Visual Fixation in the ICU: A Strong Predictor of Long-Term Recovery After Moderate-to-Severe Traumatic Brain Injury*

Caroline Arbour, RN, PhD[1,2]; Andrée-Ann Baril, BSc[1,3]; Harrison J. Westwick, MD, MSc[1,3]; Marie-Julie Potvin, PhD[1,4]; Danielle Gilbert, MD, FRCPC[1,3]; Jean-François Giguère, PhD, MD[1]; Gilles J. Lavigne, DMD, PhD[1,5]; Alex Desautels, MD, PhD, FRCPC[1,3]; Francis Bernard, MD, FRCSC[1,3]; Steven Laureys, MD, PhD[6]; Nadia Gosselin, PhD[1,2]

Objective: Posttraumatic amnesia is superior to the initial Glasgow Coma Scale score for predicting traumatic brain injury recovery, but it takes days/weeks to assess. Here, we examined whether return of visual fixation—a potential marker of higher cognitive function—within 24 hours of ICU admission could be used as an early predictor of traumatic brain injury recovery.

Design: Two-phase cohort study.

Setting: Level-I trauma ICU.

Patients: Moderate-to-severe traumatic brain injury discharged alive between 2010 and 2013.

Interventions: None.

Measurements and Main Results: Return of visual fixation was assessed through standard behavioral assessments in 181 traumatic brain injury patients who had lost the ability to fixate at ICU admission (phase 1) and compared with posttraumatic amnesia duration and the initial Glasgow Coma Scale score to predict performance on the Glasgow Outcome Scale-Extended 10–40 months after injury ($n = 144$; phase 2a). A subgroup also completed a visual attention task ($n = 35$; phase 2b) and a brain MRI after traumatic brain injury ($n = 23$; phase 2c). With an area under the curve equal to 0.85, presence/absence of visual fixation at 24 hours of ICU admission was found as performant as posttraumatic amnesia (area under the curve, 0.81; difference between area under the curve, 0.04; $p = 0.28$) for predicting patients' Glasgow Outcome Scale-Extended score. Conversely, the initial Glasgow Coma Scale score was not (area under the curve, 0.63). Even when controlling for age/medication/CT scan findings, fixation remained a significant predictor of Glasgow Outcome Scale-Extended scores (β, −0.29; $p < 0.05$). Poorer attention performances and greater regional brain volume deficits were also observed in patients who could not fixate at 24 hours of ICU admission versus those who could.

Conclusions: Visual fixation within 24 hours of ICU admission could be as performant as posttraumatic amnesia for predicting traumatic brain injury recovery, introducing a new variable of interest in traumatic brain injury outcome research. (*Crit Care Med* 2016; 44:e1186–e1193)

Key Words: Glasgow Coma Scale; outcome prediction; posttraumatic amnesia; traumatic brain injury; visual fixation

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[1]Hôpital du Sacré-Cœur de Montréal, Montreal, QC, Canada.

[2]Department of Psychology, Université de Montréal, Montreal, QC, Canada.

[3]Université de Montréal, Faculty of Medicine, Montreal, QC, Canada.

[4]Department of Psychology, Université du Québec à Montréal, Montreal, QC, Canada.

[5]Université de Montréal, Faculty of Dental Medicine, Montreal, QC, Canada.

[6]Coma Science Group, GIGA, Cyclotron Research Centre and Neurology Department, University and University Hospital of Liege, Liege, Belgium.

This study was conducted in a level-I trauma ICU at Hôpital du Sacré-Coeur de Montréal, Montreal, QC, Canada.

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For information regarding this article, E-mail: caroline.arbour@mail.mcgill.ca

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In the first hours after admission, the Glasgow Coma Scale (GCS) score is used by clinicians to estimate traumatic brain injury (TBI) severity and recovery (1). However, the GCS score is not a consistent predictor of long-term outcome after TBI (2, 3). Duration of posttraumatic amnesia (PTA) conversely is considered by many experts as the most robust predictor of TBI recovery, but it can only be established through repeated cognitive assessments and over many days/weeks (2–5). In recent years, several early predictors of TBI recovery have been identified including age, the GCS motor subscore, pupil reactivity, and CT (6, 7). Although these predictors were found useful for outcome estimation in large cohorts of TBI patients, they could have higher predictive value in milder TBI compared with severe ones (8). These predictors were also found less robust than PTA to estimate TBI outcome (9). Thus, there is a need to identify additional predictors of recovery in moderate-to-severe TBI to refine existing models and make them more performant at the individual level (10).

In the ICU, examination of the integrity of the visual system through standard behavioral assessment can be used to screen and monitor TBI recovery (11, 12). Although the mechanisms of visual disruption after TBI are not fully understood, the principal brain areas responsible for the exhibition of eye movements including the frontal eye field (FEF), parietal eye field (PEF), and supplementary eye field (SEF), as well as the midbrain and the pons, are vulnerable to brain trauma (13). In addition, acute and persistent impairments in voluntary-mediated eye movements such as intentional saccades and eye tracking were found to be a strong predictor of poor functional and attentional outcomes after mild TBI (14, 15). Unfortunately, assessment of saccades and eye tracking requires to be sustainably awake, which is not always possible in ICU TBI patients who are sedated and subjected to drowsiness (12). Visual fixation, which refers to the ability of maintaining an image of interest on the fovea, is an interesting alternative for this specific patient group as it involves cortical and subcortical structures but requires less complex coordination than saccades (16). Despite these advantages, the usefulness of visual fixation as a predictor of moderate-to-severe TBI recovery has never been explored.

This two-phase study examined whether return of visual fixation in the ICU (phase 1) could predict long-term recovery after TBI (phase 2). We hypothesized that the more rapid the recuperation of visual fixation in the ICU the less disabilities TBI patients would exhibit in the months after the injury. This study also aimed at testing whether the presence/absence of visual fixation within 24 hours of ICU admission could be as performant as PTA duration and the initial GCS score to predict long-term recovery in TBI patients. A 24-hour period for the return of visual fixation was selected as it is generally sufficient for intoxicated patients to "sober up" and be more compliant to behavioral commands, yet not long enough for them to develop substance-withdrawal syndrome (17). Periodic cessation of sedation for neurologic examination is also regularly performed during that time frame. Finally, 24 hours was judged sufficient for ICU clinicians to detect any forced gaze deviation due to space-occupying lesions or stroke.

MATERIALS AND METHODS

TBI Participants

One hundred and eighty-one moderate-to-severe TBI patients (≥ 16 yr old) discharged alive from a level-I trauma ICU between 2010 and 2013 were included retrospectively in this cohort study (phase 1). Although most patients received a bolus of neuromuscular blocking agent for intubation in the emergency department, those receiving repeated doses of blocking agents within the first 24 hours of ICU admission or with any other condition preventing bilateral eyelid opening or visual fixation were not considered for inclusion (details about eligibility screening are available in **Fig. 1**). Functional recovery was prospectively assessed through semistructured telephone interviews in 144 TBI patients or families 10–40 months after injury (phase 2a). Among patients found eligible for further testing during the interview, a subsample agreed to be submitted to a visual attention task ($n = 35$; phase 2b) and a MRI of the head ($n = 23$; phase 2c). This study was approved by the hospital research ethics committee. All participants in phase 2b and/or 2c were able to provide written inform consent.

Sociodemographic and Clinical Variables

Participants' sociodemographic and clinical information including the cumulative doses of analgesics and sedatives received in the first 24 hours of ICU admission was gathered from the medical charts.

TBI Severity, PTA Assessment, and CT Scan Findings

In all participants ($n = 181$), an alteration of consciousness extending 30 minutes and abnormal CT scan findings were

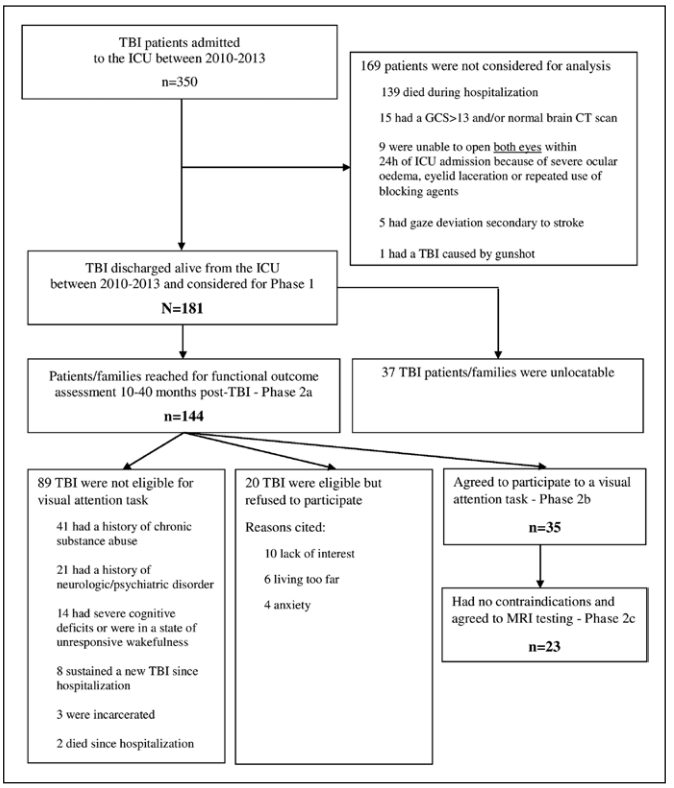

Figure 1. Flow diagram of screening and exclusion criteria for phase 1 and phase 2. GCS = Glasgow Coma Scale, TBI = traumatic brain injury.

documented (6). TBI severity was confirmed with the GCS score. The GCS is a 3- to 15-point scale used to assess patients' level of consciousness. Scoring is based on best motor response (6 points), best verbal response (5 points), and eye opening (4 points) (18). The initial GCS score (i.e., the lowest GCS score gathered in the first 24 hr after injury and before intubation) was used for TBI severity instead of the postresuscitation GCS score, as the latter was found to lack sensitivity for the discrimination of good versus poor TBI outcome when greater than 8 (19). Patients presenting an initial GCS score between 3 and 8 were considered patients with severe TBI, and those with a GCS score between 9 and 12 moderate TBI. ICU patients with an initial GCS of 13 and a positive CT scan were also considered moderate TBI, based on results from a recent large-scale study (20).

As per protocol in the study setting, PTA resorption was assessed daily by occupational therapists using the Galveston Orientation and Amnesia Test (GOAT) starting the day patients were able to communicate and exhibited a score of 6 on the GCS motor subscale (i.e., showing the patient has reached the minimum perceptivity level to be assessed for PTA). Duration of PTA was established when the ability to store new information was resumed, corresponding to a GOAT scores of 75 or above for two consecutive days (1, 21, 22).

The brain CT scan of each participant gathered during the first 24 hours of hospital admission was reviewed by a resident in neurosurgery (H.J.W.) who was blinded to patients' clinical information. Occurrence of any structural abnormalities including midline shift, hemorrhage, swelling, or periocular edema was documented. The Marshall and Rotterdam scores assessing for brain edema, midline shift, and also intraventricular, epidural, and/or arachnoid bleeding were computed (23, 24). For TBI patients who had an MRI, Firsching et al (25) grading of brainstem lesion was performed.

Phase 1–Return of Visual Fixation in the ICU

Information about presence/absence of visual fixation at 24 hours post-ICU admission was gathered in TBI patients' medical record (n = 181) as it was part of nurses' routine assessments in the study setting and was made every 4 hours in accordance with the standardized procedure of the Coma Recovery Scale–Revised (11). Briefly, nurses presented their face at the center of the patient's visual field (at 6–8 inch of distance) and gave him/her the instruction to look at them. Visual fixation was considered present in patients able to hold mutual eye contact with nurses for more than 2 seconds. In nonresponding patients, this procedure was repeated for up to two trials as nurses alternated between patients' center, right, and left visual fields to compensate for any loss of vision on one side. Although this procedure may also have triggered saccades in some patients, nurses only documented the capacity of the patients to hold mutual gaze, rather than any dynamic movement of the eyes. Assessment was performed sedation free whenever patients could tolerate it (i.e., not become agitated). It is also common practice for nurses in this setting to speak loud, call the patient by his/her name, and if needed, vigorously massage the shoulders/chest of patients during assessment of fixation. For each patient, the amount of hours from ICU admission until visual fixation recovery was computed.

Consistency in assessment of visual fixation was tested after study completion as retrospective interrater reliability testing is recommended for medical records' review studies assessing the usefulness of new outcome models (26). Although there is no standard recommendation for the proportion of raters or abstracted data that should be considered for retrospective reliability, several studies report as few as 10% (26). In this study, interrater reliability was tested between 10 pairs of ICU nurses on six recovering TBI patients. Taken together, these nurses had contributed to the assessment of 40% of patients included in the study (i.e., 72/181). For each pair of nurses, one was asked to perform visual fixation assessment while the other stood near to witness patient's reaction. Each nurse was asked to report the presence or absence of fixation individually. Cohen's κ coefficient for each pair of nurses was ranging between 0.66 and 0.96 and considered satisfactory (27).

Phase 2a–Long-Term Functional Recovery

Functional recovery was assessed with the Glasgow Outcome Scale–Extended (GOS-E) through semistructured telephone interviews 10–40 months after TBI. The GOS-E score ranges from 1 to 8 and classifies recovery based on patient's level of consciousness, independence, and work ability as death (score 1), unresponsive wakefulness syndrome (score 2), lower/upper severe disability (scores 3 and 4), lower/upper moderate disability (scores 5 and 6), and lower/upper good recovery (scores 7 and 8) (28). Good functional recovery was defined as a GOS-E score greater than 5, showing return to preinjury functioning with no or little residual impairments.

Phase 2b–Visual Attention Performance

The unstructured symbol portion of the Mesulam and Weintraub Cancellation Test (MWCT) was used to assess visual attention function in eligible TBI patients at 10–40 months after injury (29, 30). TBI patients were asked to circle target symbols as fast as they can while ignoring others. Performance was measured by the time (s) taken to perform the task.

Phase 2c–Regional Volume Deficits

Among patients who participated in the visual attention task, those without contraindications were submitted to a brain MRI using a Magnetom Trio TIM 3 Tesla MRI scanner (Siemens Healthcare, Erlangen, Germany) at the Institut universitaire de gériatrie de Montréal within the same month of GOS-E and visual attention assessments. Considering visual fixation recovery could be related to cerebral volume loss in areas involved in this ocular activity, regional volumes of the FEF, PEF, SEF, midbrain, and the pons were extracted using voxel-based morphometry on segmented T1 images (for further details about image preprocessing, see **Supplemental Digital Content I**, http://links.lww.com/CCM/B947) (31, 32).

Statistical Analysis

Receiver operating characteristic curve analysis was performed to test whether return of visual fixation in the ICU (hr), PTA duration (d), and the initial GCS score could predict a GOS-E score greater than 5. Positive likelihood ratio (PLR: sensitivity/100 – specificity) and negative likelihood ratio (NLR: 100 – sensitivity/specificity) were also computed. Then, correcting for age, cumulative doses of analgesics and sedatives received within 24 hours of ICU admission, and also CT scan findings (Marshall and Rotterdam scores), multiple regression was used to examine whether return of visual fixation (hr), PTA duration (d), and the initial GCS score could predict participants' GOS-E score. Because of the small number of participants who took part in phase 2b, a reduced regression model without potential confounders (i.e., age/medication/CT scan findings) was used to test whether return of visual fixation in the ICU (hr), PTA duration, and the initial GCS score could predict participants' performance on MWCT. Finally, percentages of regional volume deficits in TBI participants (n = 23) compared with matched controls (n = 23) (for details about control selection and pairing, see **Supplemental Digital Content II**, http://links.lww.com/CCM/B948) were calculated using the formula {[(Control – TBI)/TBI] × 100} (33). This computation was performed in our five regions of interest (FEF, PEF, SEF, midbrain, and pons), for gray matter (GM) volumes, with a Bonferroni corrected p value of 0.01. Statistics were computed using SPSS 22.0 (SPSS, Chicago, IL) and MedCalc 15.4 (MedCalc Software bvba, Ostend, Belgium).

TABLE 1. Participants' Characteristics at Phase 1 and Phase 2a

	Phase 1 (n = 181)			Phase 2a (n = 144)		
Variables, n (%) or Mean (sd)	Fixation at 24 Hr Present n = 105	Fixation at 24 Hr Absent n = 76	Group Difference t or χ^2 Test	Fixation at 24 Hr Present n = 64	Fixation at 24 Hr Absent n = 80	Group Difference t or χ^2 Test
Gender (male), *n* (%)	78 (74)	61 (80)	NS	46 (72)	63 (79)	NS
Age	36 ± 16	37 ± 15	NS	34 ± 14	37 ± 15	NS
ICU stay (d)	6 ± 5	20 ± 12	$p < 0.001$	7 ± 5	20 ± 13	$p < 0.001$
Initial Glasgow Coma Scale score	8 ± 3	7 ± 3	NS	8 ± 3	7 ± 3	NS
Hours to visual fixation recovery	11 ± 6	186 ± 144	$p < 0.001$	22 ± 6	214 ± 189	$p < 0.001$
Length of posttraumatic amnesia (d)	6 ± 5	24 ± 17	$p < 0.001$	7 ± 5	33 ± 28	$p < 0.001$
Months since traumatic brain injury	–	–	–	26 ± 10	24 ± 11	NS
Cumulative dose of fentanyl received in the first 24 hr of ICU admission (μg)	1,021 ± 1,021	1,375 ± 1,322	NS	1,326 ± 1,208	1,630 ± 1,375	NS
Cumulative dose of diprivan received in the first 24 hr of ICU admission (mg)	1,772 ± 1,410	1,762 ± 1,603	NS	1,731 ± 1,387	1,804 ± 1,504	NS
CT scan findings, *n* (%)						
Midline shift	12 (11)	10 (13)	NS	8 (13)	9 (11)	NS
Compressed cisterns	17 (16)	11 (15)	NS	10 (16)	16 (20)	NS
Subdural hemorrhage	43 (41)	36 (47)	NS	26 (41)	42 (53)	NS
Subarachnoid hemorrhage	30 (29)	39 (51)	$p < 0.05$	22 (34)	45 (56)	$p < 0.05$
Swelling	54 (51)	42 (55)	NS	26 (41)	41 (51)	NS
Periocular edema-unilateral	14 (13)	14 (18)	NS	10 (16)	14 (18)	NS
Periocular edema-bilateral	0 (0)	5 (7)	$p < 0.05$	0 (0%)	5 (6)	NS
Surgical decompression, *n* (%)	33 (31)	26 (34)	NS	10 (16)	15 (19)	NS
Cerebrospinal fluid drainage, *n* (%)	54 (51)	31 (41)	NS	22 (34)	27 (34)	NS
Marshall CT score	3 ± 1	3 ± 2	NS	3 ± 1	3 ± 1	NS
Rotterdam CT score	3 ± 1	3 ± 1	NS	3 ± 1	3 ± 1	NS
Firsching et al (25) MRI score[a]	1 ± 1	2 ± 1	$p < 0.05$	1 ± 1	2 ± 1	$p < 0.05$

NS = non significant.

[a]Firsching et al (25) score could be computed in only 20 patients involved in phases 1 and 2a.

RESULTS

Sample

Our sample at phases 1 and 2a is consisted mostly of young to middle-aged males (**Table 1**). The ability to fixate was absent in all patients at time of ICU admission and recovered on average 96 hours (ranging from 5 to 330 hr) later. Etiology of TBI included passenger in a motor vehicle collision (58%; $n = 105$), fall (25%; $n = 45$), hit or run over by a motor vehicle (11%; $n = 20$), and assault (6%; $n = 11$). No differences in sociodemographic, initial GCS score, and cumulative doses of fentanyl (Baxter Healthcare, Deerfield, IL) or diprivan (Hospira, Lake Forest, IL) received in the first 24 hours of ICU admission were found between patients who could fixate and those who could not. Compared with patients who could fixate however, those who could not had higher incidence of subarachnoid hemorrhage on CT scans and more extensive brainstem injuries as per Firsching et al (25) grades. Five patients who could not fixate at 24 hours had bilateral periocular edema but were still kept in the study as they never lost the ability to open their eyes and had no gaze deviation/stroke according to their files. At phase 2b, our sample dropped to 35 as 89 patients were considered ineligible for further testing and 20 refused to participate, but no differences were found between these subgroups (**Table 2**).

Prediction of Long-Term Recovery (Phases 2a, 2b, and 2c)

With an area under the curve (AUC) of 0.85 and 0.81, respectively, return of visual fixation at 24 hours of ICU admission (sensitivity, 80%; specificity, 73%; PLR, 3.0 [95% CI, 2.2–3.5]; NLR, 0.3 [95% CI, 0.1–0.6]) and PTA duration at 11 days (sensitivity, 68%; specificity, 85%; PLR, 4.5 [95% CI, 4.0–5.3]; NLR, 0.4 [95% CI, 0.3–1.1]) were found as performant for the prediction of a GOS-E score greater than 5 (difference between AUC,

TABLE 2. Traumatic Brain Injury Patients' Characteristics Based on Their Inclusion/Exclusion Status in Phase 2b

Variables, *n* (%) or Mean (SD)	Ineligible for Phase 2b, *n* = 89	Refused to be in Phase 2b, *n* = 20	Included in Phase 2b, *n* = 35	Subgroup Difference, Analysis of Variance or χ^2 Test
Gender (male), *n* (%)	72 (81)	15 (71)	22 (67)	NS
Age	38 ± 15	35 ± 14	33 ± 15	NS
ICU stay (d)	14 ± 13	14 ± 12	15 ± 14	NS
Initial Glasgow Coma Scale score	8 ± 3	7 ± 3	8 ± 3	NS
Hours to visual fixation recovery	169 ± 158	191 ± 150	163 ± 159	NS
Length of posttraumatic amnesia (d)	18 ± 16	17 ± 16	17 ± 15	NS
Cumulative dose of fentanyl received in the first 24 hr of ICU admission (μg)	1,440 ± 1,397	1,314 ± 1,263	1,321 ± 1,287	NS
Cumulative dose of diprivan received in the first 24 hr of ICU admission (mg)	1,973 ± 1,783	1,852 ± 1,778	2,028 ± 1,833	NS
CT scan findings, *n* (%)				
Midline shift	10 (11)	8 (13)	4 (13)	NS
Compressed cisterns	13 (15)	10 (16)	5 (17)	NS
Subdural hemorrhage	37 (42)	25 (40)	17 (57)	NS
Subarachnoid hemorrhage	34 (38)	24 (39)	11 (37)	NS
Swelling	47 (53)	32 (52)	17 (57)	NS
Periocular edema-unilateral	14 (16)	4 (20)	6 (17)	NS
Periocular edema-bilateral	5 (6)	0 (0)	0 (0)	NS
Surgical decompression, *n* (%)	31 (35)	18 (29)	10 (33)	NS
Cerebrospinal fluid drainage, *n* (%)	41 (46)	29 (46)	15 (50)	NS
Marshall CT score	3 ± 1	3 ± 1	3 ± 1	NS
Rotterdam CT score	3 ± 1	3 ± 1	3 ± 1	NS
Firsching et al (25) MRI score[a]	1 ± 1	3 ± 1	1 ± 1	NS

NS = non significant.

[a]Firsching et al (25) score could be computed in only 18 patients.

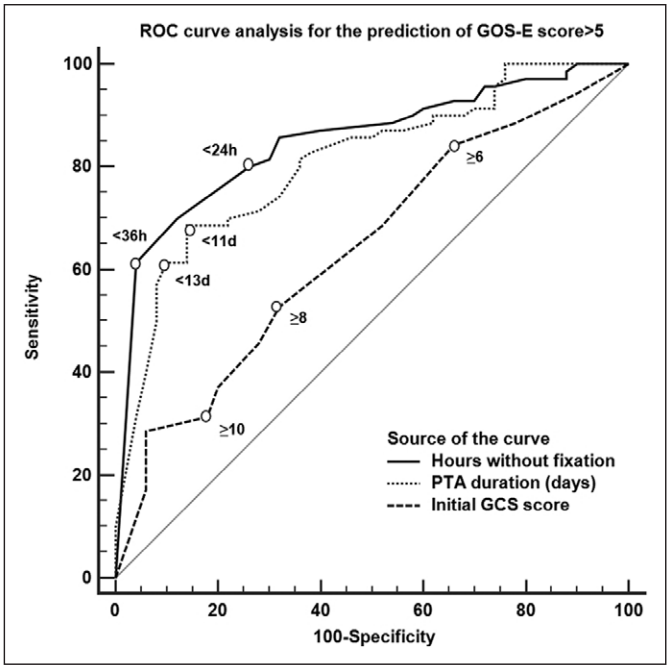

Figure 2. Receiver operating characteristic (ROC) curves for the prediction of good functional recovery by visual fixation, posttraumatic Amnesia (PTA), and the initial Glasgow Coma Scale (GCS) score. Numbers adjacent to the curve indicate cut-off values for the area under the curve. GOS-E = Glasgow Outcome Scale-Extended.

0.04; 95% CI, –0.03 to 0.12; $p = 0.28$) (**Fig. 2**). The initial GCS score conversely was a poor predictor of patients' functional outcome (AUC, 0.63). Even when correcting for age, medication (fentanyl/diprivan), and CT scan findings (Marshall/Rotterdam scores), return of visual fixation in the ICU (β, –0.29; $p = 0.04$) and PTA duration (β, –0.35; $p = 0.01$) remained significant predictors of GOS-E scores. On a smaller scale, patients who could not fixate at 24 hours of ICU admission took significant longer time to complete the MWCT task in the months after TBI, compared with those who could (104.13 ± 39.69 vs 72.42 ± 13.71 s; t, 2.89; $p = 0.04$). Again, in contrast to the GCS, return of fixation in the ICU (β, 0.26; $p = 0.04$) and PTA duration (β, 2.39; $p = 0.01$) were found to be significant predictors of MWCT scores after TBI. Finally, when percentages of the difference in regional GM volumes between each pair of TBI and matched control were considered (i.e., 23 pairs), patients who could not fixate at 24 hours of ICU admission ($n = 13$) had significant more pronounced GM volume deficits in the SEF, the midbrain, and the pons, compared with those who could ($n = 10$) (**Fig. 3**).

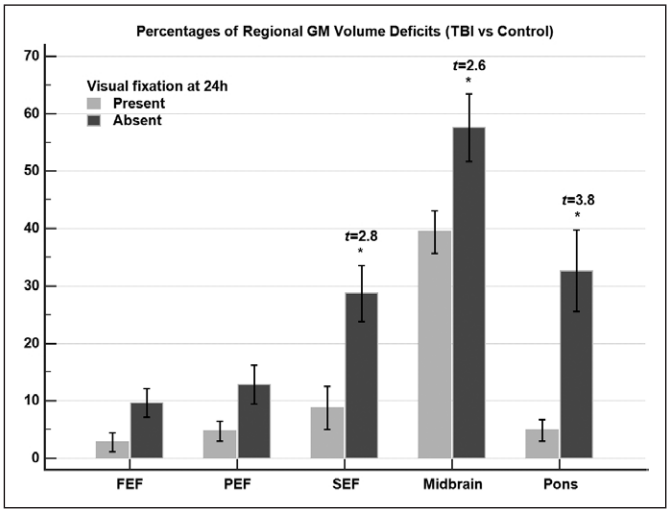

Figure 3. Percentages of regional volume deficit between pairs of traumatic brain injury (TBI) and matched control according to the return of visual fixation in the ICU. The *error bars* represent 1 SE mean. *Represents significant group difference at a Bonferroni corrected *p* value of 0.01. FEF = frontal eye field, GM = gray matter, PEF = parietal eye field, SEF = supplementary eye field.

Prediction of Death Versus Survival

Although visual fixation seems a good predictor of TBI long-term recovery, it could also be useful for predicting intrahospital death/survival. To test this hypothesis, we proceeded to a post hoc review of the medical records of all TBI patients deceased in the ICU ($n = 52$) over a 12-month period (January 2013 to December 2013). Of all patients who died during hospitalization, only one was able to fixate at 24 hours of ICU- admission. The others never recovered fixation ability. Causes of death included brain death ($n = 20$), brain hemorrhage ($n = 20$), renal failure ($n = 6$), sepsis ($n = 4$), and cardiac arrest ($n = 2$). TBI patients recovering fixation ability during the first 24 hours of ICU admission could therefore have as little as a 2% chance of succumbing to their injuries during hospitalization.

DISCUSSION

This study is the first to show that presence/absence of visual fixation at 24 hours of ICU admission could be as performant as PTA for the prediction of TBI patients' long-term functional recovery. Fixation could also be useful to predict specific attention deficits and volume losses in specific brain regions after TBI. Altogether, our findings suggest that visual fixation is an important marker of neurologic recovery, and while further testing is needed, could be considered alongside other admission variables for inclusion in TBI prognosis models.

As opposed to the initial GCS score, return of visual fixation in the ICU and PTA duration were both found to be moderate-to-strong predictors of good functional recovery in our sample of TBI patients. Accordingly, patients who were able to fixate at 24 hours of ICU admission were found 3.0 times more likely to return (at least part-time) to their preinjury occupation in the months following TBI, compared with those who could not. At a descriptive level, 86% of patients who were able to fixate at 24 hours had a good functional recovery (based on a GOS-E score > 5), as opposed to 10% of patients who were not. In contrast, the GCS score's ability to predict TBI patients' PTA duration, as well as long-term functional recovery, was hardly better than chance with an AUC equal to 0.63. Even when we reconducted our analysis with the GCS motor subscore (as it could be more robust that the total score for outcome prediction), it was not performant enough (AUC, 0.68) to predict TBI patients' functional outcome (34).

This study is not the first to highlight the limitations of the GCS score for the prediction of outcome in critically ill TBI patients (35, 36). Probably contributing to this phenomenon is the fact that although the GCS provides meaningful information about brainstem reflexes, it provides little about higher cognitive functioning in mechanically ventilated patients in whom the verbal subscale cannot be assessed (37). Visual fixation on the other hand can be initiated reflexively (from the PEF via the superior colliculus of the midbrain) or intentionally (from the FEF via the paramedian pontine reticular formation) (31). Also important for the maintenance and duration of fixation is the activity of the omnipause neurons arising from the rostral pole of the midbrain, and to a lesser extend the FEF, the SEF, and the pons, reflecting the wide distribution of neural circuits within the brain that can influence fixation (32). In terms of functionality, we know that the fronto-parietal network involved in sustained attention is also involved in intentional visual fixation (38, 39). Based on this assumption, return of visual fixation after brain injury could be indicative of higher cognitive functioning and recovering consciousness (40). Supporting this hypothesis is the fact that patients who could not fixate at 24 hours of ICU admission had poorer performance in the months following TBI on the visual attention task, compared with those who could. However, there is also a possibility that visual fixation may simply be reflexive at this stage of TBI recovery as visual fixation was found useless for discriminating patients in unresponsive wakefulness syndrome from those in minimally conscious state (41, 42).

Although it may not always be a marker of consciousness, recovery of visual fixation in the ICU is at least indicative of preserved brainstem function. Indeed, among patients who were submitted to MRI testing, those who could not fixate at 24 hours of ICU admission had significant more pronounced GM deficits than those who could in the midbrain and the pons. Patients who could not fixate at 24 hours of ICU admission also had more extensive brainstem lesions as per higher Firsching et al (25) scores. Unfortunately, MRI scans were available in only 11% of our sample limiting the extrapolation we can make on the subject. Aside from the brain injury itself, visual fixation recovery after TBI could be affected by several cooccurring factors (28). It is important to point out that although we controlled for the potential effects of analgesics and sedatives on our results, 82% of visual fixation assessments were performed during a periodic cessation of sedation. Also, 74% of our TBI participants were under preventive doses of anticonvulsant at the time of assessment, limiting the potential interference of seizure in our results. Furthermore, none of the patient showed clinical signs suggestive of simple or complex partial seizures.

This study is not without limitations. First, establishment of visual fixation in the ICU was made retrospectively based on nurses' documentation in medical files. Although this method is recommended in medical records' review studies, inconsistencies in the assessment of fixation could still have interfered with the results. A second potential limitation relates to the type of stimulus employed to assess visual fixation. The use of a mirror in particular could have resulted in higher positive response rate compared with faces (41, 42). Finally, circuitry of visual fixation is complex, and further studies with functional neuroimaging are critical for underpinning the corticocortical and corticosubcortical connections relevant to its utility as a surrogate marker of recovery in TBI. Till then, we cannot stress enough on the importance not to use visual fixation in isolation for the prediction of TBI outcome.

CONCLUSIONS

Working with reliable predictors of recovery in moderate-to-severe TBI is essential for ICU clinicians. In this study, recovery of visual fixation within 24 hours of ICU admission was found to be a strong predictor of PTA and TBI patients' long-term recovery. With further testing, visual fixation could eventually be considered alongside other admission variables for inclusion in TBI outcome algorithms, as well as for the stratification of severe and less-severe TBI in the reviewing process of randomized control trials (43).

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