditory Startle										
0 – None										
VISUAL FUNCTION SCALE	#	TCC	#	TCC	#	TCC	#	TCC	#	TCC
5 – Object Recognition▪										
4 – Object localization: Reaching*										
3 – Visual Pursuit*										
2 – Fixation*										
1 – Visual Startle										
0 – None										
MOTOR FUNCTION SCALE	#	TCC	#	TCC	#	TCC	#	TCC	#	TCC
6 – Functional Object Use†										
5 – Automatic Motor Response*										
4 – Object Manipulation*										
3 – Localisation to Noxious Stimulation*										
2 – Flexion Withdrawal										
1 – Abnormal Posturing										
0 – None										
OROMOTOR/VERBAL FUNCTION SCALE	#	TCC	#	TCC	#	TCC	#	TCC	#	TCC
3 – Intelligible Verbalization▪										
2 – Vocalization/Oral Movement										
1 – Oral Reflexive Movement										
0 – None										
COMMUNICATION SCALE	#	TCC	#	TCC	#	TCC	#	TCC	#	TCC
2 – Functional: Accurate†										
1 – Non-functional: Intentional▪										
0 – None										
AROUSAL SCALE	#	TCC	#	TCC	#	TCC	#	TCC	#	TCC
3 – Attention										
2 – Eye Opening w/o Stimulation										
1 – Eye Opening with Stimulation										
0 – Unarousable										
TOTAL SCORE										

* Denotes Minimally Conscious State Minus (MCS-)
▪ Denotes Minimally Conscious State Plus (MCS+)
† Denotes emergence from Minimally Conscious State (eMCS)
TCC Test Completion Code

BRAIN STEM REFLEX GRID ©2004

Administer daily during the acute phase, then weekly

Mark all that apply	Date					
	Assessment	**1**	**2**	**3**	**4**	**5**
Pupils	Nonreactive: pupils do not constrict in response to light and do not dilate in the dark					
Corneal Reflex	Absent					
	Present in one or both eyes					
Eye Position and Movement	No spontaneous or elicited eye movement					
	Skew or Conjugate Gaze Deviation: At rest, one or both eyes are either positioned up or to the left/right, rather than midline					
	Dysconjugate Gaze: eyes do not move together in the same direction					
	Roving: slow, conjugate, lateral, back and forth eye movements					
Oculocephalic Reflex	None: eyes move in the same direction as head or stay fixed at midline					
	Abnormal: response is present but sluggish or unilateral					
	Normal: eyes move in the direction opposite the head					
Postural Responses (Indicate limb)	Abnormal Extension					
	Abnormal Flexion					

Notes:

AROUSAL FACILITATION PROTOCOL (AFP) ©2004

GUIDELINES

1) The goal of this intervention is to prolong the length of time the patient maintains arousal (i.e. eye opening)

2) The protocol is administered any time the patient is observed to:

   - Exhibit sustained eyelid closure **AND/OR**

   - Stops following commands for a period of at least one minute

3) Readminister the arousal facilitation protocol when

   - Sustained eye closure re-occurs **OR**

   - Behavioral responsiveness ceases despite sustained eye opening

INTERVENTIONS

Deep Pressure:

1) Present deep pressure stimulation unilaterally to the face, neck, shoulder, and sternocleidomastoid muscles. The muscle should be firmly grasped at its base between the thumb and forefinger. While squeezing the muscle firmly, it should be "rolled" back and forth through the fingertips three to four times. This procedure should be repeated sequentially working from the facial musculature to the sternocleidomastoid. The examiner should assure that there are no intravenous lines, local injuries (e.g. fractures, contusions, decubiti) or systemic complications (e.g. heterotopic ossification) before administering deep pressure.

2) Administer same on contralateral side.

AUDITORY FUNCTION SCALE ©2004

Score	Item	Method	Response
4	**Consistent Movement to Command**	1.Observe frequency of spontaneous movement for a one minute interval (See **Baseline Observation and Command Following Protocol** on page 7) 2. Choose at least 1 object-related and 1 non-object related command from the **Command Following Protocol.** The type of command chosen (eye, limb, oral) should be based on patient's physical capacity and should be of low spontaneous frequency. If at least 2 out of four commands are passed, and time permits, an additional command may be attempted. The command should be repeated once during the 10 second response interval. **a. Object-Related Eye Movement Commands:** Present 2 common objects simultaneously and approximately 16 inches apart within the patient's field of view. Ask the patient to look at the object named (i.e. 'Look at the [name object]'). Next, reverse the positions of the 2 objects and ask the patient to look at the **same** object again (i.e. 'Look at the [name object]'). Administer two additional trials using the same 2 objects and repeat the above procedure with instruction to look at the **other** object on both trials. Two trials per object should be administered for a total of 4 trials. **b. Object-Related Limb Movement Command**: Present 2 common objects simultaneously and approximately 16 inches apart within the patient's field of view and within arm's (or leg's) length and ask the patient to touch the object named with their hand (or foot). Next, reverse the positions of the 2 objects and ask the patient to touch the **same** object again. Administer two additional trials using the same two objects and repeat the above procedure with instruction to touch **the other object on both trials**. Two trials per object should be administered for a total of four trials. This command may also be attempted using head movement. **c. Non-Object Related Commands:** Select at least 1 eye movement, limb movement or oral movement/vocalization command and present it over 4 trials at 15 second intervals. The same command should be used for all 4 trials. Movements that occur between commands (i.e. after the response interval has elapsed) should be noted but not scored.	Clearly discernible and accurate responses occur within 10 seconds on all 4 trials administered This item is credited only when **all 4 trials of 2 different commands** are passed. When more than one type of command from each category is attempted, scoring is based on successfully completing all 4 trials of any two different commands (e.g., 2 object-related, 2 non-object related or one of each).
		Continued	

AUDITORY FUNCTION SCALE ©2004

Score	Item	Method	Response
3	**Reproducible Movement to Command**	Same as the Consistent Movement to Command item	**3 clearly discernible and accurate** responses occur over the 4 trials on any one of the object ***or*** non-object related commands.
2	**Localisation to Sound**	Standing behind the patient and out of view, present an auditory stimulus (e.g. patient's name, voice, noise) from the right side for 5 seconds. Perform a second trial presenting the auditory stimulus from the left side. Repeat above procedure for a total of 4 trials, 2 on each side. If needed, reorient the head to midline between trials.	Head and/or eyes orient toward the location of the stimulus on **both** trials in at least one direction (ie, twice to the right or twice to the left) within 10 seconds of stimulus presentation. This item is scored when there is clear evidence of head and/or eye movement. It is not dependent on the degree or duration of movement.
1	**Auditory startle**	Present a loud noise (eg, whistle, clap) directly above the patient's head and out of view. Administer 4 trials.	Eyelid flutter or blink occurs immediately following the stimulus on at least **2** trials. If the eyes are closed, a shoulder shrug or other body startle response can be scored.
0	**None**	See above	No response to any of the above.

BASELINE OBSERVATION AND COMMAND FOLLOWING PROTOCOL ©2004

Baseline Observations of Spontaneous Behaviours and Resting Posture		
Eye-Opening		
Visual Tracking		
Sticking out tongue		
Opening mouth		
Closing mouth		
Vocalizations (eg. 'ah')		
Resting Posture	RUE:	LUE:
	RLE:	LLE:

Commands	Trial 1	Trial 2	Trial 3	Trial 4
Object Related Commands: Eye Movement				
Look at the (*object* #1, *object* #2)				
Object Related Commands: Limb Movement				
Take the (*object* #1, *object* #2)				
Kick the (*object* #1, *object* #2)				
Non-Object Related Commands: Eye Movement				
Look away from me				
Look up (*at ceiling*)				
Look down (*at floor*)				
Non-Object Related Commands: Limb Movement				
Touch my hand				
Touch your nose				
Move your (*body part*)				
Non-Object Related Commands: Oral Movement/Vocalization				
Stick out your tongue				
Open your mouth				
Close your mouth				
Say 'ah'				
Related Commands: Oral Movement/Vocalization				
Other Command 1:				
Other Command 2:				

Notes:

Updated 2020

VISUAL FUNCTION SCALE ©2004

Score	Item	Method	Response
5	**Object Recognition**	Same as Consistent Movement to Command on Auditory Function Scale, Section 2a and b (see page 5.)	If the Auditory Function score was >2 AND the command used was object-related, score 5 for the Visual Function Scale. If an object-related command was not administered, administer the Object Recognition item. If the Auditory Function score was < 2 AND the command used was object-related, continue with the Object Localization item below
4	**Object Localization: Reaching**	**1**. Identify the arm or leg with the greatest range of movement. **2**. For upper extremity reaching, select common objects (e.g. comb, toothbrush, etc.) For lower extremity assessment, select a ball suitable for kicking. **3.** Present the object approximately 8 inches to the left or right of the limb's resting position. The object should be placed in a position that is not obstructed from view. The patient should be instructed to 'Touch the [**name object**]' with the appropriate arm or leg. **4**. The command may be repeated once within the assessment interval. Do not provide any tactile cues, as these may stimulate random limb movement. **5**. Present an object twice to the left of the limb and twice to the right of the limb in random order for a total of 4 trials	Score the **direction in which the limb first moves** within a 10 second observation period, or score as no movement. The limb does not need to make contact with the object, only to move toward it; and Movement must occur in the correct direction in **3** of the 4 trials administered.

Continued

VISUAL FUNCTION SCALE ©2004

Score	Item	Method	Response
3	**Visual Pursuit**	Hold a mirror 4-6 inches directly in front of the patient's face and verbally encourage the patient to fixate on the mirror. Tilt the mirror slowly 45 degrees to the right and left of the vertical midline and 45 degrees above and below the horizontal midline. Repeat the above procedure so that a total of 2 trials are administered in each hemispace (ie twice up, twice down, twice left and twice right).	Eyes must follow the mirror for 45 degrees **without loss of fixation** on **2** occasions in any direction. *If visual pursuit is not scored, the procedure may be repeated assessing one eye at a time (using an eye patch).*
2	**Fixation**	Present a brightly colored or illuminated object 6 to 8 inches in front of the patient's face and then rapidly move to upper, lower, right and left visual fields, respectively for a total of 4 trials.	Eyes change from initial fixation point and refixate on the new target location for more than 2 seconds. At least **2** episodes of fixation are required.
1	**Visual Startle**	Present visual threat by passing finger 1 inch in front of patient's eye. Be careful not to touch eyelashes or create a breeze (manually open eyes if necessary). Conduct 4 trials per eye.	Eyelid flutter or blink following presentation of visual threat on at least **2** trials with either eye.
0	**None**	See above	No response to any of the above

MOTOR FUNCTION SCALE ©2004

Score	Item	Method	Response
6	**Functional Object Use**	Select 2 common objects (e.g. comb, cup). Place one of the objects in the patient's hand and instruct the patient to 'Show me how to use a [name object]'. Next, place the second object in the patient's hand and restate the same instruction. Repeat the above procedure using the same objects so that a total of 2 trials are administered with each object.	Movements executed are generally compatible with both objects' specific function (e.g. comb is placed on or near the head) on all **4** trials administered. *If the patient is unable to hold the object because of neuromuscular involvement, this should be noted on the record form and the item should not be scored.*
5	**Automatic Motor Response**	Observe for automatic motor behaviors patterns such as nose scratching, grasping bedrail, crossing legs, grabbing tubes, that occur spontaneously during the examination. If spontaneous automatic motor behaviors are not observed, present a familiar gesture (e.g. wave) in association with the following series of alternating commands: 1) 'Show me how to wave' (**demonstrate gesture**) 2) 'I'm going to wave again. Do not move at all. Just hold still' (**demonstrate gesture)** 3) 'Show me how to wave' (**demonstrate gesture**) 4) 'I'm going to wave again. Do not move at all. Just hold still' (**demonstrate gesture)** For patients with limited ability to move their limbs, objects associated with oromotor activity may be used (e.g. spoon). Place the object in front of the patient's mouth **without making contact**. Administer the following series of commands: 1) 'Show me how to use [**name object**]' 2) 'I am going to show you [**name object**] again. Do not move at all. Just hold still'. 3) 'Show me how to use [**name object**]' 4) 'I am going to show you [**name object**] again. Do not move at all. Just hold still'.	At least **2** episodes of automatic motor behavior are observed within the session and each episode can be clearly differentiated from a reflexive response. Patient performs the gesture (e.g. waves) or oromotor pattern on *Trials 2 and 4* (regardless of performance on trials 1 and 3).

Continued

MOTOR FUNCTION SCALE ©2004

Score	Item	Method	Response
4	**Object Manipulation**	Place a baseball size ball on the **dorsal** surface of one of the patient's hands. Roll the ball across the index finger and thumb without touching the undersurface of the hand or fingers. While moving the ball, instruct the patient to "Take the ball". Repeat the above for a total of 4 trials.	The following criteria must be met on **3** of the 4 trials administered: **1**.The wrist must rotate and the fingers should extend as the object is moved along the dorsal surface of the hand; and **2**. The object must be grasped and held for a minimum of 5 seconds. The object cannot be held by means of a grasp reflex or increased finger flexor tone.
3	**Localization to Noxious Stimulation**	Extend all four extremities. Apply pressure to the finger or toe of an extremity (use best extremity on each side of the body) for a minimum of 5 seconds (i.e. squeeze the finger or toe between your thumb and index finger). Administer 2 trials on each side for a total of 4 trials.	The non-stimulated limb must locate and make contact with the stimulated body part at the point of stimulation or with the examiner's hand on at least **2** of the 4 trials.
2	**Flexion withdrawal**	Extend all 4 extremities. Apply deep pressure to nailbeds of each extremity (i.e. press the ridge of a pencil into the cuticle). Administer 1 trial per extremity.	There is **isolated** flexion withdrawal of at least one limb. The limb must move **away** from the point of stimulation. If quality of response is uncertain, the trial may be repeated.
1	**Abnormal Posturing**	Observe response to above method	Slow, stereotyped flexion **or** extension of the upper and/or lower extremities occurs immediately after the stimulus is applied.
0	**None**	Observe response to method above	There is no discernible movement following application of noxious stimulation, secondary to hypertonic **or** flaccid muscle tone.

OROMOTOR/VERBAL FUNCTION SCALE ©2004

Score	Item	Method	Response
3	**Intelligible verbalization**	**1**. Tell patient: 'I would like to hear your voice'. This should be followed by an attempt to directly elicit speech using the verbal prompts shown below. At least one prompt should be selected from the Aural Set and at least one from the Visual Set. A maximum of 4 prompts can be administered. **2**. A maximum of 3 trials should be administered for each prompt chosen from the Aural and Visual Sets. Prompts should be administered at 10 second intervals. **Aural Set:** a) 'Your name is ___' b) 'You live in ___' c) 'One, two, three, ___' **Visual Set:** a) 'This is a ___' (Hold up a common object in front of the patient's right and then left visual field for 10 seconds). b) 'I holding___ fingers' (Hold up 4 or 5 fingers in front of the right and then left visual field for 10 seconds). c) 'This is a ___' (Point to your nose while positioned at the patient's visual midline).	Each of the following criteria must be met: **1.** Each verbalization must consist of at least one consonant-vowel-consonant (C-V-C) triad. For example, 'ma' would not be acceptable, but 'mom' would. Make sure objects chosen have a C-V-C sequence; *and* **2**.**Two different words** must be documented by the examiner to ensure that a repetitive word-like sound is not mistaken for a word. Words need not be appropriate or accurate for the context, but must be fully intelligible; *and* **3**.Words produced by writing or alphabet board are acceptable. *Verbalisations that occur spontaneously or at other times during the assessment and meet the above criteria should also receive a score of 3.*
2	**Vocalization/ Oral movement**	Observe for non-reflexive oral movements, spontaneous vocalizations or vocalizations that occur during administration of vocalization commands (see page 5)	At least **1** episode of non-reflexive oral movement (i.e., suggesting an attempt to speak, mouth opening other than yawning, lip licking, or any other oral movement that cannot be accounted for by reflexes) and/or vocalization occurs spontaneously or in response to application of sensory stimulation *Yawning is scored as reflexive oral movement.*
1	**Oral reflexive movement**	Present tongue blade between patient's lips and/or teeth	There is clamping of jaws, tongue pumping or chewing movement spontaneously or following introduction of tongue blade into mouth.
0	**None**	See above	No response to any of the above.

COMMUNICATION SCALE ©2004

Administer only if a score of 3 or 4 is achieved on the auditory subscale, a score of 3 is achieved on the Verbal/Oromotor Scale, or there is evidence of spontaneous communication (e.g., gestural or verbal yes/no responses during the exam).

Score	Item	Method	Response
2	**Functional: Accurate**	Administer the 6 Situational Orientation questions from the Communication Assessment Protocol (page 12). The examiner may use the Visual Set, Auditory set or both sets, if appropriate. Repeat the question once within 10 seconds.	Clearly discernible and accurate responses (e.g head nods/shakes, thumbs up) occur within 10 seconds on all **6** of the Visual **or** Auditory Situational Orientation questions from the Communication Assessment Protocol (see page 14)
1	**Non-functional: Intentional**	Same as above	A clearly discernible communicative response* (e.g head nods/shakes, thumbs up) must occur within 10 seconds on at least **2** of the 6 Situational Orientation questions of either set (irrespective of accuracy).
0	**None**	See above	No discernible verbal or non-verbal communication responses occur at any time.

Situational Orientation		
Visually Based		**Aurally Based**
Am I touching my ear right now? (touch nose)		Am I clapping my hands right now? (do not clap)
Am I touching my nose right now? (touch nose)		Am I clapping my hands right now? (clap)
Am I touching my ear right now? (touch ear)		Am I clapping my hands right now? (clap)
Am I touching my ear right now? (touch nose)		Am I clapping my hands right now? (do not clap)
Am I touching my nose right now? (touch ear)		Am I clapping my hands right now? (clap)
Am I touching my ear right now? (touch ear)		Am I clapping my hands right now? (do not clap)

AROUSAL SCALE ©2004

Score	Item	Method	Response
3	**Attention**	Observe consistency of behavioral responses following verbal or gestural prompts	There are **no more than 3 occasions** across the duration of the evaluation in which the patient fails to respond to a verbal or gestural prompt.
2	**Eye opening w/o Stimulation**	Observe status of the eyelids across length of assessment	Eyes remain open across the length of the examination without the need for tactile, pressure or noxious stimulation
1	**Eye opening with stimulation**	Same as above	Tactile, pressure or noxious stimulation must be applied at least once during the examination in order for the patient to sustain eye opening (the length of time the eyes remain open may vary and is not considered in the scoring)
0	**Unarousable**	See above	No eye opening noted. Note, if the eyes do not open but MCS behaviors are scored, the Arousal subscale is scored as "not testable"

ASSESSMENT OF CONTINGENT BEHAVIOR ©2004
(Supplementary Item)

Score	Item	Method	Response
Not scored	**Contingent Vocalization/ Gesture/ Affective Response**	**1**. Vocalizations, gestures and affective responses are assessed through a combination of reports from family and clinicians, and direct observations from treating staff. Family and clinical staff should be questioned about any vocalizations, gestures or affective responses (i.e., (smiling, laughing, frowning, crying) that are observed to occur spontaneously or in response to a specific stimulus. **2**. If above response is based on report, staff should attempt to directly elicit the behavior again with the assistance of the individual who reported it. **3**. If affective responses are observed during direct examination, the examiner should attempt to re-elicit the behavior using the same eliciting stimulus previously noted to produce the behavior. Examples of appropriate eliciting stimuli include verbal requests ('What's your name?'), limb gestures (waves), facial gestures (sticking out tongue) and pictures (family photos). **4.**The examiner should document: **a**. The nature of the eliciting stimulus (e.g. Verbal: 'Are you feeling sad?', Limb gesture: handshake); **b**. Specific characteristics of the behavioral response (e.g. facial grimace with tearing of the eyes, smiling, moaning); **c**. Number of times the behavior has been observed to occur within 10 seconds of the eliciting stimulus; **d**. Number of times the behavior has been observed to occur spontaneously; **e**. The time frame allowed for '**c**' and '**d**' should be specified and approximately the same.	A vocalization, gesture or affective response occurs significantly more often in response to a specific eliciting stimulus, than when the stimulus is absent. *Contingent responses do not include those that occur following administration of noxious stimuli.*

Test Completion Codes (TCC)

A TCC should be assigned to each CSR-R subscale to indicate the validity of the subscale score.

Test Completion Codes	
1	test completed in full - results valid
Test attempted, not completed due to**:**	
2.1	impaired sensory function (cortical or peripheral)
2.2	aphasia
2.3	physical injury (e.g., fracture, brachial plexus, hemiparesis)
2.4	primary language barrier
2.5	illness/medical instability
2.6	examiner error
2.7	logistical reasons
2.8	other (specify):
Test not attempted due to:	
3.1	impaired sensory function (cortical or peripheral)
3.2	aphasia
3.3	physical injury (e.g., fracture, brachial plexus, hemiparesis)
3.4	primary language barrier
3.5	illness/medical instability
3.6	examiner error
3.7	logistical reasons
3.8	other (specify):

Appendix 1.2. Hypotheses concerning which other behaviors can be considered as linked to level of consciousness and which can be seen as signs of consciousness based on results of the studies

Items	Author, Date	Population	Results	(1) Link with level of consciousness → MCS > UWS but also present in some patients with UWS = cortically mediated behaviors	(2) Possible signs of consciousness = only in patients with (E)MCS based on the CRS-R or with MCS-like patterns of brain activity on neuroimaging tools (MCS*)
Leg crossing	Rémi et al., 2011	120 severe stroke patients	Leg crossing within the first 15 days after severe stroke indicates a favorable outcome which includes less neurologic deficits, better independence in daily life, and lower rates of death.	?	?
Grimaces and cry in response to nociception	Chatelle et al., 2018	85 patients with DOC (28 UWS, 57 MCS) diagnosed with one session of the CRS-R	UWS: grimace: 18%, cry: 4%; MCS: grimace: 47%; cry: 11%	X	?
Resistance to eye opening (REO)	van Ommen et al., 2018	79 patients with DOC (23 UWS, 15 MCS-, 41 MCS+) diagnosed with repeated CRS-R	* % of presence of REO: UWS = 26%; MCS- = 53%; MCS+ = 12% * Among the six patients in UWS with REO, five showed neuroimaging results that were more compatible with the diagnosis of MCS	X	?
Learning test procedure	Lancioni et al., 2014	7 patients with DOC (2 UWS, 5 MCS) diagnosed with one session of the CRS-R	* The response frequencies of the A and B phases as well as of the B and C phases were statistically significant for all participants → all participants showed signs of learning.	X	X
Olfactory sniffing signals	Arzi et al., 2020	43 patients with DOC (146 sessions) (21 UWS, 22 MCS) diagnosed with repeated CRS-R and/or the CNC scale.	* The sniff response had a specificity of 100% for the recovery of consciousness. All patients with a sniff response ultimately showed signs of consciousness and all patients with UWS who remained unconscious did not have a sniff response.	X	X
Auditory localization	Carrière et al., 2020	186 patients with DOC (64 UWS, 28 MCS-, 71 MCS+, 23 EMCS) diagnosed with	* Auditory localization was present in 45% of DOC patients: 13% of UWS, 46% of MCS-, 62% of MCS+ and 78% of EMCS.	X	X

		repeated CRS-R assessment	* At the whole sample (n=125), difference in the survival rate between patients with and without auditory localization, with 80% of patients with auditory localization still alive compared to 55% of patients without auditory localization * In UWS patients, 29% (2/7) of LOCA patients recovered some signs of consciousness compared to 8% (3/38) of NO-LOCA patients * At the brain level, no significant differences between UWS LOCA and NO-LOCA patients with FDG-PET. However, higher functional connectivity in brain regions supporting awareness in UWS LOCA patients compared to UWS NO-LOCA patients (MRI and EEG). Patients with UWS LOCA patients also show brain similarities with MCS- patients, compared to UWS NO-LOCA.		
Habituation to the auditory startle reflex (hASR)	Hermann et al., 2020	96 DOC patients (48 UWS and 48 MCS) diagnosed with clinical assessment (neurological examination and CRS-R) and structural brain imaging	* Habituation was present in 36 of 48 (75%) MCS patients but only in 17 of 48 (35%) UWS patients * hASR correlated with MCS-like patterns of brain activity on neuroimaging tools and its presence was associated with an increase of white matter structural integrity that is predictive of motor and cognitive recovery * hASR predicts 6-month improvement of consciousness	X	X

Note. X = presence; ? = not clearly determined hitherto; UWS=Unresponsive Wakefulness Syndrome; MCS=Minimally Conscious State; EMCS=Emergence from the Minimally Conscious State; REO=Resistance to eye opening; hASR=Habituation to the auditory startle reflex; CNC=Coma–Near Coma scale; LOCA=patients showing auditory localization; NO-LOCA=patients who showed no auditory localization; FDG-PET=Fluorodesoxyglucose Positron Emission Tomography; MRI= Magnetic Resonance Imaging; EEG=Electroencephalography

Appendix 2: Additional information related to Chapter 1

Appendix 2.1 Search strategy and selected criteria

We searched Ovid Medline (Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to January 13, 2021) for articles published in English until June 31, 2020, without date restrictions. The search was completed with Scopus and Google Scholar. The results were selected and extracted by the first author (EM).

We did not include review articles, book chapters, commentaries, letters to the editor or case report.

Additional references were collected and reviewed from the included articles' reference lists.

<u>Section 1.2: Swallowing task during neuroimaging studies with healthy participants</u>

We used the following search terms: ("deglutition" or "swallowing.mp") AND ("functional magnetic resonance imaging" or "MRI" or "fMRI" or "positron emission tomography" or "PET").

Inclusion criteria: English research studies with healthy human adults > 18 years without dysphagia (within-group effects), who performed a swallowing task with a neuroimaging technique.

Of 850 papers, 31 matched our inclusion criteria. Twenty-eight studies were found with the Ovid Medline search and three studies were found by reviewing the included articles' references.

We excluded studies using magnetoencephalography, functional near-infrared spectroscopy, synthetic aperture magnetometry, movement-related cortical potentials or cortical stimulation.

<u>Section 2: Sleep and anesthesia</u>

We used the following search terms: ("deglutition" or "swallowing.mp" or "deglutition disorders" or "dysphagia.mp") AND ("sleep" (explode) or "anesthesia" (explode) or "deep sedation").

Of 527 papers, 16 matched our inclusion criteria (nine in the field of sleep and seven in anesthesia): exploration of swallowing or swallowing-related components in healthy adults or patients with neurological impairments (> 18 years) during sleep, general anesthesia or deep sedation.

We excluded studies using local anesthesia, analgesia or "light" sedation (i.e., 50% nitrous oxide in oxygen).

Section 3: Swallowing components in patients with brain injuries with a link to level of consciousness

We used the following search terms: ("deglutition" or "swallowing.mp" or "deglutition disorders" or "dysphagia.mp") AND ("brain injuries" or "cognition disorders" or "consciousness" or "consciousness disorders" or "unconsciousness" or "coma, post-head injury" or "persistent vegetative state" or "minimally conscious state.mp.").

Of 311 papers, 17 matched our inclusion criteria: exploration of swallowing or swallowing-related components (e.g., type of feeding, extubation failure, tracheotomy, risk of pneumonia) in adult patients (> 18 years) with acquired brain injury who underwent a consciousness assessment. One study (Millwood et al., 2005) not identified in PubMed was added to the analysis with a search in Google Scholar.

We excluded studies using neurological examinations such as the Glasgow Coma Scale, Glasgow Outcome Scale, National Institutes of Health Stroke Scale, Canadian Neurological Scale or Functional Independence Measure-Cognitive Score.

Section 4: Assessment and treatment of swallowing in patients with disorders of consciousness

We used the following search terms: ("deglutition" or "swallowing.mp" or "deglutition disorders" or "dysphagia.mp") AND ("brain injuries" or "cognition disorders" or "consciousness" or "consciousness disorders" or "unconsciousness" or "coma, post-head injury" or "persistent vegetative state" or "minimally conscious state.mp") AND ("diagnosis" or "scale.mp" or "assessment.mp" or "speech therapy" or "rehabilitation" or exercise therapy" or "neurological rehabilitation").

Of 127 papers, 6 matched our inclusion criteria: description of scale, tool or techniques to assess or manage swallowing disorders in patients with severe brain injuries. One reference (Brady & Pape, 2011) was added with Google Scholar.

Appendix 2.2 Description and results of the 31 identified studies with healthy human adults without dysphagia who performed a swallowing task with a neuroimaging technique

Author, Date	Number of participants (Age)	Type of neuroimaging; Design; Brain location focus	Aim(s) of the study	Brain location focus	Contrast studied	Swallowing monitoring	Mean spatial Coordinates	BA	Activations (swallowing tasks only, group data)
Voluntary swallowing studies									
Birn et al., 1998	6 (Not reported)	BOLD fMRI; Block and event-related	Measure the magnetic field changes during swallowing and speaking	Cortical	(1) Saliva swallowing every 10 s and alternately held the larynx in the maximal superior excursion for 5 s (Mendelsohn's maneuver) (2) Speaking out loud (alternately say the words "one" and "two" every 5 s)	None reported	N	N	Greatest magnetic field change in the "inferior region of the brain"
Birn et al., 1999	6 (Not reported)	BOLD fMRI; Block and event-related	Demonstrate that acquiring the average response from a brief stimulus (event-related) allows to distinguish the motion-induced signal changes that occur following the brief stimulus and prior to neuronal activation-induced signal changes	Cortical	(1) Speaking out loud (2) Saliva swallowing on command (3) Jaw clenching (4) Tongue movement	None reported	N	N	(2) Motor cortex under the region of the finger tapping motor representation
Hamdy, Mikulis, et al., 1999	10 (mean 32; 22–61 yrs)	BOLD fMRI; Single event-related	Identify cortical activity associated with human volitional swallowing	Cortical, subcortical	Volitional water swallow (5 ml water bolus into the oral cavity every 30 s) in supine position	Sound recorder	Y	Y	Areas activated: B anterorostral cingulate cortex (BA 23, 31–33), B sensorimotor cortex (BA 4, 6), B insula (BA 16), B frontal opercular cortex (BA 44), B premotor cortex (BA 6, 8), B temporal cortex (BA 21,22), B parietal cortex (BA 5), L caudate nucleus, L putamen, B posterior cingulate cortex (BA 23, 31), B prefrontal cortex (BA 10), B occipital cortex (BA 18) and B precuneus (BA 7, 31)
Hamdy, Rothwell, et al., 1999	8 (mean 48; 35–65 yrs)	$H_2{}^{15}O$ PET	Obtain precise whole brain information on the functional	Cortical	Water infused orally continuously at rates of 30, 60, or 90 ml/min and visual cue	Mylohyoid EMG	Y	Y	Group PET analysis identified increased regional cerebral blood flow (P<0.001) within:

			neuroanatomy of swallowing						B sensorimotor cortex (BA 3, 4, 6), R insula (BA 16), R orbitofrontal cortex (BA 11), R temporal cortex (BA 38), L temporal cortex and amygdala (B 38, 34), L frontal cortex and cingulate (BA 6, 32), L superiomedial cerebellum and dorsal brainstem
Mosier, Patel, et al., 1999	8 (mean 39)	BOLD fMRI; Block	Determine patterns of cortical activity during swallowing in healthy adults	Cortical	(1) 10 s volitional saliva swallow under command (2) 10 s volitional water swallow (3 ml self-administered water with a catheter against tonsillar pillars) (3) 15 s volitional saliva swallow (4) Finger tap	MRI surface electrodes	N	P	(1) (2) (3) B Primary motor cortex (midinferior lateral precentral gyrus) (BA 4), primary somatosensory cortex (BA 1, 2, 3), B SMA (BA 6), B prefrontal cortex, B superior temporal gyrus, B insula, B transverse temporal gyrus, B cingulate gyrus, B association areas, B sensorimotor integration areas, B thalamus, and B internal capsule
Mosier, Liu, et al., 1999	8 (mean 34)	BOLD fMRI; Block	Investigate the motor control of swallowing	Cortical	Same as 1999a	MRI surface electrodes	N	P	Activation occurred predominately in the midlateral precentral gyrus (BA 4), primary somatosensory cortex (BA 1, 2, 3), supplementary motor cortex (BA 6), prefrontal cortex (BA 9, 10), transverse temporal gyrus (BA 42), cingulate gyrus, insular cortex, and internal capsule (BA 24,31), speech areas (BA 44, 45), as well as in other association areas (BA 39,40), superior temporal gyrus (BA 22), and sensorimotor integration areas (BA 5, 7) The relative distribution of activation appears to change with different tasks. Each area is activated sometimes in the right hemisphere, sometimes in the left.
Zald & Pardo, 1999	(1) 8 (mean 30; 20–51 yrs) (2) 11 (mean 28; 20–52 yrs)	$H_2{}^{15}O$ PET	More precisely define a swallowing network (then the brainstem and inferior precentral gyrus)	Cortical, subcortical	(1) Voluntary saliva swallowing at approximately every 4 s during 90 s scan period vs. eyes closed resting (2) Moving the tongue from side to side	None reported	Y	Y	(1) B Inferior precentral gyrus, R anterior insula, and L cerebellum
Zald & Pardo, 2000	(1) 23 (mean 26; 18–38 yrs) (2) 8 (not reported) (3) 11 (25–62 yrs)	$H_2{}^{15}O$ PET	Examine the neural correlates of attempting to taste water	Cortical, subcortical	(1) Intraoral stimulation with water (2) Volitional saliva swallowing every 5 s (3) Odor task	None reported	Y	Y	Portions of the L anterior insula, R operculum/Rolandic cortex (BA 3,4), L precentral gyrus (BA 4,6), R postcentral gyrus (BA 43) and cerebellum (cerebellar vermis and lobules IV & V of the cerebellar hemispheres) remain significantly activated in the contrast between “tasting” water (1) and swallowing (2)

Kern, Birn, et al., 2001	14 (five subjects in each study; 21–42 yrs)	BOLD fMRI; Block and event-related	Elucidate cortical representation of 3 swallowing-related motor events (lip pursing, tongue rolling, jaw clenching) and compare to volitional swallowing	Cortical	(1) Areas activated in swallowing-related motor tasks (2) Areas activated in volitional saliva swallow (3) Areas activated in both	None reported	N	P	(2) Areas activated during block trial and/or single trial: BA 7, 19, 23, 30, 32, insula, operculum, anterior cingulate
Mosier & Bereznaya, 2001	8 (Not reported)	BOLD fMRI; Block	Determine whether the cortical organizational scheme for volitionally initiated swallowing was characterized (a) by a hierarchical dual-projection model from insular and sensorimotor areas to subcortical areas, or (b) by a heterarchical collection of independent modules operating in parallel.	Cortical, subcortical	(1) Volitional saliva swallow 10 s (2) Volitional saliva swallow 15 s (3) Volitional water swallow (3) Finger tapping task	MRI–surface electrodes	N	N	* (1) (2) (3) 5 functional clusters: (1) sensorimotor areas and cingulate gyrus; (2) inferior frontal gyrus, S2, corpus callosum, basal ganglia and thalamus; (3) premotor cortex and posterior parietal cortex; (4) cerebellum; and (5) insula. * Activation in these areas was not statistically different among swallowing tasks. * Two parallel loops defined by connections to either the cerebellum or insula and connected through the sensorimotor-cingulate module.
Fraser et al., 2002 (part 3)	8 (mean 26; 23–34 yrs)	BOLD fMRI; Block	Identify the optimal stimulus parameters promoting swallowing motor cortex reorganization in health; Determine its functional significance to swallowing; Examine its effects on swallowing motor cortex organization in acute cerebral injury; Determine its functional relevance in driving swallowing recovery after acute cerebral injury	Cortical	(1) Two 8 min functional scans: 1 min of 12 water swallows (5 ml at 5 s intervals) with visual cue (2) 1 min without swallowing	None reported	Y	Y	Areas in which a significant change in BOLD was associated with swallowing: B sensorimotor cortex (BA 1–4), anterior cingulate/SMA (BA 6, 32), B posterior cingulate (BA 31), B prefrontal gyrus (BA 10–11), B temporal lobe (BA 22), B thalamus, cerebellum
Komisaruk et al., 2002	7 (22–57 yrs)	BOLD fMRI; Block	To ascertain whether current functional MR imaging (fMRI) methods provide adequate sensitivity and resolution to reveal functional activation of specific cranial nerve nuclei in the medulla oblongata	Lower brainstem and cervical spinal cord regions	(1) Tongue tapping (2) Smile-pucker (3) Gaze shifting (4) Face brushing (5) Finger tapping (6) Mendelsohn maneuver (two swallowing cycles with prolonged laryngeal elevation for 3 s)	None reported	/	/	(6) Nucleus ambiguus activated 78% of the time during Mendelsohn maneuver and activation of inferolateral aspect of the motor cortex, just superior to the lateral sulcus (homuncular pharyngeal region)

			and pons of the lower brainstem		(7) Taste				
Suzuki et al., 2003	11 (24–42 yrs)	BOLD fMRI; Block	To investigate activation of cerebellum and basal ganglia during swallowing	Cortical, subcortical	(1) One saliva swallowing every 10 s (2) No swallow	None reported	Y	Y	B sensorimotor cortex (BA 3, 4, 6, 43, and 44), B insula (BA 13), B superior temporal gyrus (BA 22), B anterior cingular gyrus (BA 24, 32), L cerebellum (posterior lobe), B putamen, B globus pallidus, B subtantia nigra
Martin et al., 2004	14 (mean 28)	BOLD fMRI; Single event-related	Elucidate the specialized roles of the cortical and subcortical foci involved in swallowing	Cortical, subcortical	(1) Voluntary saliva swallowing (2) Voluntary tongue elevation (3) Finger opposition	MRI–surface electrodes	Y	Y	***** Largest groupwise activation: L lateral postcentral gyrus, L parietal operculum (BA 43), L supramarginal gyrus (BA 40) ***** Second prominent area: anterior cingulate gyrus (BA 32, 24), SMA (BA 6), precuneus (BA 7), cuneus (BA 18, 19), R frontoparietal operculum/insula * Modest activation: R precentral gyrus (BA 4), L pericentral cortex (BA 3, 4) * Smalls areas of activation: B middle frontal gyrus (BA 46, 9) and B superior temporal gyrus (BA 21, 22).
Harris et al., 2005	8 (mean 32 29–37 yrs)	FDG PET	Collect data on the normal metabolic brain response to swallowing, subcortical regions involved in swallowing, brain organization when swallowing while upright and compare and contrast two different analysis methods for FDG data	Cortical, subcortical	5 ml volitional water swallow (visual cue every 20 s) for 30 minutes	None reported	Y	Y	L sensorimotor cortex (BA 3, 4, 6), R prefrontal cortex (BA 10), R temporal cortex (BA 39), B lateral postcentral gyrus (BA 43), L precuneus (BA 31), B occipital cortex (BA 17–18–19), L anterior insula (BA 13), L thalamus and, L cerebellum
Toogood et al., 2005	8 (mean 23.8; 22–26 yrs)	BOLD fMRI; Single event-related	To differentiate cortical areas processing the act of swallowing from those processing aspects of the visually-cued experimental context, employing a “Go, No-Go” experimental paradigm	Cortical, subcortical	(1) Voluntary saliva swallow, “do swallow” condition (with visual cue) (2) “Don’t swallow” condition (with visual cue)	MRI–surface electrodes	N		Positive index value (greater number of voxels activated in associated with “Do Swallow” compared with “Don’t Swallow” condition): precentral gyrus, postcentral gyrus, anterior cingulated cortex (BA 24, 32), insula/operculum.
Martin et al., 2007	9 (mean 74.2 66–82 yrs)	BOLD fMRI; Single event-related	To examine the neural representations of voluntary swallowing of saliva and	Cortical	(1) Saliva swallow (once every 40 s with visual cue)	MRI–surface electrodes	Y	Y	Results with P < 0.03: (1) Precentral and postcentral gyrus, SMA, ACC, medial frontal gyrus

			swallowing of water in healthy older adults		(2) Water swallow (3 ml once every 40 s with visual cue)				(2) Precentral gyrus, pericentral, middle frontal gyrus, SMA, ACC, cuneus, precuneus, lingual gyrus Brain regions preferentially activated by water-swallowing task compared to saliva-swallowing task: B middle frontal gyrus, R superior frontal gyrus
Malandraki et al., 2009	10 (mean 21.7)	BOLD fMRI; Single event-related	To identify the neural activations of the different components of swallowing in healthy young adults	Cortical, subcortical	(1) Voluntary swallowing of 3 ml of water with visual cue (2) Planning of a swallow without execution (3) Tapping of the tip of the tongue against the alveolar ridge (4) Throat clearing	MRI–surface electrodes	N	P	(1) Precentral and postcentral gyrus, inferior parietal lobules, cingulate gyrus, Heschl's gyri (transverse temporal gyrus), midbrain, insula (BA 13), cuneus and precuneus, premotor area, cerebellum (anterior lobe, posterior lobe) [(2) superior frontal gyrus (premotor area BA 6), cingulate gyrus]
Malandraki et al., 2010	Young: 10 (mean 21.7) Old: 9 (mean 70.2)	BOLD fMRI; Single event-related	Test the hypothesis that activation in the primary motor, primary somatosensory and premotor cortices is less lateralized in the older group of participants compared with the young adults in all four swallowing-related tasks examined	ROI	(1) Voluntary swallowing of 3 ml of water with visual cue (2) Planning of a swallow without execution (3) Tapping of the tip of the tongue against the alveolar ridge (4) Throat clearing	MRI-surface electrodes	N	Y	* Young group: during swallowing there was a significant right-hemisphere activation preference in BAs 3a, 3b, and 4p * Elderly group: large equally bilateral activation in the sensorimotor and premotor cortical regions during swallowing and planning * Differences in laterality preference between the young and older adults were minimal and not statistically significant for most tasks and areas examined except during swallowing in BA 4p
Babaei et al., 2012	16 (20–34 yrs)	BOLD fMRI (distinction between positive and negative BOLD signals); Single event-related	To characterize systematically swallow-related positive and negative BOLD brain activity and evaluate their reproducibility across two sessions	Cortical, subcortical	Voluntary saliva swallow (visual cue), 21 random single trial swallows across two sessions.	None reported	Y	Y	Significantly positive BOLD activations in both sessions: B SMA, premotor (B), sensorimotor (B), Rolandic operculum (B), anterior and posterior insula (B), ventrolateral prefrontal (B), middle cingulate (B), inferior parietal lobe (B), dorsal striatum (R), R thalamus, L cerebellum
Lowell et al., 2012	14 (mean 52)	fMRI connectivity	To determine the functional interactions of several brain regions that are critical to the cortical control of swallowing, specifically the insula, primary sensorimotor cortex, and IFG, and to determine	ROI	Volitional saliva swallow (visual cue), once every 10 s (three swallows per block)	MRI–surface electrodes	Y	P	* Of the total volume of significant correlations for each seed region during volitional swallowing, positive correlations represented 98.0% for the insula as the seed region, 97.8% for the primary motor cortex as the seed region, 92.9% for the primary somatosensory cortex as the seed region, and 97.4% for BA 44 as the seed region * Lateralization: L insula, L inferior frontal gyrus, L primary motor cortex, functional

			whether laterality of functional interactions is evidenced for each region during swallowing						connectivity equivalent between L and R for primary somatosensory cortex
Babaei et al., 2013	16 (20–34 yrs)	BOLD fMRI (distinction between positive and negative BOLD signals); Single event-related	Characterize functional connectivity of neural network of swallowing, and evaluate its reproducibility and modulation during rest or task performance	Cortical, subcortical	(1) voluntary saliva swallow (with visual cue) (2) control visual task (3) resting state	None reported	Y	Y	Significantly positive BOLD activations: B prefrontal operculum (BA 44, 45), B middle cingulate (BA 24), B anterior and posterior insula (BA 13), B SMA (BA 6, 8), B premotor (BA 6, 8), B sensorimotor (BA 1-4), B Rolandic operculum (BA 43, 4), B inferior parietal (BA 40), R dorsal striatum, R thalamus, R red nucleus, L cerebellum
Luan et al., 2013	20 (mean 23.1)	BOLD fMRI; Single event-related	To use graph-theoretic approaches to examine the interaction between brain regions during voluntary saliva swallowing in healthy young adults and compare network properties between and within subjects	Cortical, subcortical with 45 ROI selected in each hemisphere	Voluntary saliva swallowing, once every 44 s	None reported	N	N	B anterior cingulate and paracingulate gyri, B paracentral lobule, B median cingulate and paracingulate gyri, B inferior parietal but supramarginal and angular gyri, B posterior cingulate gyrus, B superior parietal gyrus, B cuneus, L postcentral gyrus, B middle frontal gyrus, R precentral gyrus, B dorsolateral superior frontal gyrus, B precuneus, L fusiform gyrus, L lenticular nucleus and putamen, B hippocampus, B SMA, B insula, B supramarginal gyrus, B lingual gyrus, B superior temporal gyrus, B middle occipital gyrus, B thalamus, B superior occipital gyrus
Mihai et al., 2014	16 (mean 24.9; 20–33 yrs)	BOLD fMRI; Single event-related	To investigate changes in activation over time during a water swallowing task in young healthy subjects	ROI	Volitional water swallow	Pneumatic cushion transformed in electric signal	Y	N	Consecutive activations at the premotor cortex, SMA, and bilateral thalamus, continuing on to primary motor and sensory cortex, insula, and cerebellum and reaching the brainstem shortly before subsiding.
Windel et al., 2015	Young group: 24 (mean 24.2; 20–33 yrs) Old group: 27 (mean 64.8; 55–75 yrs)	BOLD fMRI; Single event-related	To characterize the neural representation of swallowing in healthy seniors compared to healthy young participants with a large sample size, high resolution functional imaging methods, and motor performance during imaging	Cortical, subcortical, brainstem	Voluntary water swallowing (with visual cue), 20 swallows	Pneumatic cushion transformed in electric signal	Y (only for old group)	Y	No significant difference between subject groups apart from the seniors in the frontal pole 1 of BA 10. Coordinates of highest activation for seniors: L superior temporal gyrus, R Broca pars triangularis, B sensorimotor cortex, secondary somatosensory cortex (L), B SMA, B Broca pars opercularis, anterior and medial cingulate cortex, L hippocampus, L insula, pons

Toogood et al., 2017	7 (mean 27.7)	BOLD fMRI; Single event-related	It was hypothesized that swallowing preparation would preferentially activate the premotor cortex, SMA, and ACC, whereas the sensorimotor cortex and insula would be activated during both swallowing preparation and execution	ROI	(1) Prepare to swallow (2) Voluntary saliva swallow (3) Do not prepare to swallow (4) Do not swallow (with visual cue)	MRI surface electrodes	P	Y	(2) B insula, L ventrolateral precentral and postcentral gyri (BA 3, 4, 6), a smaller R ventrolateral precentral gyrus activation along the central sulcus (BA 4), L precentral gyrus (BA 4/6), R precentral gyrus within the central sulcus, R postcentral gyrus (BA 3, 1), and a small area of the L premotor cortex. Areas of activation outside the ROIs corresponded to the superior, middle, and inferior frontal gyri, inferior parietal lobule, cuneus, and precuneus.
Kober et al., 2019	11 (mean 29.18)	BOLD fMRI; Block; Whole brain analysis and ROI in the second phase	To investigate whether execution of swallowing movements leads to comparable brain activation patterns than those elicited by imagery of swallowing movements	Cortical, subcortical	Session 1: (1) Voluntary saliva swallow vs. rest, (2) Mental imagery of swallow vs. rest, (3) Voluntary saliva swallow vs. Mental imagery of swallow Session 2: (4) Mental imagery of swallow with neurofeedback vs. rest (5) Mental imagery of swallow vs. mental imagery of swallow with neurofeedback	None	Y	N	(1) (2) B Lateral pre- and postcentral gyrus, B inferior and middle frontal gyrus, B premotor areas, primary motor areas, B SMA, B insula, B cerebellum, L globus pallidus
Lin et al., 2019	40 (mean 69.1; 52–82 yrs)	fMRI; GMV; Whole-brain VBM analysis, Cerebellum-specific VBM analysis and Cerebellum ROI analysis	To investigate the association between swallowing efficiency and gray matter volume in healthy older adults	Cortical, subcortical	Swallowing efficiency (repetitive saliva swallowing test for 30 s)	Tactile palpation	Y	/	Swallowing efficiency positively correlated with the GMV of the L cerebellum, controlled for age, gender and total intracranial volume. No significant finding in the cortical regions or the brainstem.
Spontaneous swallowing study									
Paine et al., 2011	3 (None reported)	BOLD fMRI; dynamic and MRI acquisition block (SimulScan)	To test the feasibility of using SimulScan to effectively image oropharyngeal structures and functional brain activation during swallowing	Cortical, subcortical	Spontaneous saliva swallowing	ROI in the oropharynx area	N	Y	Significant activations: sensorimotor regions (BA 3, 4), SMA and middle and superior frontal gyrus (BA 6, 9), insular cortex (BA 13), Heschl's gyri (BA 42), superior and inferior parietal lobules, anterior and posterior cingulated gyrus (BA 24, 30, 31), thalamus, midbrain, cuneus, cerebellar regions in both anterior and posterior lobes

Studies using both voluntary and spontaneous swallowing tasks									
Kern, Jaradeh, et al., 2001	8 (24–27 yrs)	BOLD fMRI; Single event-related	Compare the cerebral cortical representation of experimentally induced pharyngeal reflexive swallow with that of volitional swallow	Cortical, subcortical	(1) Volitional saliva swallows every 30 s (cued with tactile stimulation) (2) Reflex water bolus swallow (injection of a predetermined threshold volume in the pharynx once every 30 s)	EMG	N	Y	*Area activated in at least half of the subjects: (1) BA 4, 6, 18, 19, 30, insula, anterior cingulate (BA 24, 32, 33) (all areas activated B). (2) BA 1, 4, 6 * Reflexive swallowing has greater activated cortical volume in L hemisphere, and volitional swallowing has greater volume in R hemisphere ($p<0.05$)
Martin et al., 2001	14 (mean 28)	BOLD fMRI; Single event-related; Whole-brain analysis	Define the cerebral cortical representation of human swallowing; compare the patterns of cortical activation associated with "automatic" and "volitional" swallowing; test the hypothesis that there is a functional lateralization for swallowing	Cortical, subcortical	(1) Naive saliva swallow (2) Voluntary saliva swallow (3) Volitional water swallow (once 3 ml per minute in the mouth)	Oscilloscope with pressure transducer driven by expanding magnetic resonance	Y	Y	Areas significantly activated: (1) B precentral and postcentral gyrus, R insula (2) Precentral and postcentral gyrus (B), caudal anterior cingulate gyrus (R) (3) Precentral and postcentral gyrus (B), insula (R), caudal anterior cingulate gyrus (R) (1) (2) vs. (3) The three swallowing tasks produced similar regions of activation. However, activation of the caudal ACC was significantly more likely in association with the voluntary saliva swallow and the water bolus swallow than with the naive saliva swallow. Activation of the intermediate ACC more common in association with the voluntary swallowing tasks compared with the naive swallowing task.

Note. Abbreviations: BA = Brodmann area; N = no; Y = yes; P = partially; IFG = inferior frontal gyrus; SMA = supplementary motor area; ACC = anterior cingulate cortex; ROI = region of interest; R = right activation; L = left activation; B = bilateral activation; GMV = grey matter volume; VBM = voxel-based morphometry; BOLD = blood oxygen level dependent; fMRI = functional magnetic resonance imaging; PET = positron emission tomography; EMG = electromyography; MRI = magnetic resonance imaging; FDG = fluorodeoxyglucose

Appendix 2.3 Description of the consciousness scales used in the studies identified in Section 3

Rancho Los Amigos (RLA) Scale (Hagen et al., 1987b): This scale describes eight levels of cognitive functioning based on the presence or absence of a range of behaviors such as responsiveness to auditory, visual or tactile stimulations, presence or absence of sleep/wake cycle, response to command, ability to recognize family and friends, attention, memory, etc. Some authors (Hansen, Engberg, et al., 2008; O'Neil-Pirozzi et al., 2003) extrapolated the level of the RLA score to diagnostic criteria and compared RLA level II with UWS, RLA level III with MCS and an RLA level higher than III with EMCS. However, the RLA was created before the establishment of diagnostic criteria for patients with MCS (Giacino et al., 2002) and therefore does not precisely determine the patient's level of consciousness.

Full Outline of UnResponsiveness (FOUR) (Wijdicks et al., 2005): This scale consists of four components (eye, motor, brainstem, and respiration). Each component has a maximum score of 4. It allows patients with coma and UWS to be distinguished but includes only one criterion (motor response to noxious stimulation) for MCS diagnosis (Giacino et al., 2002) and none to distinguish MCS from EMCS.

Wessex Head Injury Matrix (WHIM) (Shiel et al., 2000): This scale contains 58 behavioral items divided into four sections. According to the WHIM, patients with UWS have a score between 1 and 15, MCS between 16 and 46 and emerging from post-traumatic amnesia (PTA) between 47 and 62. However, the WHIM classification does not meet all of the Aspen Workgroup diagnostic criteria (Seel et al., 2010). There is a risk of misdiagnosing a patient as having UWS when he/she would have received an MCS diagnosis with another scale (Schnakers et al., 2008).

Sensory Modality Assessment and Rehabilitation Technique (SMART) (Gill-Thwaites & Munday, 1999): The SMART examines eight modalities (visual, tactile, auditory, olfactory, gustatory stimuli, wakefulness, functional motor, communicative abilities) with a classification according to five levels of response (no response, reflexive, withdrawal, localizing, discriminating responses). The SMART does not allow one to establish a precise DOC diagnosis based on level of responsiveness. Indeed, response levels 1, 2 and 3 can be observed in patients with coma or UWS, response level 4 in patients with UWS or MCS, and response level 5 in patients with MCS or EMCS (Chatelle et al., 2010).

Coma Recovery Scale – Revised (CRS-R) (Giacino et al., 2004)*:* This scale contains six subscales (auditory, visual, motor, oromotor, communication, arousal). It is the currently recommended behavioral assessment of level of consciousness in patients with DOC. It has well-defined administration and scoring procedures that facilitate consistent use, it provides interpretive guidelines for scores and it is the only scale that allows one to differentiate UWS, MCS, and EMCS based on the Aspen Workgroup criteria (Seel et al., 2010).

Appendix 3: Additional information related to Chapter 3

STROBE Statement – Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	2, 3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3, 4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4, 5
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	Fig 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Fig 1
		(b) Give reasons for non-participation at each stage	Fig 1
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 2
		(c) Summarise follow-up time (eg, average and total amount)	Table 2
Outcome data	15*	Report numbers of outcome events or summary measures over time	NA

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	6-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	9, 10

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Appendix 4: Additional information related to Chapter 4

Appendix 4.1 English version of the SWADOC's Administration Guide

Supplementary Material 1. English version of the SWADOC's Administration Guide

Note: Non-validated translation for understanding only

Administration Guide

The SWADOC is a swallowing assessment protocol adapted for patients with disorders of consciousness (DOC). It was designed because of the lack of tools to assess swallowing-related components that were adapted to the specific features of patients with DOC (no response to commands in some cases and inability to communicate functionally). The purpose of the SWADOC is to explore certain components related to the oral and pharyngeal phases of swallowing and a series of prerequisites and other components related to swallowing. It cannot be the sole basis for judging the possibility of resuming eating, in whole or in part. In our opinion, such a decision regarding patients with DOC can only be made after an objective examination of swallowing (videofluoroscopic or nasofibroscopic examination).

The tool is non-invasive and can be used in clinical practice at patients' bedside, as an initial assessment and then repeatedly to track patients' progress.

This protocol can be used by clinicians working with patients with DOC, as a basis for both quantitative and qualitative analysis of their swallowing, which is useful in formulating their treatment plan. In addition, the quantitative items (SWADOC-scored) allow one to compute a total score and subscores for the oral and pharyngeal phases of swallowing, which can constitute a baseline for assessing the efficacy of a treatment for the patient.

This guide includes: (1) some general information to be read prior to the assessment; (2) a list of the necessary materials; (3) the items to be checked during the medical history taking; (4) specific information concerning the scoring of quantitative items; and (5) the SWADOC-scored grid (only quantitative items). You will then find a table with instructions for administering and scoring each item, both qualitative and quantitative. Finally, the appendices contain further information on the tests or protocols cited and bibliographic references.

1. **General comments**

- It is preferable for the patient to be in a sitting position during the assessment.
- While the test is being administered, the therapist must inform the patient about each stimulation to be administered.
- Before starting the patient's assessment, it is important to be sure that none of the following factors applies. If one of them does, the assessment should be delayed. Similarly, if one of these factors arises during the assessment, the assessment must be stopped: fever, ongoing infection, oxygen desaturation, unstable heart rate, autonomic crisis, and inability to keep the patient awake (a maximum of 3 arousal protocols may be applied during an assessment).

2. Materials needed for the assessment

- 2 stopwatches ⏲
- Flashlight
- Teaspoon
- Cotton swab soaked in a cold, sweet solution
- 5 mL of cold, colored thickened solution with IDDSI level 3 texture (moderately thick)[1]

3. Quantitative items

- Level 3 is the expected standard. The higher the total score, the better preserved the patient's swallowing ability is.
- A patient at time "T" cannot be at several different levels for the same item. If a patient responds at several levels, score him/her at the highest one (e.g., if a patient is able to open his/her mouth when the spoon approaches – level 2 – and on command – level 3 – the score will be level 3).
- To calculate the total score and subscores: assign 3 points for every level 3 item, 2 points for every level 2 item, 1 point for every level 1 item, and 0 points for every level 0 item. Add the scores for all items in the oral phase to calculate the oral subscore, add the scores for all items in the pharyngeal phase to calculate the pharyngeal subscore, and add the oral and pharyngeal subscores to calculate the total score.

4. Medical history

The information required for the medical history should be collected from the patient's file or from the care team.

Date and time of administration: **Patient's last and first names:** **Sex:** **Date of birth:** **Current residence:** **Receiving speech therapy:** yes / no - **Frequency:** - **Place:** at a center / at home - **Type:**	**Nutritional status:** - Current weight: - BMI (weight/height²): - Weight loss or gain during the last month: .... – during the last 6 months: .... **FILS score**[2] *(see Appendix 1)* and corresponding level: ………… For a FILS score of less than 7, specify the **enteral feeding method:** ☐ gastrostomy ☐ jejunostomy ☐ nasogastric tube For a FILS score of more than 3, specify the **IDDSI score**[1] (or equivalent – *see Appendix 2*) **for foods:** ………. **Help required during meals:** yes / no – if yes, from whom: ………………………….

Date of accident: **Type of accident:** □ Vascular □ Traumatic □ Anoxic □ Other: **Location of brain lesion:** **Glasgow score at time of accident:** - Eye opening: - Verbal response: - Motor response:	**Hydration:** □ enteral □ oral In case of oral hydration, specify the **IDDSI score**[1] **for drinks:** **ENT problems before accident:** yes / no – specify: …………………………………………………………………… **ENT problems since accident:** yes / no – specify: …………………………………………………………………… **Ongoing or recent lung infections:** yes / no – specify: …………………………………………………………………… **Respiratory kinesiotherapy:** yes / no – if yes, specify the frequency of sessions: …………………………………………………………………… **Medication that may affect:** □ consciousness □ swallowing □ salivation – specify: …………………………………………………………………… **Hypersalivation:** yes / no – **Treatment of hypersalivation:** □ toxins □ patches Patient able to produce: □ spontaneous sounds □ words □ reliable communication **Communication code:** yes / no – specify: …………………………………………………………………… **Scores on the SECONDs**[3,4] **or the CRS-R**[5] at the time of assessment and corresponding level: ……………………………………….

5. Presentation grid for quantitative items (SWADOC-scored)

	Items	Level 0	Level 1	Level 2	Level 3
Oral phase	**1. Initiation of mouth opening**	□ Mouth opening impossible or only with the therapist's active assistance	□ Mouth opening upon lip stimulation	□ Mouth opening upon presentation of spoon	□ Mouth opening upon command (min 2/3)
	2. Endo-buccal secretions	□ Substantial amount of secretions (80%–100%)	□ Moderate amount of secretions (20%–80%)	□ Few secretions (0%–20%)	□ Moist mouth but without significant secretions
	3. Lip prehension	□ No lip prehension (no reaction or tightening of lips)	□ Incomplete lip prehension spontaneously or upon verbal stimulation	□ Appropriate lip prehension but not consistently or only upon verbal stimulation	□ Consistently correct, spontaneous lip prehension
	4. Tongue propulsion	□ No tongue movement: passive movement of the bolus to the pharyngeal level, stagnation in mouth or expulsion when drooling	□ A few tongue movements but not sufficient to propel the bolus	□ Pathological tongue propulsion, possibly with post-swallowing stasis	□ Appropriate tongue propulsion
Pharyngeal phase	**1. Initiation of saliva swallowing reflex**	□ No saliva swallowing spontaneously or upon stimulation	□ Saliva swallowing only upon stimulation	□ Saliva swallowing spontaneously and upon stimulation	□ Saliva swallowing upon command (min 2/3)
	2. Latency of swallowing reflex triggering upon stimulation	□ No triggering or cannot be completed	□ > 10 seconds	□ 5 to 10 seconds	□ 0 to 5 seconds
	3. Tracheostomy	□ Tracheostomy with inflated cuff	□ Tracheostomy with cuff, ongoing deflation	□ Tracheostomy without cuff or with permanently deflated cuff	□ Tracheostomy with ongoing weaning, or no tracheostomy
	4. Bronchial congestion	□ Frequent bronchopneumonia or heavy congestion	□ Moderate congestion	□ Little congestion	□ No congestion
SWADOC-scored – oral phase: /12		**SWADOC-scored – pharyngeal phase: /12**		**SWADOC-scored – total: /24**	

6. Protocol for assessing swallowing in patients with disorders of consciousness

Procedure for examination	Instructions	Scoring (qualitative items – quantitative items oral phase – quantitative items pharyngeal phase)	Materials
1. Arousal	When you enter the room, check the patient's arousal: → If the patient is awake, introduce yourself and start the assessment: **Greet the patient** orally, using his/her first name and touching his/her hand or arm. **Introduce yourself** and explain why you are there: for example, "Hello, my name is… I'm a speech therapist. I've come to see how you're doing and suggest some stimulation activities and exercises for you." → If the patient is asleep, try to wake him/her by using any kind of sensory stimulation: changing his/her position, increasing the light in the room, touching or speaking to him/her, etc. If this does not work, use the CRS-R[6] arousal protocol. At the end of the assessment, note how long the patient kept his/her eyes open.	**Waking time:** □ 0%–25% □ 25%–50% □ 50%–75% □ 75%–100% **Stimulation needed:** □ Auditory – specify: ……………………………………………………………… □ Tactile – specify: ……………………………………………………………… □ Visual – specify: ………………………………………………………………	
2. Resting position of the head, eyes, masseters and lips	**Resting position:** Note the position of the head, lips and masseters at rest, whether there is any facial or lip paralysis, and whether the eyes are open. If members of the care team or the family are present, ask whether this is the "usual" head position. Position yourself on the side where the patient's gaze is oriented, based on the head position.	→ **Patient's position:** □ in bed □ in (wheel)chair → **Resting head position:** - *Verticality:* □ Neutral □ Flexion □ Extension - *Horizontality:* □ Neutral □ R rotation □ L rotation □ R tilt □ L tilt → **Lips at rest:** □ Normal contact □ No contact □ Hypertonic contact (tightening) → **Masseter tone at rest:** □ Relaxed (normal) □ Hypertonia □ Hypotonia □ Contracted-relaxed → **Paresis, if any:** □ facial □ labial □ none + *side:* □ left □ right → **Eyes open:** □ Both eyes □ Possible to open both eyes but one eye open preferentially: □ L □ R □ Only possible to open one eye → **Spontaneous head movements:** □ yes □ no → **Resting respiration:** □ mouth □ nose □ tracheostomy	

3. External stimulation of orofacial area	→ **Passive head mobilization:** Place an open hand at the base of the skull and try to lightly move the head in different directions. → **Head support:** Remove the cushion or lift the head if it is flexed and note whether the head can be supported for the next 10 seconds.	→ **Passive head mobility:** □ Possible without resistance □ Possible but with resistance and tension felt □ Impossible → **Head support:** □ Satisfactory □ Possible briefly (<3 seconds) □ Impossible	
	→ **Firm pressure** *(see Appendix 4)*: Apply a series of firm pressures and relaxations at a steady pace, with open palms on the face = forehead and top of skull, both temples, eye and top of skull, both cheeks, mouth and top of skull Signs of discomfort may include grimacing, attempts to avoid contact, etc. → **Light touch** *(see Appendix 4)*: With your index finger, stroke different areas of the face, spacing stimulations 5 seconds apart = temples to forehead, cheeks, chin, upper lip, lower lip. Signs of discomfort could include pressing the tongue against the palate. NB: To be taken into account in assessing the sensitivity profile.	→ **Firm pressure:** □ No reaction □ Sign of discomfort + Specify the type of sign: …………………………………………………………… → **Light touch:** □ No reaction □ Sign of discomfort + Specify the type of sign: ……………………………………………………………	
4. Mouth opening	⏱ **Item B1. Initiation of mouth opening:** 1. Ask the patient "Open your mouth" 3 times, leaving a minimum of 10 seconds between requests. Level 3 is achieved if the patient opens his/her mouth a minimum of twice. 2. If there is no reaction to the request to open the mouth, bring a spoon up to the patient's mouth – repeat 3 times if the patient does not react within 10 seconds. 3. If there is no reaction 10 seconds after the third presentation of the spoon, rub the spoon, and then your index finger, back and forth on the lower lip. 4. If there is no reaction after 10 seconds, press your thumb against the lower jaw (active assistance). If the patient opens his/her mouth constantly, a greater mouth opening reaction to the approach of the spoon is expected. If there is not this reaction, score 0. **NB**: If the patient does not open his/her mouth with active assistance from the therapist, take this into account in assessing the tonicity profile as "T+ hypercontraction."	□ *Level 3*: Opens mouth upon command (min 2/3) □ *Level 2*: Opens mouth upon presentation of spoon □ *Level 1*: Opens mouth upon lip stimulation □ *Level 0*: Cannot open mouth or only with active assistance by therapist	Empty spoon Stopwatch
	Amplitude of mouth opening: To determine whether food can pass through, verify that the mouth opening (obtained in item B1) equals at least 2 fingers (index and middle fingers)	**Amplitude of mouth opening:** □ 2 fingers □ more than 2 fingers □ less than 2 fingers	

5. Mouth cavity observations	Describe the patient's **oral hygiene and dental condition.**	→ **Oral hygiene:** □ satisfactory □ dry □ coated → **Describe teeth:** □ Full set of teeth □ No teeth □ Partial set of teeth + specify: → **Dental condition:** □ Good □ Tartar □ Gingivitis □ Bleeding □ Worn □ Bruxism □ Food residue → **Dental prosthesis:** □ yes □ no → **Appliance for bruxism:** □ yes □ no → **Drooling:** □ yes □ no **If yes:** □ left □ right	Flashlight
	Item B2. Endo-buccal secretions: Observe the presence and amount of saliva or dry or moist mucus secreted in the patient's mouth cavity: cheeks, buccal vestibule, floor of the mouth, tongue and oropharynx. Determine whether the amount of saliva and mucus secreted in the mouth in relation to the size of the mouth cavity is approximately 0%–20%, 20%–80% or 80%–100% or if there are no secretions. NB: If the mouth cannot be opened, try to observe secretions at other times (e.g., when the patient yawns). Score 0 if the item cannot be assessed.	□ *Level 3*: Moist mouth without significant secretions □ *Level 2*: Few visible secretions (0%–20%) □ *Level 1*: Moderate amount of secretions (20%–80%) □ *Level 0*: Substantial amount of secretions (80%–100%)	Flashlight
	Describe the **appearance** of the saliva or mucus secretions in the mouth: texture, color, etc.	**Appearance of secretions:**	
6. Initiation of saliva swallowing reflex	◷ **Item P1. Initiation of saliva swallowing reflex:** 1. Ask the patient "Swallow your saliva," making an exaggerated head movement and placing your hand on your throat to indicate movement of the larynx. Make this request 3 times, leaving a minimum of 10 seconds between requests. Level 3 is achieved if the patient swallows a minimum of twice. 2. If there is no reaction to the request, move on to item "P2. Latency of swallowing reflex triggering upon stimulation." Then score item P1 on the basis of the swallowing upon stimulation observed for item P2, and on the basis of saliva swallowing observed during the examination.	□ *Level 3*: Swallows saliva upon command (min 2/3) □ *Level 2*: Swallows saliva spontaneously and upon stimulation □ *Level 1*: Swallows saliva only upon stimulation □ *Level 0*: No saliva swallowing spontaneously or upon stimulation	Stopwatch
	If applicable, specify whether the verbal command **triggered incomplete swallowing** (tongue movements or laryngeal raising without triggering of swallowing):	□ Swallowing started upon verbal command but not completed	

7. Triggering of saliva swallowing reflex upon stimulation	⏱ **Item P2. Latency of triggering swallowing reflex upon stimulation:** Brush a cotton swab soaked in a cold, sweet solution across the following areas, 3 times each: (1) tongue apex, (2) base of the tongue, (3) velum (soft palate), and (4) posterior pharyngeal wall. **NB:** If the mouth cannot be opened, stimulate the lips. Record the reaction time after each stimulation. If there is no lip or tongue movement and swallowing does not occur upon stimulation, **wait 10 seconds** before moving on to the next area. If a lip or tongue movement occurs after stimulation, **wait 30 seconds** maximum before moving on to the next area.	□ *Level 3*: 0 to 5 seconds □ *Level 2*: 5 to 10 seconds □ *Level 1*: > 10 seconds □ *Level 0*: No triggering or not successful	Cotton swab soaked in cold, sweet solution Stopwatch
	NB: Stop the stopwatch when the patient triggers a complete swallow (and not merely movements). Note the **time taken** to trigger swallowing in this area in P2. Note which areas triggered swallowing and which ones triggered incomplete swallowing (larynx raised jerkily, start of tongue propulsion, etc.). **Criteria for stopping** scoring the item**:** 1. Triggering of a swallowing reflex 2. Occurrence of a gag reflex 3. No reaction after stimulation of the posterior pharyngeal wall	**Area(s) that triggered swallowing:** □ Lips □ Tongue apex □ Base of tongue □ Velum □ Posterior pharyngeal wall □ No swallowing **Area(s) that triggered incomplete swallowing:** □ Lips □ Tongue apex □ Base of tongue □ Velum □ Posterior pharyngeal wall □ No incomplete swallowing	
	If swallowing is triggered during the stimulations in item P2 but there is no gag reflex, continue the stimulations in P2 to see whether **the gag reflex exists and where it is triggered**. NB: To be taken into consideration in the assessment of the sensitivity profile.	**Gag reflex:** □ yes □ no **Area(s) that triggered gag reflex:** □ Lips □ Tongue apex □ Base of tongue □ Velum □ Posterior pharyngeal wall **Other signs of discomfort:** …………………………………………………………………	Cotton swab soaked in cold, sweet solution
	If swallowing occurs, note the **quality of laryngeal raising:**	**Laryngeal raising:** □ yes □ no □ Abnormal: 0 incomplete 0 slow 0 jerky	

8. Functional test	◷ **Items B3. Lip prehension and B4. Tongue propulsion:** • Prepare a teaspoon containing 5 mL of cold, moderately thick colored solution (IDDSI level 3 texture) (NB: 5 mL = approx. 1 teaspoon). • Restart the initiation of mouth opening protocol (item B1) and present the prepared spoon. • Observe the lip prehension of the spoon (**item B3**). If the patient does not react, stimulate him/her verbally by saying "Take the spoon." • If there is no mouth opening or lip prehension upon presentation of the spoon but it is possible to open the mouth passively, place the contents of the spoon on the patient's tongue and observe the reactions. • Start the stopwatch when lip prehension occurs or the liquid is placed on the tongue. • Observe the tongue propulsion (**item B4**), placing one hand under the floor of the patient's mouth to feel any tongue movements. • Check for the existence of any post-swallowing oral stasis. If the patient does not present any lip or tongue reaction **after 10 seconds**, score 0. If the patient presents complete lip prehension (level 3 for item B3), do two more trials with an empty spoon to verify the stability of prehension. If the patient continues to succeed at this item, score level 3; if the patient fails the second or third time, score level 2. **NOTE: If the patient does not show any saliva swallowing upon stimulation (level 0 for item P1), no spontaneous swallowing is observed or the patient has a strong bite reflex or trismus, the functional test should not be carried out.** In this case, "tongue propulsion" should be scored 0 and "lip prehension" should be tested with an empty spoon. **NB:** Similarly, if the functional test cannot be done because the mouth will not open, the "tongue propulsion" and "lip prehension" items must be scored 0.	**B3. Lip prehension:** ☐ *Level 3*: Consistently correct, spontaneous lip prehension ☐ *Level 2*: Appropriate lip prehension but not consistently or only upon verbal stimulation ☐ Level 1: Incomplete lip prehension spontaneously or upon verbal stimulation ☐ *Level 0*: No lip prehension (no reaction or tightening of lips) **B4. Tongue propulsion:** ☐ *Level 3*: Appropriate tongue propulsion ☐ *Level 2*: Pathological tongue propulsion, possibly with post-swallowing stasis ☐ *Level 1*: A few tongue movements but not sufficient to propel the bolus ☐ *Level 0:* No tongue movement: passive transfer of the bolus to the pharyngeal level, stagnation in mouth or expulsion when drooling	Stopwatch Teaspoon 5 mL of cold, colored thickened solution with IDDSI level 3 texture (moderately thick)

	In addition to the lip prehension and tongue propulsion items above, note whether there is any **triggering of swallowing and/or coughing and/or going down the wrong way (inhalation).**	→ **Triggering of swallowing reflex:** □ yes □ no → **Triggering time after the liquid has touched the tongue:** … sec → **Multiple swallows:** □ yes □ no → **Coughing episode:** □ yes □ no If yes: □ before swallowing □ after swallowing □ remotely → **Signs of increased congestion or dyspnea:** □ yes □ no → **Other signs of inhalation:** ……………….....................................	
	Note the characteristics of triggering of **tongue movements:**	Spontaneous tongue movements: → **Not associated with attempts to swallow:** □ yes □ no → **During attempts to swallow** saliva: □ yes □ no → **In response to stimulation** of the face, lips or tongue itself: □ yes □ no + If yes, specify the stimulation that triggered tongue movements: …………………………………...	
	Note signs of any **primitive reflexes** upon mouth opening and lip prehension:	→ **Bite reflex:** □ yes □ no → **Sucking reflex:** □ yes □ no → **Chewing reflex:** □ yes □ no	
	In case of swallowing, note the **quality of laryngeal raising.**	**Laryngeal raising:** □ yes □ no □ Abnormal: O incomplete O slow O jerky	
	Item P3. Tracheostomy: Question the care team, look at the patient's file and/or observe the patient's tracheostomy.	□ *Level 3*: Tracheostomy with ongoing weaning – tube can be plugged with a finger – or no tracheostomy □ *Level 2*: Tracheostomy without a cuff or with a permanently deflated cuff □ *Level 1*: Tracheostomy with a cuff, ongoing deflation □ *Level 0*: Tracheostomy with an inflated cuff If there is no tracheostomy, did the patient have one in the past? □ yes □ no	Patient's file

9. Respiration	**Item P4. Respiration and upper and lower airway congestion:** Question the care team, look at the patient's file and/or observe the patient. To assess the level of congestion in the upper and lower airways, look for the **severity of the following signs of congestion** in the patient: noisy or whistling breathing, coughing that indicates the presence of mucus, etc. It is also important to consider the **number of intraoral or endotracheal aspirations** done by the care team or the patient himself/herself. Finally, the need for **respiratory kinesiotherapy treatment** should be considered.	□ *Level 3*: no congestion □ *Level 2*: little congestion □ *Level 1*: moderate congestion □ *Level 0*: frequent bronchopneumonia or heavy congestion	Patient's file
	If **congestion** exists, specify the type.	→ **Breathing aid systems:** □ humidifiers □ oxygen In case of oxygen treatment, number of liters or %: ………………… → **Upper airway congestion:** □ yes □ no – specify: …………………………………………………………………… → **Lower airway congestion:** □ yes □ no – specify: …………………………………………………………………… → **Frequency of aspirations:** …………………………………………………………………… → **Frequency of respiratory kinesiotherapy:** ……………………………………………………………………	
10. Voice Articulation Language	Note the ability to produce **spontaneous sounds, articulate words or reliable communication** (according to the SECONDs, correct responses to 5 simple closed-ended autobiographical questions):	→ **Spontaneous noises/sounds:** □ yes □ no → **Articulate words:** □ yes □ no → **Reliable communication:** □ yes □ no	
11. Tonicity and sensitivity profiles	**Tonicity profile**: Observe the patient's facial appearance at rest, during tactile stimulations and during initiation of mouth opening tests.	□ *T– profile: hypotonicity*: mouth continuously open, drooling □ *T+ profile: hypertonicity/tightness*: clenches teeth continuously and/or during tactile stimulation, resists mouth opening □ *T neutral profile*: no signs of hypotonicity or hypertonicity	
	Sensitivity profile: Observe reactions to external and internal stimulation in the orofacial area and the gag reflex.	□ *S– profile: hyposensitivity*: no reaction to tactile stimulation, weak gag reflex or none □ *S+ profile: hypersensitivity*: startles, grimaces during light touch tactile stimulation, exaggerated gag reflex □ *S neutral profile*: no signs of hyposensitivity or hypersensitivity	

SWADOC-scored – Total : /24	**SWADOC-scored – oral phase: /12** **SWADOC-scored – pharyngeal phase: /12**	**Tonicity profile: T+ / Tn / T–** **Sensitivity profile: S+ / Sn / S–**
Comments:		

APPENDICES

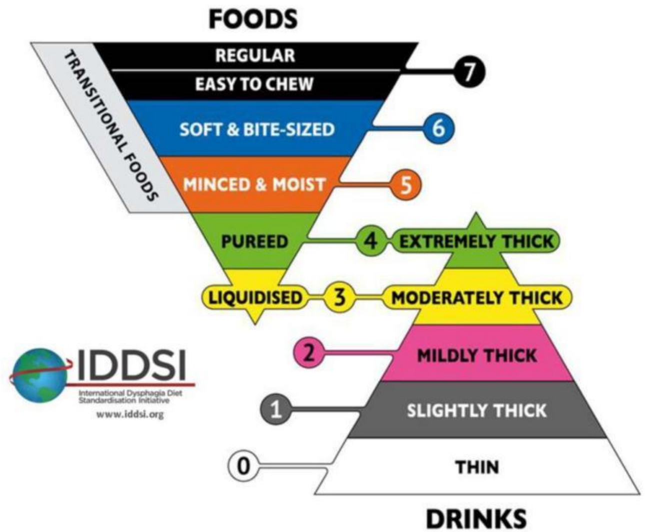
Appendix 1: items of the *Food Intake Level Scale* (FILS)[2]

No oral intake
Level 1: No swallowing training is performed except for oral care.
Level 2: Swallowing training not using food is performed.
Level 3: Swallowing training using a small quantity of food is performed.
Oral intake and alternative nutrition
Level 4: Easy-to-swallow food less than the quantity of a meal (enjoyment level) is ingested orally.
Level 5: Easy-to-swallow food is orally ingested in one to two meals, but alternative nutrition is also given.
Level 6: The patient is supported primarily by ingestion of easy-to-swallow food in three meals, but alternative nutrition is used as a complement.
Oral intake alone
Level 7: Easy-to-swallow food is orally ingested in three meals. No alternative nutrition is given.
Level 8: The patient eats three meals by excluding food that is particularly difficult to swallow.
Level 9: There is no dietary restriction, and the patient ingests three meals orally, but medical considerations are given.
Level 10: There is no dietary restriction, and the patient ingests three meals orally (normal).

Comments:
- Swallowing training: Training conducted by an expert, well-instructed caregiver, or the patient himself/herself to improve the swallowing function.
- Easy-to-swallow food: Food that is prepared so that it is easy to swallow even without mastication, for example, meat and vegetables are gelatinized or homogenized in a mixer.
- Alternative nutrition: Non-oral nutrition such as tube feeding and drip infusion.
- Food that is particularly difficult to eat: dry and brittle food, hard food, water, and so on.
- Medical considerations: guidance, tests, examinations, and so on, for symptoms suggestive of swallowing disorders such as choking and the feeling of food remaining in the pharynx.

Appendix 2: International Dysphagia Diet Standardisation Initiative (IDDSI)[1]

For the corresponding FILS scores, note the textures of food and drinks offered to patients using the IDDSI terminology.



Appendix 3: arousal protocol of the Coma Recovery Scale Revised (CRS-R) [5,6]

AROUSAL FACILITATION PROTOCOL (AFP) ©2004

GUIDELINES

1) The goal of this intervention is to prolong the length of time the patient maintains arousal (i.e. eye opening)

2) The protocol is administered any time the patient is observed to:

   - Exhibit sustained eyelid closure **AND/OR**

   - Stops following commands for a period of at least one minute

3) Readminister the arousal facilitation protocol when

   - Sustained eye closure re-occurs **OR**

   - Behavioral responsiveness ceases despite sustained eye opening

INTERVENTIONS

Deep Pressure:

1) Present deep pressure stimulation unilaterally to the face, neck, shoulder, and sternocleidomastoid muscles. The muscle should be firmly grasped at its base between the thumb and forefinger. While squeezing the muscle firmly, it should be "rolled" back and forth through the fingertips three to four times. This procedure should be repeated sequentially working from the facial musculature to the sternocleidomastoid. The examiner should assure that there are no intravenous lines, local injuries (e.g. fractures, contusions, decubiti) or systemic complications (e.g. heterotopic ossification) before administering deep pressure.

2) Administer same on contralateral side.

Appendix 4: External stimulations of the orofacial area

Objective:
This subtest assesses the patient's reactions to facial tactile stimulation. It is mainly intended to determine the patient's sensitivity and tonicity "profiles" in reaction to stimulations in order to guide the patient's treatment.
This subtest is inspired by the orofacial sensitivity subtest of the Comprehensive Assessment Measure for the Minimally Responsive Individual (CAMMRI)[7] in the case of light touch and by the stimulation methods for sensory processing disorder (sensory dysorality) proposed by Catherine Senez[8] for firm pressure ("going around the house").

Materials:
- Latex/vinyl gloves

Test administration:
Tell the patient you are going to touch different areas of his/her face.
Follow the specific order in the data form for the areas targeted. First do the firm pressure test, followed by the light touch test.

1) **Firm pressure**

Using both hands, with the palms open and placed on the patient's head, engage in a series of sequences of contact, pressure, relaxation of pressure and removal of hands. The pressures must succeed each other at a steady pace, and very quickly. The pressure applied should be moderate to firm in one location in the area to be stimulated (do not stroke the whole area).

Description of the stimulation:
- Forehead and top of skull
- Both temples
- One eye and top of skull (cup your hand to avoid touching the eye)
- The other eye and top of skull
- Both cheeks
- Mouth and top of skull

2) Light touch

During light stimulation, stroke with your index finger. Touch each area only once. Space the simulations 5 seconds apart.

Areas to stimulate	Description of the stimulation
a) Temples/ forehead	Stroke continuously from the temple to the midline of the face, on one side and then the other
b) Cheeks	Start at the height of the middle of the ear, follow the cheekbone and stop in the mid-eye area
c) Chin	With your index finger flattened, move up the length of the chin
d) Upper lip	Stroke the lip from left to right
e) Lower lip	Stroke the lip from left to right

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Guide de passation

L'outil SWADOC est un protocole d'évaluation de la déglutition adapté aux patients en état de conscience altérée (ECA). Il a été conçu suite au constat du manque d'outils adaptés aux spécificités des patients ECA (absence de réponse à la commande pour certains et absence de communication fonctionnelle) permettant d'apprécier une série de composants en lien avec la déglutition. L'outil SWADOC a pour objectif d'explorer certains composants en lien avec la phase orale et pharyngée de la déglutition ainsi qu'une série de prérequis et autres composants en lien avec la déglutition. Il ne permet pas de statuer à lui seul sur la possibilité d'une reprise alimentaire, partielle ou totale. Une telle décision auprès des patients ECA ne peut, à notre avis, être prise qu'après un examen objectif de la déglutition (vidéofluoroscopie ou nasofibroscopie de la déglutition).

L'évaluation est non-invasive et utilisable en pratique clinique au chevet des patients, en évaluation initiale puis de manière répétée pour suivre l'évolution du patient.

Ce protocole pourra être utilisé par les cliniciens intervenant auprès des patients ECA, comme une base d'analyse à la fois quantitative et qualitative de leur déglutition, utile dans la formulation de leur projet thérapeutique. De plus, les items quantitatifs (SWADOC-scored) permettent de calculer un score global et des sous-scores de la phase buccale et de la phase pharyngée, qui pourront constituer une ligne de base à l'évaluation de l'efficacité d'une prise en charge auprès du patient.

Ce guide comprend : 1) Une série d'informations générales préalables à l'évaluation 2) Le matériel nécessaire, 3) Les éléments à relever lors de l'anamnèse, 4) Quelques spécificités concernant la cotation des items quantitatifs, 5) La grille SWADOC-scored (items quantitatifs uniquement). Vous trouverez ensuite le tableau reprenant les consignes de passation et de cotation de chaque item, qualitatif comme quantitatif. Enfin, vous trouverez en annexe des précisions sur les tests ou protocoles cités, ainsi que les références bibliographiques.

1. **Remarques générales**

- Il est préférable que le patient soit en position assise lors de l'évaluation
- Au fil de la passation de l'évaluation, le thérapeute informera le patient sur chaque stimulation qui lui est proposée
- Avant de commencer l'évaluation du patient, il convient de s'assurer qu'aucun des éléments suivants n'est présent. Si un de ces éléments est présent, il convient de reporter l'évaluation. De même, si un de ces éléments apparaît au cours de l'évaluation, il convient d'arrêter l'évaluation : fièvre, infection en cours, désaturation en oxygène, instabilité de la fréquence cardiaque, crise neurovégétative, impossibilité à stimuler le patient pour qu'il reste éveillé (on réalisera au maximum 3 protocoles d'éveil lors d'une évaluation)

2. **Matériel nécessaire à l'évaluation**

- 2 chronomètres 🕓
- Lampe de poche
- Cuillère à café
- Coton-tige imbibé d'une solution sucrée et froide
- 5 mL de solution colorée épaissie froide texture IDDSI3 (modérément épais)[1]

3. **Items quantitatifs**

- Le niveau 3 est la norme attendue. Plus le score global est élevé, plus les capacités de déglutition du patient sont préservées.
- Un patient à un instant « t » ne peut pas se trouver dans plusieurs niveaux différents pour un même item. Dans le cas où un patient valide plusieurs niveaux, on lui accorde le niveau le plus élevé lors de la cotation (par exemple, si un patient est capable d'ouvrir la bouche à l'approche de la cuillère –niveau 2- et sur commande –niveau 3-, on cote le niveau 3)
- Pour calculer le score global et les sous-scores : compter 3 pour chaque sous-item de niveau 3, 2 pour chaque item de niveau 2, 1 pour chaque item de niveau 1 et 0 pour chaque item de niveau 0. Additionner le score de chaque item de la phase buccale pour calculer le sous-score buccal, additionner le score de chaque item de la phase pharyngée pour calculer le sous-score pharyngé, et additionner les sous-scores buccal et pharyngé pour calculer le score global.

4. **Anamnèse**

Les informations requises pour l'anamnèse sont à recueillir dans le dossier du patient, ou auprès de l'équipe soignante.

Date et heure de passation : **Nom et prénom du patient :** **Sexe** : **Date de naissance** : **Endroit où réside le patient actuellement** : **Suivi logopédique** : oui / non - **Fréquence** : - **Lieu** : en centre / à domicile - **Type** :	**Statut nutritionnel** : - Poids actuel : - IMC (poids/taille²) : - Perte ou prise de poids au cours du dernier mois : .... - au cours des 6 derniers mois : ….... **Score à la FILS**[2] *(voir annexe n°1)* et niveau correspondant : ………… Pour un score FILS inférieur à 7, préciser le **mode d'alimentation entérale** : ☐ gastrostomie ☐ jéjunostomie ☐ sonde naso-gastrique Pour un score FILS supérieur à 3, préciser le **score IDDSI**[1] (ou équivalent -*voir annexe n°2*) **pour les aliments** : ……….

Date de l'accident : **Type d'accident** : □ Vasculaire □ Traumatique □ Anoxique □ Autre : **Localisation de l'atteinte cérébrale** : **Score de Glasgow au moment de l'accident** : - Ouverture des yeux : - Réponse verbale : - Réponse motrice :	**Aide requise lors des repas** : oui / non – si oui par qui : ………………………… **Hydratation** : □ entérale □ per os En cas d'hydratation per os, préciser le **score IDDSI**[1] **pour les liquides** : **Antécédents ORL préalables à l'accident** : oui / non – préciser : ……………………………………………………………… **Affections ORL depuis l'accident** : oui / non – préciser : ……………………………………………………………… **Infections pulmonaires en cours ou récentes** : oui / non – préciser : ……………………………………………………………… **Prise en charge en kinésithérapie respiratoire** : oui / non – si oui, préciser la fréquence des séances : ……………………………………………………………… **Médication pouvant affecter :** □ l'état de conscience □ la déglutition □ la salivation – préciser : ……………………………………………………………… **Hypersalivation** : oui / non – **Traitement de l'hypersalivation** : □ toxines □ patchs Patient capable de produire : □ sons spontanés □ mots □ communication fiable **Code de communication** : oui / non – préciser : ……………………………………………………………… **Scores à la SECONDs**[3,4] **ou à la CRS-R**[5] au moment de l'examen, et niveau correspondant : ………………………………………

5. Grille de présentation des items quantitatifs (SWADOC-scored)

	Items	Niveau 0	Niveau 1	Niveau 2	Niveau 3
Phase buccale	**1. Initiation d'ouverture buccale**	◻ Ouverture de la bouche impossible ou seulement sur aide active du thérapeute	◻ Ouverture buccale sur stimulation labiale	◻ Ouverture buccale à l'approche de la cuillère	◻ Ouverture buccale sur commande (min 2/3)
	2. Sécrétions endo-buccales	◻ Sécrétions en quantité significative (80-100%)	◻ Sécrétions en quantité modérée (20-80%)	◻ Peu de sécrétions (0-20%)	◻ Bouche humide mais sans sécrétions significatives
	3. Préhension labiale	◻ Aucune préhension labiale (pas de réaction ou serrage des lèvres)	◻ Préhension labiale incomplète en spontané ou sur stimulation verbale	◻ Préhension labiale adéquate mais non-systématique ou uniquement sur stimulation verbale	◻ Préhension labiale correcte et spontanée systématiquement
	4. Propulsion linguale	◻ Aucun mouvement lingual : passage passif du bolus au niveau pharyngé, stagne en bouche ou ressort en bavage	◻ Quelques mouvements linguaux mais insuffisants pour propulser le bolus	◻ Propulsion linguale pathologique avec présence possible de stases post-déglutition	◻ Propulsion linguale adéquate
Phase pharyngée	**1. Initiation du réflexe de déglutition salivaire**	◻ Pas de déglutition de salive que ce soit sur stimulation ou spontanément	◻ Déglutition de salive uniquement sur stimulation	◻ Déglutition de salive spontanée et sur stimulation	◻ Déglutition de salive sur commande (min 2/3)
	2. Latence de déclenchement du réflexe de déglutition sur stimulation	◻ Pas de déclenchement ou non-réalisable	◻ > 10 sec	◻ Entre 5 et 10 secondes	◻ Entre 0 et 5 secondes
	3. Trachéotomie	◻ Trachéotomie avec ballonnet gonflé	◻ Trachéotomie avec ballonnet en cours de sevrage	◻ Trachéotomie sans ballonnet ou avec ballonnet dégonflé en permanence	◻ Trachéotomie en cours de sevrage, ou absente
	4. Respiration et encombrement haut et bas	◻ Bronchopneumonies fréquentes ou encombrement important	◻ Encombrement modéré	◻ Peu d'encombrement	◻ Pas d'encombrement
SWADOC-scored phase buccale: /12		**SWADOC-scored phase pharyngée: /12**		**SWADOC-scored total: /24**	

6. Protocole d'évaluation de la déglutition chez les patients en état de conscience altérée

Enchaînement de l'examen	Consignes	Notation (items qualitatifs – items quantitatifs phase buccale – items quantitatifs phase pharyngée)	Matériel
1. Eveil	En entrant dans la chambre, vérifier l'éveil du patient : → Si le patient est éveillé, se présenter et commencer l'évaluation : **Saluer le patient** oralement en utilisant son prénom et en touchant sa main ou son bras. **Se présenter** et expliquer la raison de notre présence : par exemple, « Bonjour, je m'appelle… Je suis logopède/orthophoniste. Je viens voir comment vous allez et vous proposer quelques stimulations et exercices. » → Si le patient sommeille, essayer de le réveiller en utilisant n'importe quel type de stimulation sensorielle : changer sa position, la luminosité de la pièce, le toucher, lui parler, etc. Si cela ne fonctionne pas, utiliser le protocole d'éveil de la CRS-R[5] *(voir annexe n°3)*. A la fin de l'évaluation, noter dans quelle mesure le patient a gardé les yeux ouverts.	**Temps d'éveil** : □ 0-25% □ 25-50% □ 50-75% □ 75-100% **Stimulations nécessaires** : □ Auditives – préciser : …………………………………………………………… □ Tactiles – préciser : …………………………………………………………… □ Visuelles – préciser : ……………………………………………………………	
2. Position au repos de la tête, des yeux, des masséters et des lèvres	**Position au repos** : noter la position de la tête, des lèvres et des masséters « au repos » ainsi que la présence éventuelle d'une paralysie faciale ou labiale, et l'ouverture des yeux Si des membres de l'équipe soignante ou la famille sont présents, demander si c'est la position de la tête « habituelle ». Se positionner du côté où le regard est orienté d'après la position de la tête.	→ **Position du patient** : □ au lit □ au fauteuil → **Position de la tête « au repos » :** - *Verticalité* : □ Neutre □ Flexion □ Extension - *Horizontalité* : □ Neutre □ Rotation D □ Rotation G □ Inclinaison D □ Inclinaison G → **Lèvres au repos :** □ Contact normal □ Lèvres sans contact □ Contact hypertonique (serrage) → **Tonus des masséters au repos :** □ Relâché (normal) □ Hypertonie □ Hypotonie □ Contracté-relâché → **Parésie éventuelle :** □ faciale □ labiale □ pas de parésie + *côté* : □ gauche □ droite → **Ouverture des yeux :** □ Deux yeux □ Ouverture possible des deux yeux mais un œil ouvert préférentiellement : □ G □ D □ Ouverture d'un seul œil possible → **Mouvements spontanés de la tête** : □ oui □ non → **Respiration au repos** : □ buccale □ nasale □ trachéotomie	

3. Stimulations externes de la sphère oro-faciale	→ **Mobilisation passive de la tête** : poser une main ouverte au niveau de la base du crâne et tenter de mobiliser légèrement la tête dans les différentes directions → **Soutien de la tête** : retirer le coussin ou relever la tête si elle est en flexion et noter si le soutien de la tête est possible pendant les 10 secondes qui suivent	→ **Mobilité passive de la tête** : □ Possible sans résistance □ Possible mais avec résistance et tensions ressenties □ Impossible → **Soutien de la tête** : □ Satisfaisant □ Possible mais bref (<3sec) □ Impossible	
	→ **Pressions fermes** *(voir annexe n°4)* : réaliser une série de pressions fermes - relâchements de pression à un bon rythme, paumes ouvertes au niveau de la face = front-sommet du crâne, deux tempes, œil-sommet du crâne, deux joues, bouche-sommet du crâne Des exemples de manifestations d'incommodités pourraient être des grimaces, des tentatives d'évitement du contact, etc. → **Toucher léger** *(voir annexe n°4)* : effleurer avec l'index différentes zones de la face, en espaçant chaque stimulation de 5 secondes = tempes vers front, joues, menton, lèvre supérieure, lèvre inférieure. Des exemples de manifestations d'incommodités pourraient être le fait de coller sa langue au palais. NB : A prendre en compte dans l'évaluation du profil de sensibilité	→ **Pressions fermes :** □ Aucune réaction □ Manifestation d'incommodité + Préciser le type de manifestation : …………………………………………………………………… → **Toucher léger** : □ Aucune réaction □ Manifestation d'incommodité + Préciser le type de manifestation : ……………………………………………………………………	
4. Ouverture buccale	◷ **Item B1. Initiation d'ouverture buccale :** 1. Demander au patient « Ouvrez la bouche » 3 fois, en laissant minimum 10 secondes entre chaque demande. Le niveau 3 est atteint si le patient ouvre la bouche lors de minimum 2 demandes. 2. En l'absence de réaction à la commande d'ouverture buccale, approcher une cuillère de sa bouche – à répéter 3 fois si le patient ne réagit pas au bout de 10 secondes 3. En l'absence de réaction 10 secondes après la 3ème approche de la cuillère, faire des allers-retours avec la cuillère puis avec l'index sur sa lèvre inférieure 4. En l'absence de réaction au bout de 10 sec, appuyer avec le pouce sur sa mâchoire inférieure (aide active) Si le patient a une ouverture buccale constante, on recherchera une réaction d'ouverture buccale plus grande à l'approche de la cuillère. En l'absence de cette réaction, on cotera le niveau 0. **NB** : Si le patient n'ouvre pas sa bouche sur aide active du thérapeute, on tiendra compte de cette information pour l'évaluation du profil de tonicité en « T+ hypercontraction »	□ *Niveau 3* : Ouverture buccale sur commande (min 2/3) □ *Niveau 2* : Ouverture buccale à l'approche de la cuillère □ *Niveau 1* : Ouverture buccale sur stimulation labiale □ *Niveau 0* : Ouverture de la bouche impossible ou seulement sur aide active du thérapeute	Cuillère vide Chronomètre

	Amplitude d'ouverture buccale : pour estimer si le passage d'aliments est possible, vérifier que cette ouverture buccale (obtenue à l'item B1) est au moins égale à 2 doigts (index et majeur)	**Amplitude d'ouverture buccale** : □ égale à 2 doigts □ supérieure à 2 doigts □ inférieure à 2 doigts	
5. Observations intra-buccales	Décrire **l'hygiène buccale et l'état dentaire** du patient	→ **Hygiène buccale** : □ satisfaisante □ sécheresse □ chargée → **Décrire la dentition :** □ Dentition complète □ Edentition totale □ Edentition partielle + préciser : → **Etat dentaire** : □ Correct □ Tartre □ Gingivite □ Saignements □ Dents « limées » □ Bruxisme □ Résidus alimentaires → **Prothèse dentaire** : □ oui □ non → **Prothèse pour bruxisme** : □ oui □ non → **Présence de bavage** : □ oui □ non **Si oui** : □ gauche □ droite	Lampe de poche
	Item B2. Sécrétions endo-buccales : Observer la présence et la quantité de sécrétions salivaires ou bronchiques sèches ou humides dans la bouche du patient : dans les joues, les sillons labiaux, sur le plancher de bouche, sur la langue et dans l'oropharynx. On détermine si la quantité de sécrétions salivaires et bronchiques en bouche par rapport à la taille de la cavité orale est plutôt de l'ordre de 0-20%, de 20-80% ou de 80-100% ou si elles sont absentes. NB : si aucune ouverture buccale n'est possible, tenter d'observer la présence éventuelle de sécrétions salivaires à d'autres moments (lors de bâillements par exemple). Noter 0 si l'item n'a pas pu être évalué.	□ *Niveau 3* : Bouche humide mais sans sécrétions significatives □ *Niveau 2* : Peu de sécrétions visibles (0-20%) □ *Niveau 1* : Sécrétions en quantité modérée (20-80%) □ *Niveau 0* : Sécrétions en quantité significative (80-100%)	Lampe de poche
	Décrire **l'aspect** des sécrétions salivaires ou bronchiques intra-buccales : texture, couleur, etc.	**Aspect des sécrétions** : ………………………………………………..	
6. Initiation du réflexe de déglutition salivaire	🕓 **Item P1. Initiation du réflexe de déglutition salivaire :** 1. Demander au patient « Avalez votre salive », en faisant un mouvement exagéré de tête et en plaçant notre main sur notre gorge pour indiquer le mouvement du larynx. Faire cette demande 3 fois, en laissant minimum 10 secondes entre chaque demande. Le niveau 3 est atteint si le patient déglutit lors de minimum 2 demandes. 2. En l'absence de réaction à la commande, passer à l'item « P2. Latence de déclenchement du réflexe de déglutition sur stimulation ». Puis coter l'item P1 sur la base des déglutitions sur stimulation observées à l'item P2, ainsi que sur la base des déglutitions salivaires observées pendant l'examen.	□ *Niveau 3* : Déglutition de salive sur commande (min 2/3) □ *Niveau 2* : Déglutition de salive spontanée et sur stimulation □ *Niveau 1* : Déglutition de salive uniquement sur stimulation □ *Niveau 0* : Pas de déglutition de salive que ce soit sur stimulation ou spontanément	Chronomètre
	Le cas échéant, préciser si la commande verbale a **amorcé une déglutition non aboutie** (mouvements de langue ou ascensions laryngées sans déclenchement de la déglutition) :	□ Déglutition amorcée par la commande verbale mais non aboutie	

7. Déclenchement du réflexe de déglutition salivaire sur stimulation	🕓 **Item P2. Latence de déclenchement du réflexe de déglutition salivaire sur stimulation :** Faire trois allers-retours de gauche à droite avec un coton-tige imbibé d'une solution sucrée et froide sur les différentes zones, dans l'ordre suivant : 1) Apex lingual, 2) Base de langue, 3) Voile du palais, 4) Mur postérieur pharyngé **NB :** si aucune ouverture buccale n'est possible, stimuler les lèvres. Chronométrer le temps de réaction après chaque stimulation. Si aucun mouvement labial ou lingual ni déglutition ne survient après une stimulation, **attendre 10 secondes** pour passer à la zone suivante. Si un mouvement labial ou lingual survient suite à la stimulation, **attendre 30 secondes** maximum puis passer à la zone suivante. NB : On arrête le chronomètre quand le patient déclenche une déglutition aboutie (et pas uniquement des mouvements). Noter le **temps** mis pour le déclenchement de la déglutition dans cette zone en P2. Noter quelles zones ont déclenché une déglutition et quelles zones ont amorcé une déglutition non aboutie (élévation laryngée en plusieurs à coups, début de propulsion linguale, etc). **Critère d'arrêt** de cotation de l'item **:** 1. Déclenchement d'un réflexe de déglutition 2. Survenue d'un réflexe nauséeux 3. Pas de réaction après stimulation au niveau du mur postérieur pharyngé	□ *Niveau 3* : entre 0 et 5 secondes □ *Niveau 2* : entre 5 et 10 secondes □ *Niveau 1* : > 10 sec □ *Niveau 0* : Pas de déclenchement ou non-réalisable **Zone(s) ayant déclenché une déglutition :** □ Lèvres □ Apex lingual □ Base de langue □ Voile du palais □ Mur postérieur pharyngé □ Absence de déglutition aboutie **Zone(s) ayant amorcé une déglutition non aboutie** : □ Lèvres □ Apex lingual □ Base de langue □ Voile du palais □ Mur postérieur pharyngé □ Absence de déglutition non aboutie	Coton-tige imbibé d'une solution sucrée et froide Chronomètre
	Si une déglutition se déclenche au cours des stimulations de l'item P2 mais pas un réflexe nauséeux, continuer les stimulations de l'item P2 pour rechercher la présence d'un **réflexe nauséeux et sa zone de déclenchement**. NB : A prendre en compte dans l'évaluation du profil de sensibilité	**Réflexe nauséeux** : □ oui □ non **Zone ayant déclenché le réflexe nauséeux :** □ Lèvres □ Apex lingual □ Base de langue □ Voile du palais □ Mur postérieur pharyngé **Autres signes d'incommodité** : …………………………………………………………………………	Coton-tige imbibé d'une solution sucrée et froide
	En cas de déglutition, noter la **qualité de l'ascension laryngée**	**Ascension laryngée :** □ Présente □ Absente □ Présente anormalement : O incomplète O ralentie O en plusieurs à-coups	

8. Test fonctionnel	◷ **Items B3. Préhension labiale et B4. Propulsion linguale :** • Préparer une cuillère à café contenant 5mL de solution colorée modérément épaissie (texture IDDSI3) froide (NB : 5 mL = 1 cuillère à café). • Reproposer le protocole d'initiation de l'ouverture buccale (item B1) et présenter la cuillère préparée. • Observer la préhension labiale de la cuillère (**item B3**). Si le patient ne réagit pas, le stimuler verbalement en disant : « Prenez la cuillère ». • S'il n'y a pas d'ouverture buccale et de préhension labiale à l'approche de la cuillère mais qu'il est possible d'entrouvrir la bouche passivement, déposer le contenu de la cuillère sur la langue et observer les réactions. • Lancer le chronomètre au moment de la préhension labiale ou quand le liquide est déposé sur la langue. • Observer la propulsion linguale (**item B4**), en plaçant une main sous le plancher buccal du patient pour sentir les éventuels mouvements de la langue. • Vérifier la présence éventuelle de stases buccales post-déglutition. Si le patient ne présente aucune réaction labiale ou linguale **au bout de 10 secondes**, coter 0. Si le patient présente une préhension labiale complète (niveau 3 de l'item B3), refaire deux essais avec une cuillère vide pour vérifier la stabilité de la préhension. Si le patient réussit toujours cet item, coter niveau 3 ; si le patient échoue au 2e ou au 3e essai, coter niveau 2. **ATTENTION : si le patient ne présente aucune déglutition salivaire sur stimulation (niveau 0 à l'item P1), qu'aucune déglutition spontanée n'est observée ou qu'il a un réflexe de morsure important ou un trismus, le test fonctionnel ne sera pas réalisé.** Dans ce cas, l'item « propulsion linguale » sera coté 0 et l'item « préhension labiale » sera testé avec une cuillère vide. **NB :** De même, si le test fonctionnel ne peut être réalisé car aucune ouverture buccale n'est possible, les items « propulsions linguale » et « préhension labiale » seront cotés 0.	**B3. Préhension labiale :** □ *Niveau 3* : Préhension labiale correcte et spontanée systématiquement □ *Niveau 2* : Préhension labiale adéquate mais non-systématique ou uniquement sur stimulation verbale □ Niveau 1 : Préhension labiale incomplète en spontané ou sur stimulation verbale □ *Niveau 0* : Aucune préhension labiale (pas de réaction ou serrage des lèvres) **B4. Propulsion linguale :** □ *Niveau 3* : Propulsion linguale adéquate □ *Niveau 2* : Propulsion linguale pathologique avec présence possible de stases post-déglutition □ *Niveau 1* : Quelques mouvements linguaux mais insuffisants pour propulser le bolus □ *Niveau 0 :* Aucun mouvement lingual : passage passif du bolus au niveau pharyngé, stagne en bouche ou ressort en bavage	Chronomètre Cuillère à café 5mL de solution colorée épaissie froide texture IDDSI3 (modérément épais)

	En plus des items de préhension et de propulsion linguale ci-dessus, noter la présence éventuelle d'un **déclenchement d'une déglutition et/ou d'une toux et/ou d'une fausse route.**	→ **Déclenchement d'un réflexe de déglutition** : □ oui □ non → **Temps de déclenchement après que le liquide ait touché la langue** : … sec → **Déglutitions multiples :** □ oui □ non → **Episode de toux** : □ oui □ non Si oui : □ avant déglutition □ après déglutition □ à distance → **Signes d'encombrement majoré ou dyspnée** : □ oui □ non → **Autres signes de fausse route :** ………………………………………	
	Noter les caractéristiques du déclenchement de **mouvements linguaux** :	Mouvements linguaux spontanés : → **En dehors des tentatives de déglutition** : □ oui □ non → **Lors des tentatives de déglutitions** salivaires : □ oui □ non → **En réponse à stimulation** du visage, des lèvres ou de la langue elle-même : □ oui □ non + Si oui, préciser la stimulation qui a induit les mouvements linguaux : …………………………………………………………………	
	Noter la présence d'éventuels **réflexes archaïques** à l'ouverture de la bouche et à la préhension labiale :	→ **Réflexe de morsure :** □ oui □ non → **Réflexe de succion :** □ oui □ non → **Réflexe de mâchonnement :** □ oui □ non	
	En cas de déglutition, noter la **qualité de l'ascension laryngée**	**Ascension laryngée :** □ Présente □ Absente □ Présente anormalement : O incomplète O ralentie O en plusieurs à-coups	
	Item P3. Trachéotomie : Questionner l'équipe soignante, regarder dans le dossier du patient et/ou observer la trachéotomie du patient.	□ *Niveau 3* : Trachéotomie en cours de sevrage, possibilité de boucher la canule au doigt ou absence de trachéotomie □ *Niveau 2* : Trachéotomie sans ballonnet ou avec ballonnet dégonflé en permanence □ *Niveau 1* : Trachéotomie avec ballonnet en cours de sevrage □ *Niveau 0* : Trachéotomie avec ballonnet gonflé Si pas de trachéotomie, le patient en a-t-il eu une dans le passé : □ oui □ non	Dossier du patient

9. Respiration	**Item P4. Respiration et encombrement haut et bas** : Questionner l'équipe soignante, regarder dans le dossier du patient et/ou observer le patient. Pour évaluer le niveau d'encombrement haut et bas, repérer la **sévérité des signes d'encombrement** suivants chez le patient : respiration bruyante ou sifflante, toux laissant percevoir la présence de mucus, etc. Il convient également de prendre en compte la **quantité d'aspirations intrabuccales et/ou endotrachéales** réalisées par l'équipe soignante ou le patient lui-même. Enfin, le **besoin d'un suivi en kinésithérapie respiratoire** est à prendre en compte.	◻ *Niveau 3* : pas d'encombrement ◻ *Niveau 2* : peu d'encombrement ◻ *Niveau 1* : encombrement modéré ◻ *Niveau 0* : bronchopneumonies fréquentes ou encombrement important	Dossier du patient
	En cas **d'encombrement**, préciser son type.	→ **Systèmes aidant la respiration** : ◻ humidificateurs ◻ oxygénation Si oxygénation, nombre de litres ou % : ………………………………. → **Encombrement haut** : ◻ oui ◻ non – préciser : …………………………………………………………………………… → **Encombrement bas** : ◻ oui ◻ non – préciser : …………………………………………………………………………… → **Fréquence des aspirations :** …………………………………………………………………………… → **Fréquence de la kiné respiratoire :** ……………………………………………………………………………	
10. Voix Articulation Langage	Noter la capacité à produire des **bruits spontanés, des mots articulés ou une communication fiable** (d'après la SECONDs, réponse correcte à 5 questions autobiographiques simples et fermées) :	→ **Bruits/sons spontanés** : ◻ oui ◻ non → **Mots articulés** : ◻ oui ◻ non → **Communication fiable** : ◻ oui ◻ non	
11. Profils de tonicité et de sensibilité	**Profil de tonicité** : Observer l'aspect facial du patient au repos, lors des stimulations tactiles et lors des essais d'initiation d'ouverture buccale	◻ *Profil T- : hypotonicité* : ouverture buccale en continu, bavage ◻ *Profil T+ : hypercontraction/serrage* : serre les dents en continu et/ou lors des stimulations tactiles, résiste à l'ouverture buccale ◻ *Profil T neutre* : absence de signes d'hypotonicité ou d'hypertonicité	
	Profil de sensibilité : Observation des réactions aux stimulations externes et internes de la sphère oro-faciale, et du réflexe nauséeux	◻ *Profil S- : hyposensibilité* : absence de réaction aux stimulations tactiles, réflexe nauséeux faible ou absent ◻ *Profil S+ : hypersensibilité* : sursauts, grimaces lors des stimulations tactiles de toucher léger, réflexe nauséeux exacerbé ◻ *Profil S neutre* : absence de signes d'hyposensibilité ou d'hypersensibilité	

SWADOC-scored total : /24	**SWADOC-scored phase buccale : /12** **SWADOC-scored phase pharyngée : /12**	**Profil de tonicité : T+ / Tn / T-** **Profil de sensibilité : S+ / Sn / S-**
Remarques :		

ANNEXES

Annexe 1 : items traduits de la *Food Intake Level Scale* (FILS)[2]

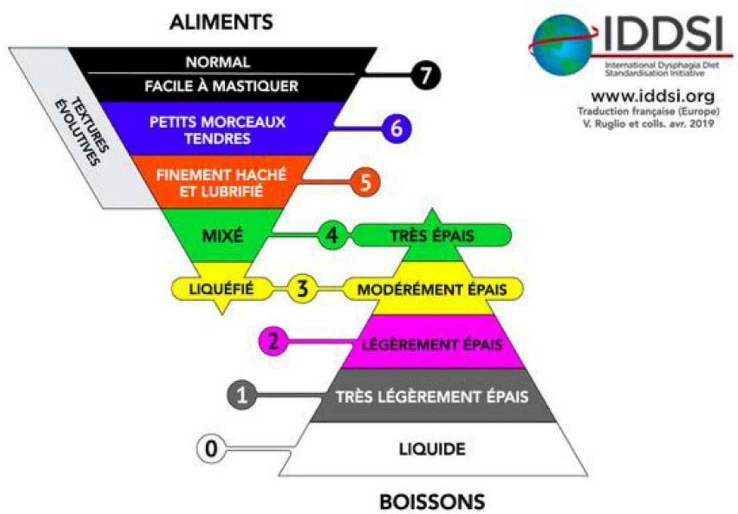
Pas d'alimentation orale
Niveau 1 : pas de stimulation de la déglutition en dehors des soins buccaux.
Niveau 2 : stimulations de la déglutition « à vide » (sans nourriture)
Niveau 3 : stimulations de la déglutition utilisant une petite quantité de nourriture
Combinaison d'alimentation orale et alimentation entérale
Niveau 4 : alimentation en texture facile et en quantité moindre qu'un repas (alimentation plaisir) ingérée oralement.
Niveau 5 : alimentation en texture facile ingérée oralement correspondant à un ou deux repas mais une alimentation complémentaire non-orale est aussi donnée.
Niveau 6 : alimentation en texture facile reçue à trois repas mais une alimentation non-orale est aussi donnée en complément.
Alimentation orale uniquement
Niveau 7 : alimentation en texture facile aux trois repas. Pas d'alimentation complémentaire non-orale.
Niveau 8 : le patient ingère trois repas en excluant les aliments qui sont particulièrement difficile à avaler.
Niveau 9 : le patient ingère trois repas sans restriction au niveau des textures mais des conseils médicaux sont donnés.
Niveau 10 : alimentation orale ordinaire aux trois repas.

Remarques sur les termes employés :

- Stimulations de la déglutition : stimulations réalisées par un thérapeute compètent dans le domaine, un soignant formé ou le patient lui-même pour améliorer sa déglutition.
- Alimentation en texture facile : aliments qui sont préparés de telle manière qu'ils sont faciles à déglutir même sans mastication par exemple de la viande et des légumes sous forme pâteuse ou homogénéisée dans un mixer.
- Alimentation non-orale : gastrostomie, sonde naso-gastrique ou alimentation parentérale.
- Aliments qui sont particulièrement difficiles à avaler : aliments secs et fragmentables, aliments durs, eau, etc.
- Conseils médicaux : conseils donnés dans le but de limiter les symptômes dysphagiques comme les épisodes de toux ou la sensation d'aliments stagnant dans le pharynx.

Annexe 2 : standardisation internationale des textures adaptées à la dysphagie (IDDSI)[1]

Pour les scores à la FILS correspondant, nous noterons les textures d'aliments et d'hydratation proposées aux patients en suivant la terminologie internationale IDDSI (International Dysphagia Diet Standardisation Initiative).



Annexe 3 : protocole d'éveil de la *Coma Recovery Scale Revised* (CRS-R)[5,6]

PROTOCOLE DE STIMULATION D'EVEIL ©2008
INDICATIONS
1) Le but de cette intervention est de prolonger la durée d'éveil du patient (ouverture des yeux). 2) Ce protocole doit être administré à chaque fois que le patient : - Démontre des périodes prolongées de fermeture des yeux ET/OU - Arrête de répondre aux questions pendant 1 minute ou plus 3) Recommencer le protocole de simulation d'éveil quand : - Une fermeture prolongée des yeux se reproduit ET/OU - Les réponses comportementales arrêtent malgré une ouverture spontanée des yeux
INTERVENTIONS
Pression profonde : 1) Effectuez une pression profonde unilatérale au niveau du visage, la nuque, la main, le torse, le dos, la jambe, et les orteils. Pendant que vous pincez le muscle de manière intense vous le « roulez » 3 à 4 fois entre l'index et le pouce. Cette procédure doit être répétée de manière séquentielle dans le sens du visage vers les orteils. Assurez-vous qu'il n'y ait pas de lignes internes, lésions locales (fractures, contusions, ulcérations) avant d'entamer la pression profonde. 2) Répéter la procédure du côté controlatéral.

Annexe 4 : stimulations externes de la sphère oro-faciale

Objectif :
Ce sous-test évalue les réactions du patient à des stimulations tactiles faciales. Il vise notamment à déterminer le « profil » de sensibilité et de tonus du patient, en réaction aux stimulations afin d'orienter la prise en charge du patient.
Ce subtest s'est inspiré du sous-test de la sensibilité oro-faciale de la Comprehensive Assessment Measure for the Minimally Responsive Individual (CAMMRI)[7] pour les stimulations légères et des méthodes de stimulation des dysoralités sensorielles de Catherine Senez[8] pour les stimulations fermes (tour de la maison).

Matériel :
- Gants en latex/vinyl

Administration du test :
Dites au patient que vous allez toucher des zones de son visage.
Suivez l'ordre spécifique du formulaire de données concernant les zones à cibler. Faites d'abord le test de la pression ferme puis celui du toucher léger.

1) **Pressions fermes**

En utilisant les deux mains, paumes ouvertes et posées sur la tête du patient, il faut réaliser une série de contacts, pressions, lâchés de pression, retraits. Les pressions devront se succéder suivant un bon rythme et très rapidement. La pression appliquée doit être modérée à ferme en un endroit de la zone à stimuler (pas d'effleurement de toute la zone).
Description de la stimulation :

- Front-sommet du crâne
- Les deux tempes
- Un œil-sommet du crâne (creuser la main pour ne pas toucher l'œil)
- L'autre œil-sommet du crâne
- Les deux joues
- La bouche-sommet du crâne

2) Toucher léger

Pendant les stimulations légères, effectuez des effleurements avec l'index. Ne touchez qu'une seule fois chaque zone d'application. Espacez chaque stimulation de 5 secondes.

Zones à stimuler	**Description de la stimulation**
a) Tempes/front	Utiliser une caresse continue de la tempe jusqu'au centre du visage, un côté puis l'autre
b) Joues	Commencer au niveau du milieu de l'oreille, suivre l'os de la joue et s'arrêter dans la zone du milieu de l'œil
c) Menton	Index à plat, remonter le long du menton
d) Lèvre supérieure	Caresser la lèvre de gauche à droite
e) Lèvre inférieure	Caresser la lèvre de gauche à droite

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Appendix 4.3 SWADOC-scored (French version)

	Items	Niveau 0	Niveau 1	Niveau 2	Niveau 3
Phase buccale	**1. Initiation d'ouverture buccale**	☐ Ouverture de la bouche impossible ou seulement sur aide active du thérapeute	☐ Ouverture buccale sur stimulation labiale	☐ Ouverture buccale à l'approche de la cuillère	☐ Ouverture buccale sur commande (min 2/3)
	2. Sécrétions endo-buccales	☐ Sécrétions en quantité significative (80-100%)	☐ Sécrétions en quantité modérée (20-80%)	☐ Peu de sécrétions (0-20%)	☐ Bouche humide mais sans sécrétions significatives
	3. Préhension labiale	☐ Aucune préhension labiale (pas de réaction ou serrage des lèvres)	☐ Préhension labiale incomplète en spontané ou sur stimulation verbale	☐ Préhension labiale adéquate mais non-systématique ou uniquement sur stimulation verbale	☐ Préhension labiale correcte et spontanée systématiquement
	4. Propulsion linguale	☐ Aucun mouvement lingual : passage passif du bolus au niveau pharyngé, stagne en bouche ou ressort en bavage	☐ Quelques mouvements linguaux mais insuffisants pour propulser le bolus	☐ Propulsion linguale pathologique avec présence possible de stases post-déglutition	☐ Propulsion linguale adéquate
Phase pharyngée	**1. Initiation du réflexe de déglutition salivaire**	☐ Pas de déglutition de salive que ce soit sur stimulation ou spontanément	☐ Déglutition de salive uniquement sur stimulation	☐ Déglutition de salive spontanée et sur stimulation	☐ Déglutition de salive sur commande (min 2/3)
	2. Latence de déclenchement du réflexe de déglutition sur stimulation	☐ Pas de déclenchement ou non-réalisable	☐ > 10 sec	☐ Entre 5 et 10 secondes	☐ Entre 0 et 5 secondes
	3. Trachéotomie	☐ Trachéotomie avec ballonnet gonflé	☐ Trachéotomie avec ballonnet en cours de sevrage	☐ Trachéotomie sans ballonnet ou avec ballonnet dégonflé en permanence	☐ Trachéotomie en cours de sevrage, ou absente
	4. Respiration et encombrement haut et bas	☐ Bronchopneumonies fréquentes ou encombrement important	☐ Encombrement modéré	☐ Peu d'encombrement	☐ Pas d'encombrement
SWADOC-scored phase buccale: /12		**SWADOC-scored phase pharyngée: /12**		**SWADOC-scored total: /24**	

Appendix 4.4 The FOTT-SAS (table adapted from Mortensen et al., 2016)

Items	Yes	No
1) Conscious and/or respond to verbal address?		
2) Abel to sit upright with some degree of head control?		
3) Oral transport of saliva?		
4) Spontaneous or facilitated swallowing of saliva?		
5) Coughing following swallowing of saliva?		
6) Gurgling breath sound following swallowing of saliva?		
7) Difficulties in breathing following swallowing of saliva?		
Based on the above questions, should oral intake be initiated? (Oral intake should be initiated if items 1-4=Yes and items 5-7=No)		

Appendix 5: original published articles

Appendix 5.1 Is oral feeding compatible with an unresponsive wakefulness syndrome

Journal of Neurology
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ORIGINAL COMMUNICATION

CrossMark

Is oral feeding compatible with an unresponsive wakefulness syndrome?

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Abstract

Objective The aim of the study is to explore the possibility of oral feeding in unresponsive wakefulness syndrome/vegetative state (UWS/VS) patients.

Method We reviewed the clinical information of 68 UWS/VS patients (mean age 45 ± 11; range 16–79 years) searching for mention of oral feeding. UWS/VS diagnosis was made after repeated behavioural assessments using the Coma Recovery Scale—Revised. Patients also had complementary neuroimaging evaluations (positron emission tomography, functional magnetic resonance imaging and electroencephalography and diffusion tensor imaging).

Results Out of the 68 UWS/VS patients, only two could resume oral feeding (3%). The first patient had oral feeding (only liquid and semi liquid) in addition to gastrostomy feeding and the second one could achieve full oral feeding (liquid and mixed solid food). Clinical assessments concluded that they fulfilled the criteria for a diagnosis of UWS/VS. Results from neuroimaging and neurophysiology were typical for the first patient with regard to the diagnosis of UWS/VS but atypical for the second patient.

Conclusion Oral feeding that implies a full and complex oral phase could probably be considered as a sign of consciousness. However, we actually do not know which components are necessary to consider the swallowing conscious as compared to reflex. We also discussed the importance of swallowing assessment and management in all patients with altered state of consciousness.

Keywords Swallowing · Dysphagia · Oral-feeding · Consciousness · Unresponsive wakefulness syndrome

Evelyne Mélotte and Audrey Maudoux contribute equally to this work as first author.

Steven Laureys, Olivia Gosseries and Audrey Vanhaudenhuyse contribute equally to this work as last author.

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Background

The unresponsive wakefulness syndrome (UWS/VS) is a disorder of consciousness characterized by the presence of eye-opening and reflexive movements, without conscious behaviours [1]. In patients with UWS/VS, cortical white and grey matters are severely affected [2]. Fluorodeoxyglucose positron emission tomography (FDG-PET) studies show impairment of metabolism in the polymodal associative cortices but relatively preserved metabolism in the brainstem [3, 4]. Swallowing is a complex sensorimotor function which is either initiated voluntary or occurs spontaneously (reflex swallowing). Each type of swallowing activates different cortical regions. Neuroimaging studies demonstrated that while the central pattern generator (CPG; localized in the brainstem) mediates the reflexive component of swallowing, many cortical regions are involved in voluntary as

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well as in reflex swallowing [5–8]. However, even if both forms of swallowing involve cortical regions activation, the network of brain regions activated during reflexive swallowing is different from that observed during volitional swallowing [5–8]. More specifically, fMRI studies in healthy volunteers showed that cerebral cortical representation of saliva and water reflexive swallow mainly involved bilateral primary sensorimotor cortices and insular cortices [5, 7]. On the other hand, during saliva and water bolus volitional swallows, there is an activation of the primary sensorimotor, premotor, prefrontal, frontal opercular, temporal and insular cortices, anterior cingulate gyrus and precuneus with a most consistent cortical activation in the primary sensorimotor cortex [5, 7, 8]. In the case of UWS/VS, patients classically receive hydration and nutrition through an enteral feeding tube. The possibility of resuming oral feeding in the UWS/VS population is greatly debated [2, 9–12], and it is actually unclear if the presence of oral feeding is compatible with the diagnosis of UWS/VS or if this observation should lead to a modification of diagnosis (i.e. minimally conscious state). In this article, we document the feasibility of oral feeding in patients with UWS/VS.

Method

We retrospectively reviewed the clinical information of 68 chronic patients in UWS/VS. These patients were sent by their institution, doctor or family to be hospitalized for a 1-week multimodal assessment in the University Hospital of Liege. From December 2006 to May 2017, 68 chronic patients in UWS/VS underwent this hospitalization week. The inclusion criteria were a chronic state (> 3 months after onset) and a diagnosis of UWS/VS. Diagnosis of UWS/VS was made after repeated behavioural assessments by trained and experienced neuropsychologists using the Coma Recovery Scale—Revised (CRS-R, [13]). The CRS-R consists of six subscales (auditory, visual, motor, and oromotor functions as well as communication and arousal) giving us 23 items ordered by degree of complexity, ranging from reflexive to cognitively mediated behaviours.

We also performed complementary clinical neuroimaging assessments. FDG-PET data were normalized to signal intensity of the skin [14]. The mean value of skin voxels was selected as intensity scaling index for each volume. The skin was chosen due to the fact that it is not affected by the brain injury and metabolic activity can easily be extracted. For resting state functional Magnetic Resonance Imaging (fMRI), spontaneous BOLD signal correlations were measured between different brain regions for the default mode, auditory, visual, sensorimotor, salience and frontoparietal networks [15]. We also used diffusion tensor imaging (DTI) to quantify the orientation and directional uniformity of water diffusion in brain tissue [16]. Finally, clinical electroencephalograms (EEG) using 19 electrodes were also acquired and interpreted by a certified neurologist. Among the 68 patients in UWS/VS (mean age 45 ± 11; range 16–79 years), etiology was traumatic in 17 cases and non-traumatic in 51 cases [anoxic encephalopathy (n = 34), ischemic or hemorrhagic stroke (n = 8), mixed etiology (n = 4), others (n = 5)]. Median interval since insult was 30 months (Q1 = 9 and Q3 = 39).

Results

Out of the 68 UWS/VS patients included in this study, according to the medical records and the questionnaires fulfilled by the family, the doctor and the nurses, only two patients could resume oral feeding (3%). The first patient received oral feeding (i.e. liquid and semi liquid) in addition to gastrostomy feeding, with a functional swallowing based on an otorhinolaryngological examination, and the second patient had full oral feeding (i.e. liquid and mixed solid food).

Case report 1

Medical history

A 17-year-old man was admitted to intensive care unit after an ethylic coma complicated by a pneumopathy caused by gastric liquid inhalation. The situation was evolving positively, allowing the patient to leave the hospital after a few days. However, a couple of days after the discharge, the patient suffered from a cardiorespiratory arrest occurring after an effort at home. Cardiorespiratory resuscitation was performed and ventilation was needed. An unconscious state was observed with a lack of evolution. One month later, the patient was discharged from intensive care unit with a diagnosis of UWS/VS and returned to his parent's home without any period in a rehabilitation centre. He received nurse care each day and physical therapy thrice a week but no swallowing care. Fourteen years after the brain injury, he came to the University Hospital of Liège. He was still considered as UWS/VS.

Oral feeding

When the patient came at the University Hospital of Liege, he was entirely fed by mouth with thick to thin liquid texture (corresponding to level 0–4 in the International Dysphagia Diet Standardisation Initiative—IDDSI Framework [17]). However, the patient still had the gastrostomy tube for complementary nutrition of about 0.5 l per day.

Otorhinolaryngological exam were performed. The fiberoptic endoscopic evaluation showed preserved laryngeal mobility and cough reflex, as well as no salivary or secretions stasis. Semi-liquid and liquid test was performed. For semi-liquid, the patient could open his mouth when the spoon touched his lips but he was not able to close it around the spoon. Antero-posterior movements of the tongue were observed and there was no buccal stasis. The initiation of swallowing reflex was delayed but no inhalation occured. Liquid was given with a syringe on lingual basis. A posterior leakage was observed, the initiation of swallowing reflex was delayed but ventricular bands close to protect the larynx and no inhalation occured.

Multimodal diagnosis assessment

CRS-R total scores ranged from 4 to 7 depending on the day (total of 6 evaluations). The patient showed spontaneous eye opening, head and legs movements, auditory startle reflex, no response to command, no visual fixation, no visual pursuit, bilateral abnormal flexion in response to noxious stimulations, oral reflex movements and vocal productions but no communication. The total CRS-R score on the day of the otorhinolaryngological exam was 5. Clinical assessments concluded that he fulfilled the criteria for a diagnosis of UWS/VS. Neuroimaging results also pointed in that direction (Fig. 1a–h). FDG-PET showed a drop in brain metabolism of 79% as compared to healthy controls, with hypometabolism in the global lateral and medial fronto-parietal network and a preservation of the brainstem and cerebellum (Fig. 1a, b). MRI revealed a global bilateral atrophy of the cerebral and cerebellar hemispheres (Fig. 1c, d). fMRI showed no spontaneous brain activity in the different resting state networks (Fig. 1c–f). DTI showed diffuse alteration of white matter connections (Fig. 1g, h). Clinical electroencephalograms (EEG) suggested a severe encephalopathy.

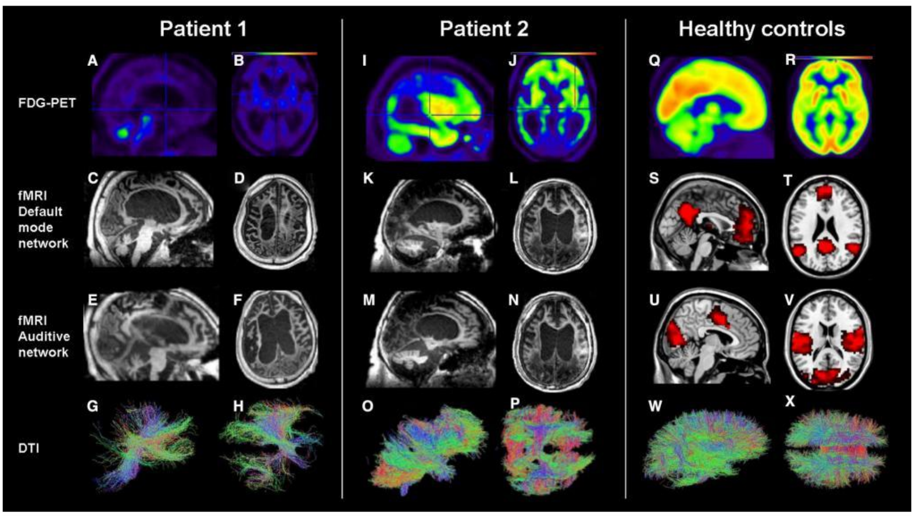

Fig. 1 Neuroimaging results (PET, fMRI default mode network, fMRI auditory network and DTI) of the two patients and healthy controls. Patient 1 (left panel): FDG-PET showed a drop in brain metabolism of 79% with hypometabolism in the global lateral and medial fronto-parietal network and a preservation of the brainstem and cerebellum (**a**, **b**). MRI revealed a global bilateral atrophy of the cerebral and cerebellar hemisphere in patient 1 (**c**, **d**). DTI showed diffuse alteration of white matter connections (**g**, **h**). Patient 2 (central panel): drop in brain metabolism of 47% with hypometabolism in the bilateral parieto-temporal associative areas but relative preservation of the brainstem, cerebellum and frontal and occipital cortex (**i**, **j**). MRI revealed a global cerebellar vermis atrophy, a mesencephalic bilateral atrophy, a parieto-occipital cortex and basal ganglia (principally left thalamic) atrophy (**k**, **l**). DTI showed loss of white matter in dorsal posterior area bilaterally and disorganisation of fibers in parietal cortex (**o**, **p**). In fMRI, performed with sedation, patient 1 and 2 showed no spontaneous brain activity in the different resting state networks (**c**–**f** and **k**–**n**, respectively)

Case report 2

Medical history

A 35-year-old man was admitted to the hospital as a result of a motor road accident (moped knocked down by a car). There was no loss of awareness or neurologic symptoms but some fractures in the hand and kneecap. Three days later, he was admitted to the intensive care unit after a cardiac arrest during a kneecap surgery. He sustained an anoxic brain injury and remained comatose during the following 10 weeks. He then recovered spontaneous eye opening and startle reflexes to loud sound and bright light. Three weeks after the brain injury, computed tomography revealed cerebral collapse on basal ganglia. He was tracheostomized during the first three months then oral feeding was gradually started. At the discharge, neurological examination retained the diagnosis of "permanent vegetative state" based on the absence of any behavioural sign of consciousness. The patient returned back home 4 months after the anoxic brain injury with a naso-gastric tube feeding. Nineteen years after the insult, the patient came to the University Hospital of Liège for a multimodal diagnosis assessment.

Oral feeding

Oral liquid and solid food feeding were gradually continued by the mother after the initial hospitalization and enteral feeding was stopped 2 weeks after the discharge. The patient never received swallowing therapy. When he came to our center, the patient was entirely fed by mouth. He also orally received hydration and medications. Solid food corresponded to level 5 (minced and moist) in the IDDSI Framework [17]. Three meals per day were administrated by the mother or the nurse with normal utensils. The patient opened his mouth when the spoon was touching his lips but was not able to close his lips around the spoon. There was no history of lung infection and his body weight was stable. The nutritional status measured by albumin indicator was normal (43gr/L norms 38–49).

Multimodal diagnosis assessment

Behavioural examinations confirmed the diagnosis of UWS/VS. The CRS-R total scores ranged from 6 to 7 depending on the day (total of 6 evaluations) and showed spontaneous eyes opening, auditory startle reflex, no response to command, no visual fixation or pursuit, no blink to threat, bilateral flexion responses to noxious stimulations, oral reflex movements and vocalizations without any communication. However, neuroimaging examinations (FDG-PET, DTI and EEG) looked atypical. FDG-PET showed a drop in brain metabolism of 47% as compared to healthy controls with relative metabolic preservation of the brainstem, cerebellum, frontal and occipital cortices and hypometabolism in the bilateral parieto-temporal associative areas (Fig. 1i, j). MRI revealed global cerebellar vermis atrophy, mesencephalic bilateral atrophy, parieto-occipital cortex and basal ganglia (principally left thalamic) atrophy. There was also a hyperintense signal in the midbrain and the pons compatible with a Wallerian degeneration. A quadriventricular dilatation was also noted as well as bilateral white matter diffuse lesions encompassing parietal and cingulate posterior cortices and precuneus (Fig. 1k, l). fMRI showed no spontaneous brain activity in any of the resting state networks (Fig. 1k–n). DTI showed a loss of white matter in dorsal posterior area bilaterally and disorganisation of fibers in parietal cortex (Fig. 1o, p). EEG depicted symmetrical reactive slow theta activity, suggesting of a medium and diffuse cerebral suffering.

Discussion

In our population, only two out of 68 patients in UWS/VS could safely resume oral feeding. This is thus a rare observation (3%) among patients in UWS/VS. We see that the period between the accident and the assessment in our center is very long. It reflects the failure of most health care system to adequately care for disorders of consciousness patients after the acute phase. A previous retrospective study showed that in 260 patients diagnosed as "permanent vegetative state", 8% could perform oral feeding [18]. However, no information was given about how the diagnosis of UWS/VS was made and if standardized behavioural assessments were used. Indeed, repeated behavioural assessment is essential to make a proper diagnosis. A recent study show that performing a single CRS-R assessment could lead to up to 35% of misdiagnosed UWS/VS [19]. In our study, repeated clinical assessments (n = 6) matched with the diagnosis of UWS/VS in both patients according to actual behavioral diagnosis criteria. For patient 1, neuroimaging results are in line with the UWS/VS diagnosis. However, atypical results were observed for patient 2 (relative metabolic preservation of frontal and occipital cortices, relatively preserved DTI and theta activity but no spontaneous resting state fMRI networks). Given the dissociation between the behaviour and the neuroimaging findings, patient 2 could be considered as being in a functional locked-in [20, 21] or in a MCS* [22, 23], or even maybe in a state of cognitive motor dissociation [24]. However, advanced diagnostic techniques during a swallowing task or by means of mental imagery tasks should be performed to confirm this alternative diagnosis. Considering that the diagnosis of UWS/VS implies the absence of any voluntary behaviour, the observation of functional swallowing in these two patients raises many questions and reflexions.

As we described above, swallowing can either occurs spontaneously (reflex swallowing) or be initiated voluntary (for a review see [25]). Reflex swallowing is classically described as an irrepressible swallowing movement occurring despite the intention to avoid swallowing, without volitional input for initiation [5] and without conscious control [25]. Reflex swallowing is classically assessed with injection of minute amounts of water directly into the pharynx [5] or "naïve" saliva swallow [7]. According to the classical view of the initiation of reflex swallow, the oral phase is bypassed. Reflex swallowing is observed as early as the 12th gestational week, before the cortical and subcortical structures have totally developed [26]. It has also been reported that swallowing can be observed in the human anencephalic foetus [27, 28]. On the other hand, voluntary swallowing corresponds to sequential eating or drinking voluntarily initiated or facilitated by the cerebral cortex [25]. Materials in the mouth (food or saliva) and the cortical drive to the tongue and the submental muscles are necessary for initiation of voluntary swallowing [25]. In voluntary swallowing studies, water or food was injected in the mouth without any verbal instruction to swallow [7, 8] or subjects were cued to swallow volitionally their saliva [5, 7].

As described in the introduction, the network of brain regions activated during reflexive swallowing is different from that observed during volitional swallowing [5–8, 29, 30]. In previous studies, voluntary and reflex swallow can be differentiated in terms of state of awareness, wakefulness, and to what extent the oral phase is involved [5–8, 25]. However, because swallowing was never studied in disorders of consciousness (DOC) population, we actually do not know what is sufficient to consider swallowing as conscious compared to reflex swallowing in this population of patients. In terms of the oral phase of the swallowing, are lip closure, mastication, tongue manipulation and propulsion necessary to consider swallowing a conscious action? This issue is still debated and future studies are needed to define what is a "conscious" swallowing and what is a reflex swallowing in DOC patients. Given the retrospective character of this study, we are not able to analyze precisely the efficacy of the oral phase. However, we can make prediction by looking at the food texture that these two patients received. The first patient was able to swallow liquid and semi-liquid textures, which does not necessarily imply a complex oral phase. On the other hand, patient 2 received solid food and this type of texture definitely implies some form of functional oral phase to propel the food. We can then consider that the swallowing of patient 2 probably reflects higher level of conscious swallowing than the swallowing of patient 1. Interestingly, these observations are in line with the atypical neuroimaging results found in patient 2. Furthermore, given that voluntary swallowing is initiated or facilitated by the cerebral cortex, we can suppose that the preservation of some cortical areas (principally in the frontal cortex) in patient 2 can contribute to better swallowing results. However, based on the current neuroimaging results, we should be careful in saying that swallowing is reflex or conscious. This precise information can only be obtained with functional imaging performed during swallowing.

The swallowing abilities of the patients with DOC should be systematically assessed and compared among the different states of consciousness. This is critical as misdiagnosis can have serious medical and ethical consequences for the patients and their family. Indeed, prognosis, treatment decisions (particularly pain treatment) and medico-legal judgements (especially end-of-life decision-making) are influenced by the diagnosis [31, 32].

Neuropathological studies seem to indicate that a correlation exists between the level of consciousness and swallowing function: the higher the cognitive function, the better the chance to achieve oral feeding [33–36]. Based on this, the atypical brain activation observed in patient 2 in addition to his capacity to perform full oral feeding should prompt us to be more careful and rethink our initial clinical UWS/VS diagnosis.

Finally, this case study emphasizes the importance of systematic observations of swallowing capacities in all patients with altered consciousness. Indeed, as shown in our study, even patients with no evident sign of consciousness can sometimes demonstrate some functional swallowing. More than 30 years ago, it was demonstrated that some assessments (pre-feeding assessment and functional assessment) could be performed in severe head-injured patients [34]. Since then, other studies showed that objective swallowing assessments [realized with instrumental assessments such as fiberoptic endoscopic exam (FEES) or videofluoroscopy (VFSS)] could be performed safely in patients regardless their level of consciousness [37–39]. Brady et al. [38] considered that the decision to introduce oral food or liquid in DOC patients should only be made after the completion of an objective swallowing evaluation. We share Brady's opinion and we insist on the importance of the realization of a systematic swallowing evaluation including instrumental assessments of swallowing such as VFSS or FEES, as they are the only reliable way to identify silent aspiration due to poor cough reflex [40]. Combined to VFSS or FEES, swallowing function clinical evaluation will give complementary information on the pre-swallowing and swallowing abilities [38, 39].

Clinicians working with DOC patients are also faced with the challenge of providing meaningful therapy. Safety and treatment efficacy of swallowing rehabilitation in patients with DOC is still debated [33, 37, 38] (for a review see [41]). Some clinicians advocate providing patients with a level II (generalized responses/vegetative state) or III (localized responses/minimally conscious) in Ranchos Los Amigos Scale (RLAS [42]) with food/liquid presentations for taste stimulation [33]. Other clinicians recommend no oral feedings until the patient's level of consciousness improves beyond level III in RLAS [34, 38, 43]. However, based on our observations, a few patients who do not show conscious behaviour according to the CRS-R can perform oral feeding even if the majority of DOC patients are fed with enteral feeding. Thus, we believe that the decision to introduce food or liquid should not rely uniquely on the observation of conscious behaviour but rather on performance observed during an objective swallowing assessment.

Several limitations of the study should be taken into account.

First, we have considered only patients who were known to be fed at the moment of their admission for the one-week multimodal assessment. This introduces a bias in our data given that we might have missed patients who can potentially be fed orally but who are not (due for example to the lack of stimulation, fear of bronchoinhalation, etc.). However, we think that this number of missed patients is probably low. In our experience, almost all families try to reintroduce oral feeding. Most of the time they are confronted to difficult situations making it impossible. This is namely the hypercontraction of masseter or bite reflex reducing considerably the chance of oral feeding, the total absence of oro-facial reaction when trying to put some food in the mouth, the absence of swallowing reflex, etc. When these difficulties are not present, further testing is usually undertaken and if judged safe, oral feeding is pursued. Therefore, the number of patients that were not fed at the moment of their admission but could have had full oral feeding is probably very low. Second, as we described before, it has been more informative if we had swallowing assessment with standardized otorhinolaryngological techniques for all UWS/VS patients. Further studies are needed to better estimate rate and characteristics of swallowing in these DOC patients. Finally, we cannot totally exclude that the absence of response on resting state fMRI in our two patients is not due to the administration of sedation during the scanning. However, this was a light sedation (0.8 mg/mL) done mainly to improve the patients' comfort in the scanner. Moreover, a recent study demonstrated that connectivity decreases due to propofol sedation are relatively small compared to those already caused by structural brain injury [44]. Another recent study also showed that administration of sedation did not prevent some patients with DOC to show fMRI responses during active imagery tasks [45].

Conclusion

Oral feeding in UWS/VS patients is rare. We here presented the case of two patients who could achieve oral feeding. Although the diagnosis based on clinical behavioural assessment suggests an UWS/VS, we found some atypical neuroimaging results in the second patient who performed full oral feeding. Resuming full oral feeding may be related to recovery of some brain functions, which probably lead to a higher level of consciousness than UWS/VS. Full oral feeding could thus potentially be considered as a sign of consciousness. However, further studies will have to explore more precisely if functional swallowing is really a sign of consciousness and if this observation can be another key element to determine the diagnosis. We suggest that only the recovery of a full and complex oral phase (including solid food) should be considered as a sign of consciousness. Indeed, in some UWS/VS patients, the rare recovery of oral feeding with liquid and semi-liquid textures could be due to the presence of reflex swallowing rather than conscious swallowing.

A systematic swallowing assessment should be performed in all DOC patients regardless of their level of consciousness. This will allow to better tract residual swallowing function in DOC patients and see if it can be related to the level of consciousness. Various therapeutic techniques should be assessed and therapeutical objectives/purposes should be developed. Finally, we would like to emphasize that in these two patients the presence of relatively preserved swallowing function does not seem to predict good prognostic in terms of functional outcomes given their long history of chronic UWS/VS condition.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by the Ethics Committee of the Medical School of the University of Liège and written consents were obtained from the legal representative of each patient.

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Original article

Swallowing in individuals with disorders of consciousness: A cohort study

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ABSTRACT

Background: After a period of coma, a proportion of individuals with severe brain injury remain in an altered state of consciousness before regaining partial or complete recovery. Individuals with disorders of consciousness (DOC) classically receive hydration and nutrition through an enteral-feeding tube. However, the real impact of the level of consciousness on an individual's swallowing ability remains poorly investigated.

Objective: We aimed to document the incidence and characteristics of dysphagia in DOC individuals and to evaluate the link between different components of swallowing and the level of consciousness.

Methods: We analyzed clinical data on the respiratory status, oral feeding and otolaryngologic examination of swallowing in DOC individuals. We analyzed the association of components of swallowing and participant groups (i.e., unresponsive wakefulness syndrome [UWS] and minimally conscious state [MCS]).

Results: We included 92 individuals with DOC (26 UWS and 66 MCS). Overall, 99% of the participants showed deficits in the oral and/or pharyngeal phase of swallowing. As compared with the MCS group, the UWS group more frequently had a tracheostomy (69% vs 24%), with diminished cough reflex (27% vs 54%) and no effective oral phase (0% vs 21%).

Conclusion: Almost all DOC participants had severe dysphagia. Some components of swallowing (i.e., tracheostomy, cough reflex and efficacy of the oral phase of swallowing) were related to consciousness. In particular, no UWS participant had an efficient oral phase, which suggests that its presence may be a sign of consciousness. In addition, no UWS participant could be fed entirely orally, whereas no MCS participant orally received ordinary food. Our study also confirms that objective swallowing assessment can be successfully completed in DOC individuals and that specific care is needed to treat severe dysphagia in DOC.

1. Introduction

After a period of coma, individuals with severe brain injury may remain in an altered state of consciousness before regaining partial or complete recovery [1]. Disorders of consciousness (DOC) consist of 3 states ranging from no awareness and no arousal to the preservation of arousal with fluctuating awareness [2]: coma, vegetative state/unresponsive wakefulness syndrome (UWS) [3] and minimally conscious state (MCS) [4]. UWS is characterized by the presence of eye-opening and reflexive movements, without conscious behaviours [3]. Individuals with MCS show reproducible but inconsistent signs of consciousness, such as command following, visual pursuit, and localization to noxious stimulation

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[4]. When they recover the ability to functionally communicate or to use objects adequately, they emerge from the MCS [4].

Swallowing disorders are relatively frequent after an acquired brain injury from traumatic or anoxic causes, ranging from 25% to 61% depending on the studies [5,6]. Oral feeding has been suggested to be related to the level of consciousness in previous studies evaluating swallowing in severe brain-injured individuals [5–17]. Individuals with DOC classically receive hydration and nutrition through an enteral-feeding tube [18]. The real impact of the level of consciousness on individuals' swallowing ability remains poorly investigated. Indeed, previous studies that assessed swallowing in individuals with severe brain injury had small sample sizes [15], focused on only one component such as the type of feeding [17] or the possibility of extubation [16] and/or they mostly used clinical assessment of consciousness that was not based on established diagnostic criteria [4] (see [5–14]). In line with this, previous literature showed that the Coma Recovery Scale-Revised (CRS-R) [19] is the current gold standard to assess the level of consciousness in DOC individuals, and multiple evaluations should be performed to decrease misdiagnosis [20]. Accurate diagnosis is challenging because of confounding factors such as aphasia and motor deficits, but it has important implications for prognosis [21], treatment management [22] and related ethical considerations [23].

Swallowing has not yet been studied systematically in DOC individuals, and to our knowledge, the link between the level of consciousness and swallowing components (e.g., lip prehension, lingual propulsion, pharyngo-laryngeal sensitivity, efficacy of the pharyngeal phase and ability to clear saliva) has never been investigated. We recently suggested that an effective oral phase of swallowing could be a determinant to consider swallowing as a conscious behavior [17]. However, in this previous study, we included only UWS participants and based our conclusion on only 2 components (i.e., presence or absence of oral feeding and type of oral feeding).

In the present work, we collected respiratory and nutritional status as well as the otolaryngological results of swallowing in a large cohort of individuals with prolonged DOC. We predicted that most individuals have severe alterations of the different components of swallowing and that some components of the swallowing process, such as the oral phase, may be linked to the level of consciousness.

2. Participants and methods

2.1. Participants

We retrospectively collected data for individuals admitted consecutively from January 2010 to August 2018 to the University Hospital of Liege (Belgium) for a 1-week multimodal assessment of consciousness for diagnostic and prognostic purposes. Fig. 1 illustrates the flow of participants in the study. Inclusion criteria were 1) recovered from coma caused by a severe acquired brain injury, 2) with a prolonged condition (> 1 month post-insult) [25,26], 3) medically stable, 4) underwent fiberoptic endoscopic examination of swallowing (FEES), 5) a diagnosis of UWS or MCS based on a minimum of 5 CRS-R tests (to avoid diagnostic errors due to fluctuations in responsiveness and to obtain a stable clinical

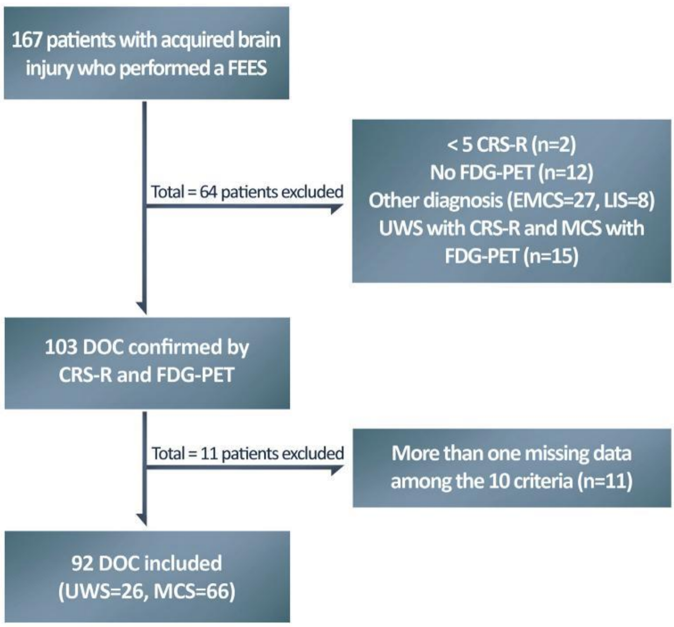

Fig. 1. Flowchart of the study. FEES: fiberoptic endoscopic evaluation of swallowing; CRS-R: Coma Recovery Scale-Revised; FDG-PET: fluorodeoxyglucose-positron emission tomography; EMCS: emergence from minimally conscious state; LIS: locked-in syndrome; DOC: disorders of consciousness; UWS: unresponsive wakefulness syndrome; MCS: minimally conscious state.

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diagnosis) [20], which was confirmed on fluorodeoxyglucose-positron emission tomography (FDG-PET) (see next sections concerning data acquisition and analyses) and 6) no more than 1 missing data item (i.e., at least 9 of 10 selected criteria regarding respiratory status, type of feeding and components of the oral and pharyngeal phases of swallowing).

We extracted demographic data (i.e., sex, age, etiology, time since insult) and DOC diagnosis from participants' medical records. Etiology was classified in terms of focal or global injury to distinguish between on one hand, ischemic, hemorrhagic and traumatic brain injury, and on the other, anoxic and metabolic encephalopathy.

The study was approved by the Ethics Committee of the Faculty of Medicine of the University Hospital of Liege, and written informed consent was obtained from all legal surrogates. We followed the principles of the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) (see Supplementary materials) [24].

2.2. Diagnosis of consciousness

The diagnosis was established after repeated behavioral assessments performed by trained and experienced clinician researchers using the CRS-R [19] and FDG-PET. The CRS-R consists of 6 subscales (auditory, visual, motor, and oromotor functions as well as communication and arousal) of 23 items ordered by degree of complexity, ranging from reflexive to cognitively mediated behaviors [27]. All participants underwent at least 5 CRS-R tests over a maximum of 10 days and the best result was kept for the behavioral diagnosis [20]. To confirm the behavioral diagnosis, FDG-PET images were visually inspected by experts and classified as compatible with UWS (when the statistical tool detected no voxels with preserved metabolism in the associative fronto-parietal network bilaterally) or compatible with MCS (with incomplete hypometabolism or partial preservation of metabolic activity detected in the fronto-parietal network). The acquisition procedure and analyses of FDG-PET data were described previously [28,29]. The brain activity map was obtained with a threshold of uncorrected $p < 0.05$ in all contrasts for single-subject analyses, as in previous studies [28,29]. We excluded individuals with a diagnosis of UWS based on the CRS-R but with FDG-PET results compatible with MCS because these individuals may present covert consciousness (referred to as MCS*) [2].

2.3. Respiratory status, type of feeding and swallowing assessments

We collected data on 10 specific criteria based on the results of the ear, nose and throat (ENT) examination (performed by SD, AM or AL) and from the questionnaires completed by the family (for the type of feeding).

For respiratory status, we reported the presence or absence of tracheostomy (criterion 1). The type of feeding (criterion 2) referred to the presence or absence of exclusive enteral-feeding. For participants who received oral feeding, we distinguished type of feeding based on the criteria of the Food Intake Level Scale (FILS) [30]. The FILS is an observer-rating scale for assessing the severity of dysphagia, examining to what degree individuals take food orally on a daily basis, ranging from 0 (no oral intake, and no swallowing training) to 10 (normal oral food intake). Scores 1 to 3 correspond to no oral intake, 4 to 6 oral intake with alternative nutrition, and 7 to 10 oral intake exclusively.

The other 8 criteria were related to the otolaryngological examination performed by ENT experts. A FEES was performed with a flexible videorhinolaryngoscope (Olympus Visera OTP-S7, Tokyo) and color monitor. We excluded all criteria that required a response to a command (e.g., assessment of the nasopharyngeal or vocal fold closure with the production of sounds, apnea, volunteer saliva swallow, cough). The first 3 criteria of the otolaryngological examination were related to the oral phase of swallowing with the presence or absence of hypertonia of jaw muscles (criterion 3), the presence or absence of an oral phase of swallowing (lip prehension or lingual propulsion; criterion 4), and the observation or not of an effective oral phase (criterion 5). Practically, we moved a spoon to in front of the individual's mouth and observed the reaction. With absence of lip prehension, we placed a 2-ml bolus in the middle of the tongue and observed if lingual propulsion occurred. We considered the oral phase effective if we detected consecutively lip prehension, lingual propulsion and no post-swallowing oral stasis. The last 4 criteria were related to the pharyngeal phase of swallowing. The presence or absence of secretions in the pharyngo-laryngeal area (criterion 6) and the salivary aspiration (criterion 7) informed on participants' ability to manage secretions. The cough reflex (criterion 8) was evaluated by stimulating the laryngeal area, and if no cough was observed, the pharyngo-laryngeal sensitivity was considered absent. Finally, we noted the presence or absence of bolus aspiration during the swallowing of 2 ml of thick and liquid textures (criteria 9 and 10, respectively). Some participants did not undergo the functional swallowing test because of a severe bite reflex, an inefficacity of the oral phase, or because it was considered too dangerous regarding other parameters (e.g., too many saliva aspirations, absence of spontaneous saliva swallowing).

2.4. Statistical analysis

We performed a descriptive analysis for each diagnosis group (UWS and MCS) in terms of sex, age, etiology and time since insult. Normality was assessed with histograms, quantile plots and Shapiro-Wilk tests. Univariate comparisons between UWS and MCS groups involved chi-square or Fisher exact test for categorical variables and Kruskal-Wallis test for non-normally distributed continuous variables. The association between each of the 10 criteria and the diagnosis groups was assessed by univariate logistic regression. These associations were further investigated by multivariable logistic regression adjusted for etiology and time since insult. The results of logistic regressions are presented as odds ratios (ORs) and adjusted ORs together with their 95% confidence intervals (CIs). $P < 0.05$ was considered statistically significant. Individuals with missing values were excluded from the analysis for the considered criteria. Statistical analyses were performed with Stata v14.2 (Stata Corp. 2015, College Station, TX).

3. Results

Among the 167 individuals identified, 92 matched our inclusion criteria (Fig. 1); 26 showed only reflexive behavior and had a diagnosis of UWS and 66 satisfied the CRS-R criteria for MCS in at least one evaluation (Table 1) Eleven of the 26 UWS participants were already included in our previous UWS studies focusing on type of feeding exclusively [17]. Diagnosis was confirmed by FDG-

Table 1
Descriptive statistics of the whole sample.

	UWS (n=26)	MCS (n=66)	P-value
Sex (F/M)	9/17	30/36	0.343
Age, years, mean (SD)	41 (12)	38 (12)	0.405
Etiology	Focal: 11 Global: 15	Focal: 49 Global: 17	0.004
Time since injury, months, mean (SD)	30 (22)	4 (34)	0.014

UWS: unresponsive wakefulness syndrome; MCS: minimally conscious state.

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PET in all included participants. The two diagnosis groups did not differ in age or sex but did differ by etiology and time since insult (Table 1), MCS participants having longer time since insult and more focal damage than UWS participants. We first present the descriptive analysis (Table 1) and then the percentage of participants for each of the 10 selected criteria, the univariate analysis for each criterion by diagnosis (p_{uni}), and the adjusted multivariate analysis ($p_{adjusted}$) for etiology and time since insult (Table 2). We also illustrate the percentage of UWS and MCS participants for each criterion in Fig. 2.

In total, 91 of 92 participants presented disorders in at least one criterion linked to the oral or pharyngeal phase of swallowing (i.e., criteria 3 to 10). Regarding respiratory status, 34 (37%) participants still had a tracheostomy at the time of assessment. As compared with MCS individuals, UWS individuals more frequently had a tracheostomy ($p_{adjusted} = 0.002$). In total, 71 (77%) participants received enteral feeding exclusively, with no significant difference between UWS and MCS groups ($p_{adjusted} = 0.254$). None of the MCS participants received exclusive ordinary solid food (FILS 10). Regarding the ENT examination, for the oral phase, 52 (56%) participants presented hypertonia of the jaw muscles, with no difference between UWS and MCS groups ($p_{adjusted} = 0.881$). In total, 43 (47%) participants showed at least one component of the oral phase of swallowing (lip prehension or lingual propulsion), with no difference between groups ($p_{adjusted} = 0.94$). However, UWS and MCS groups differed in efficacy of the oral phase of swallowing ($p_{adjusted} = 0.011$), characterized by the presence of lip prehension and lingual propulsion without post-swallowing oral stasis. For the pharyngeal phase, 34 (37%) participants had pharyngo-laryngeal secretions and 26 (28%) saliva aspiration. UWS and MCS groups differed on univariate analysis for the pharyngo-laryngeal secretions ($p_{uni} = 0.012$) and saliva aspiration ($p_{uni} = 0.019$) but not significantly on multivariable analysis (pharyngo-laryngeal secretions: $p_{adjusted} = 0.067$; saliva aspiration: $p_{adjusted} = 0.062$). For the test of the cough reflex, among the 63 participants assessed, 43 (52%) showed decreased pharyngo-laryngeal sensitivity, with significantly more MCS participants presenting a cough reflex than UWS participants ($p_{adjusted} = 0.027$). Regarding the functional test with thick and liquid texture, 16 (61%) and 53 (80%) UWS and MCS participants, respectively, performed the swallowing test with a cream texture and 12 (46%) and 42 (63%) with a liquid texture. Nine (13%) participants showed aspiration with a thick texture and 17 (31%) with a liquid texture, with no difference between groups (thick texture: $p_{adjusted} = 0.798$; liquid texture: $p_{adjusted} = 0.226$).

4. Discussion

The main aims of this study were to document the proportion and characteristics of dysphagia in individuals with DOC and to evaluate the link between different criteria of swallowing and level of consciousness. To our knowledge, this is the first study of respiratory status, oral feeding and FEES in a large cohort of individuals with DOC. In our study, all but one DOC individual (MCS) presented at least one swallowing dysfunction of the oral and/or pharyngeal phase. Also, tracheostomy, cough reflex and the efficacy of the oral phase were the 3 criteria related to consciousness. Finally, none of the UWS individuals could be fed entirely orally, whereas none of the MCS individuals received ordinary oral food.

Regarding type of feeding, none of the UWS participants could achieve a full oral feeding, most probably linked to the absence of an effective swallowing oral phase and less effective pharyngeal phase, as shown by the proportion of participants with tracheostomy. Only a small proportion (7%) of MCS participants could safely resume full oral feeding with easy-to-swallow food (i.e., FILS 7). Despite the ability of some MCS participants to resume oral feeding, a higher level of consciousness (i.e., EMCS) is probably necessary to enable a full ordinary oral food (FILS 10).

Some swallowing criteria were notably related to the level of consciousness. First, UWS and MCS participants differed in spontaneous saliva management because more UWS participants still had a tracheostomy at the time of the evaluation than MCS participants. None of the participants were respirator-dependent. The need for the tracheostomy in about one third of the participants can probably be explained by insufficient saliva

Table 2
Descriptive and statistical analysis of the 10 criteria in the UWS and MCS groups.

Criteria	UWS n (%)	MCS n (%)	p_{uni}	$p_{adjusted}$	UWS vs MCS OR	95% CI
1. Tracheostomy still in place	18/26 (69.2)	16/66 (24.2)	< 0.001	0.002	5.67	1.86–17.27
Tracheostomy removed	5	38				
Never had a tracheostomy	3	12				
2. Full enteral feeding	23/26 (88.5)	48/66 (72.7)	0.117	0.254	2.45	0.53–11.39
Partial oral feeding (FILS 7)	3	13				
Full oral feeding (FILS 7)	0	3				
Full oral feeding (FILS 7)	0	2				
Oral phase						
3. Hypertonia of the jaw muscles	15/26 (57.7)	37/66 (56.1)	0.887	0.881	1.08	0.41–2.87
4. Oral phase	12/26 (46.2)	31/66 (47.0)	0.844	0.94	0.96	0.37–2.53
5. Efficacy of the oral phase	0/26 (0)	14/66 (21.2)	0.007	0.011	0.09	0–0.63
Pharyngeal phase						
6. Pharyngo-laryngeal secretions	15/26 (57.7)	19/66 (28.8)	0.012	0.067	2.53	0.94–6.82
7. Saliva aspiration	12/26 (46.2)	14/66 (21.2)	0.019	0.062	2.65	0.95–7.38
8. Cough reflex	7/23 (30.4)	36/60 (60)	0.019	0.027	0.30	0.10–0.87
9. Cream aspiration	2/16 (12.5)	7/53 (13.2)	0.941	0.798	1.26	0.21–7.44
Not performed[a]	10	13				
10. Liquid aspiration	2/12 (16.7)	15/42 (35.7)	0.223	0.226	0.35	0.07–1.90
Not performed[a]	14	24				

p_{uni}: univariate analysis between UWS and MCS; $p_{adjusted}$: multivariable analysis between UWS and MCS adjusted for etiology and time since insult; PL: pharyngo-laryngeal; OR: odds ratio; CI: confidence interval; FILS: Food Intake Level Scale.
[a] Not performed because it was considered too risky by examiners or because of troubles in the oral phase (e.g., bite reflex, no lingual propulsion).

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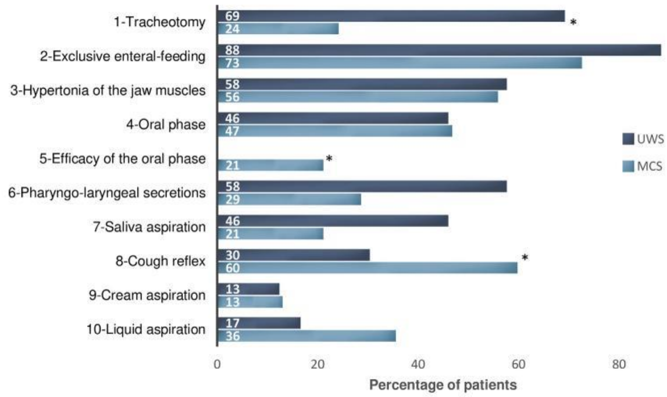

Fig. 2. Percentage of UWS and MCS patients for the 10 criteria. UWS: unresponsive wakefulness syndrome; MCS: minimally conscious state. Asterisks (*) indicate significant difference between UWS and MCS, P adjusted < 0.05.

swallowing reflexes and ineffective pharyngeal phase of swallowing. Also, we observed more pharyngo-laryngeal secretions and saliva aspiration in UWS than MCS participants although not significantly after controlling for time since injury and etiology. These findings suggest that the level of consciousness may affect the ability to correctly manage saliva.

Second, both UWS and MCS participants showed a partial oral phase of swallowing (e.g., tongue and masticatory-like movements). However, no UWS participants and only a small number of MCS participants showed an effective oral phase of swallowing (lip prehension, lingual propulsion and no post-swallowing oral stasis). From this result and as already suggested in our previous study [17], an effective oral phase should be considered a sign of consciousness and thus should be taken into account in DOC diagnosis. The oral phase of swallowing is usually described as the voluntary (conscious) part of swallowing, controlled by multiple cortical regions such as the primary sensori-motor cortex, supplementary motor area, premotor cortex (also called "cortical masticatory area"), thalamus, cingulate, putamen and insulo-opercular cortex that interact with regions in the brainstem [31–34]. Some authors showed that masticatory-like movements and rhythmic tongue activity can be produced by the recruitment of the brainstem alone [35,36]. However, although the brainstem controls basic activity patterns of the cranial motoneuron groups involved in the oral phase of swallowing (hypoglossal, trigeminal, facial, vagal), descending inputs from the central nervous system also play an important role. Indeed, for some authors [36], the activity pattern of each motoneuron is modulated by higher brain and peripheral inputs. This cortical and peripheral recruitment allows that the final motor outputs fit the environmental demand. If the components of the oral phase of swallowing (e.g., mastication) were based on only a central pattern generator in the brainstem, it would be stereotyped [37]. Thus, the presence of an effective oral phase of swallowing seems highly dependent on cortical recruitment, which would explain why UWS individuals who show severe alterations of supratentorial cerebral metabolism do not present an effective oral phase of swallowing.

Finally, the presence of a cough reflex was a criterion more present in MCS than UWS participants. As shown in neuroimaging studies [38], the cough reflex is probably not a simple pontomedullary reflex arc. Indeed, in these previous studies, the cough reflex was facilitated by cortical activations (mainly the primary motor cortex, posterior insula, paracentral lobule, posterior mid-cingulate cortex, premotor cortex). Thus, the impact of the level of consciousness highlighted in the present study might probably be linked to the importance of the underlying cortical damage. Moreover, it is now generally accepted in stroke literature that the cortex plays an important role in the control of swallowing and that damages to swallowing motor areas and/or their connection to the brainstem usually result in dysphagia [39,40].

Besides these main findings, hypertonia of the jaw muscles and the number of aspirations on cream/liquid texture did not differ between UWS and MCS groups. However, more MCS participants performed the functional test with thick and liquid texture than did UWS participants, which highlights that UWS participants seem to be generally considered more at risk of aspiration by the examiners or had more troubles in the oral phase (e.g., hypertonicity, absence of lip prehension or lingual propulsion) than MCS participants.

Our findings also agree with previous studies showing that objective swallowing assessment such as the FEES can be successfully completed in DOC individuals [7,9,15]. The ENT examination gives precious information on 2 main points, first regarding tracheostomy and second regarding the possibility of oral feeding. After the FEES, the ENT specialist suggested removing the tracheostomy for several DOC participants (8 MCS participants and 6 UWS participants) because of good saliva management and the absence of stenosis or laryngeal paralysis. In these cases, the tracheostomy was probably maintained to prevent any respiratory complications because of the lack of adequate information regarding the management of the tracheostomy or because no one tested the possibility to begin a tracheostomy weaning. A previous study reported that individuals with a tracheostomy are more likely to develop pneumonia than patients without a tracheostomy [41]. This should be kept in mind when making decisions on the need to maintain a tracheostomy in this fragile population. In this regard, the FEES can help in deciding on possible decannulation, but given the complexities of saliva management in the DOC population, the decision for tracheostomy weaning should be discussed in a multidisciplinary team. Besides tracheotomy management, the ENT examination is crucial for patients in whom we would like to start or continue oral feeding. Indeed, with the high proportion of patients with absence of cough reflex (about 54% in the whole sample), there is a high risk of silent aspiration. In

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this study, the ENT examination also advised starting partial oral feeding in 3 more UWS participants and 13 MCS participants and to stop full or partial oral feeding in 3 MCS participants. A functional swallowing test can be difficult to implement in individuals with severe trismus or total absence of an oral phase of swallowing, but as long as partial oral phase is present (e.g., partial lip prehension and lingual propulsion), thick or liquid swallowing can be tested by a qualified clinician.

Regarding the severity of dysphagia in DOC individuals, specific care such as nursing, chest physiotherapy, and speech therapy are recommended [42]. Management of swallowing should be integrated into a global approach taking into account respiration, mobility and tonicity of the face and considering emotional reactions, spasticity, and potential hypersensitivity. Clinically, we noticed that therapeutic feeding (i.e., swallowing small amounts of tasty easy-to-swallow food) can sometimes help clear excess saliva secretions in the pharyngo-laryngeal area. In addition, taste stimulation (involving only a very small amount of food or liquid that is delivered via a cotton swab in particular zones of the oral cavity) is also a good option for individuals who are at risk of aspiration. Nevertheless, the decision to introduce oral food or liquid in DOC individuals as therapeutic feeding or as a real part of the feeding should only be made after the completion of an objective swallowing evaluation [9].

There are several limitations of the study related to its retrospective, observational and single-centre design, which suggests that our data are moderately representative of the general DOC population. The presence of missing data for one criterion (cough reflex) should be acknowledged. We were also limited in the number of available criteria that could be studied. A prospective analysis, given a prescribed test protocol for DOC individuals with more detailed criteria, may yield additional information that were not covered in the current study, such as the duration of the oral phase before the swallowing reflex, the frequency of spontaneous saliva swallowing reflex [13] or the importance of secretions post-swallowing with a valid protocol such as the New Zealand secretion scale [43]. Future longitudinal studies should also investigate the recovery of dysphagia along with consciousness recovery within the same individuals.

In conclusion, this study provides promising results linking swallowing and consciousness, notably regarding the ability of (minimally) "conscious" individuals to better manage spontaneous swallowing of saliva (reflected here by the presence or absence of tracheostomy), the cough reflex and the efficiency of the oral phase of swallowing. We should continue our efforts in the assessment of the oro-facial area in DOC individuals to be able to propose appropriate and sensible care management.

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Author contributions

E.M., O.G., and S.L. contributed to conception and design of the study. E.M., S.D., A.M., and A.L., acquired the ENT data. OG, A.T., C.A. and A.V. acquired the diagnosis data. E.M., OG and D.L. analyzed the data. E.M. and O.G. drafted the manuscript. A.M., A.L., A.T., C.A., JF.K., A.V., D.L., and S.L. provided major revisions in significant proportions of the manuscript. D.L., O.G. and S.L. contributed equally.

Disclosure of interest

The authors declare that they have no competing interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.rehab.2020.04.008.

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Following severe brain injuries (e.g., traumatic or anoxic brain injury, stroke), a small proportion of patients will remain in an altered state of consciousness. Patients with prolonged (> 28 days post-insult) disorders of consciousness (DOC) can open their eyes (sometimes showing electrophysiological sleep/wake cycles) and the majority no longer need invasive ventilation. However, most of them receive artificial feeding, suggesting that consciousness affects swallowing capacities.

The aim of this thesis is to contribute to the study of the links between consciousness and swallowing. The hypotheses are that swallowing capacities are linked to level of consciousness, and that the presence of some components of swallowing constitutes a possible sign of consciousness.

Based on a literature review, we show that the sequencing of the components of swallowing falls on a continuum of voluntary to reflex behaviors. Components of the oral phase may be considered as voluntary behaviors because they are controllable and suppressible (although largely automated), components of the pharyngeal phase as somatic reflexes, and components of the esophageal phase as autonomic reflexes. The triggering of the swallowing reflex inhabits the border region between voluntary behaviors and somatic reflexes, while the opening of the upper esophageal sphincter divides somatic from autonomic reflexes. If voluntary behaviors are considered possible signs of consciousness, the presence of components of the oral phase of swallowing should be considered as revealing conscious behaviors. Moreover, we show that a range of cortical areas (mainly the primary sensorimotor cortex, premotor cortex and supplementary motor area, anterior part of the cingulate cortex, insula and cerebellum) are involved in both voluntary and spontaneous swallowing tasks.

In two retrospective studies analyzing swallowing in patients with DOC diagnosed by means of repeated behavioral assessment and neuroimaging, we demonstrate that almost all such patients present at least one dysfunction in the oral and/or pharyngeal phase. Patients who do not show behavioral signs of consciousness (unresponsive wakefulness syndrome – UWS) do not present an efficient oral phase of swallowing allowing oral feeding with solid food. Consequently, the preservation of components of the oral phase of swallowing should be considered as a sign of consciousness and be one of the diagnostic criteria for consciousness. The absence of an efficient oral phase of swallowing in patients with UWS and its presence in only a small proportion of minimally conscious (MCS) patients explain why no "typical" patients with UWS (i.e., with behavioral and neuroimaging assessments pointing in the same direction) can be fed entirely orally while no patients with MCS can eat ordinary textured food.

Furthermore, in the studied group, level of consciousness is linked to components of the pharyngeal phase (reflected by the absence of a tracheostomy, pharyngo-laryngeal secretions or saliva aspiration) and to the cough reflex. Indeed, more patients with MCS than UWS present efficient spontaneous saliva management and a cough reflex, although these components are present in some patients with UWS. For that reason, these components seem to represent cortically mediated behavior but do not constitute signs of consciousness as such.

Finally, this work highlights the lack of appropriate tools to assess and treat swallowing for patients with DOC. A protocol study for the validation of a swallowing assessment tool for patients with DOC is therefore proposed.