



A Meta-Analysis of Global Neurophysiological Measures in Disorders of Consciousness

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Introduction A known problem in neurophysiological research is the lack of reproducibility (Poldrack 2017). This is especially relevant when the research concerns disorders of consciousness (DoC), a spectrum of medical conditions where awareness is impaired following severe brain injury. The heterogeneity of clinical profiles and brain lesions in DoC patients makes it challenging to obtain reliable data, which is further complicated by the relatively small cohorts often used in DoC studies.

Aim As meta-analysis ranks among the strongest research designs based on hierarchical levels of evidence, we here use this approach to quantitatively synthesise existing findings based on EEG in DoC patients.

Methods In January 2022, using databases MEDLINE via Ovid, and Scopus and Embase via Elsevier, we conducted a literature search for resting-state EEG studies published from 2000 to 2022, involving adults (≥16 years old) with prolonged DoC (≥28 days) and a primary diagnosis of unresponsive wakefulness syndrome (UWS; presenting arousal and reflexive movements) or minimally conscious state (MCS; presenting arousal and minimal signs of awareness), based on a validated behavioural scale (Schnakers 2020). Two referees (among MM, ZW, SA and JA) independently screened abstracts and full texts of potentially relevant studies, following inclusion/exclusion criteria shown in Figure 1. Authors were contacted when statistics were not available in the published materials. Separate random effect meta-analyses were conducted to compare global EEG metrics (Figure 2) between UWS and MCS, and healthy controls (HC) using the R package 'meta'. Effect sizes were computed using Hedges' g; heterogeneity between studies was measured using the Q test and quantified with the I² statistic. The full protocol, including the search strategy using controlled vocabulary and keyword terms, is available on PROSPERO (CRD42022327151).

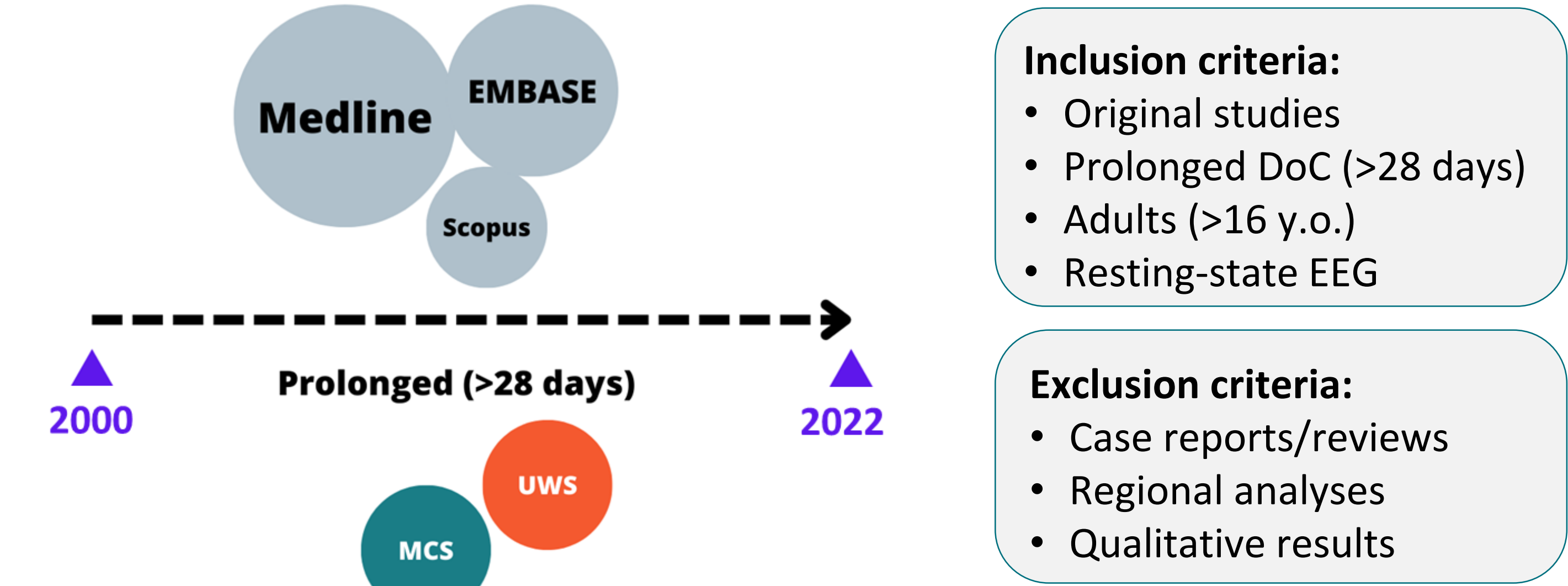


Figure 1. Schematic representation of literature search (left) and of the main inclusion and exclusion criteria used for screening (right)

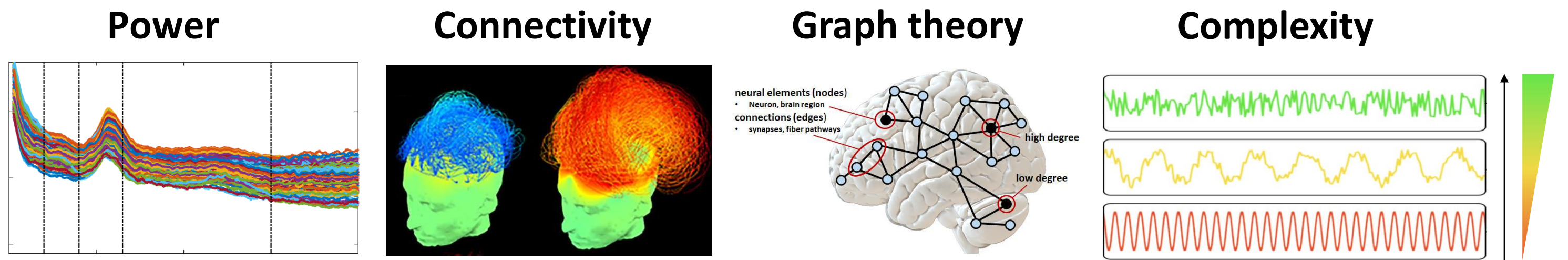


Figure 2. Main EEG measures of interest used in the studies included in the meta-analysis.

Results From a total of 4085 unique studies, 39 were found eligible for inclusion in the meta-analysis, spanning a total of 462 UWS and 484 MCS patients, as well as 188 HC (Figure 3). This included EEG studies investigating mean differences between HC, UWS and MCS in measures of power, connectivity and graph theory for δ (0.5-4Hz), θ (4-8Hz), α (8-13Hz), β (13-30Hz) and γ (>30Hz) bands. Consistent differences in EEG δ and α measures between DoC patients and HC, as well as between UWS and MCS (with smaller effect size) were found. Consistent differences in EEG θ measures between UWS and MCS (Figure 4).

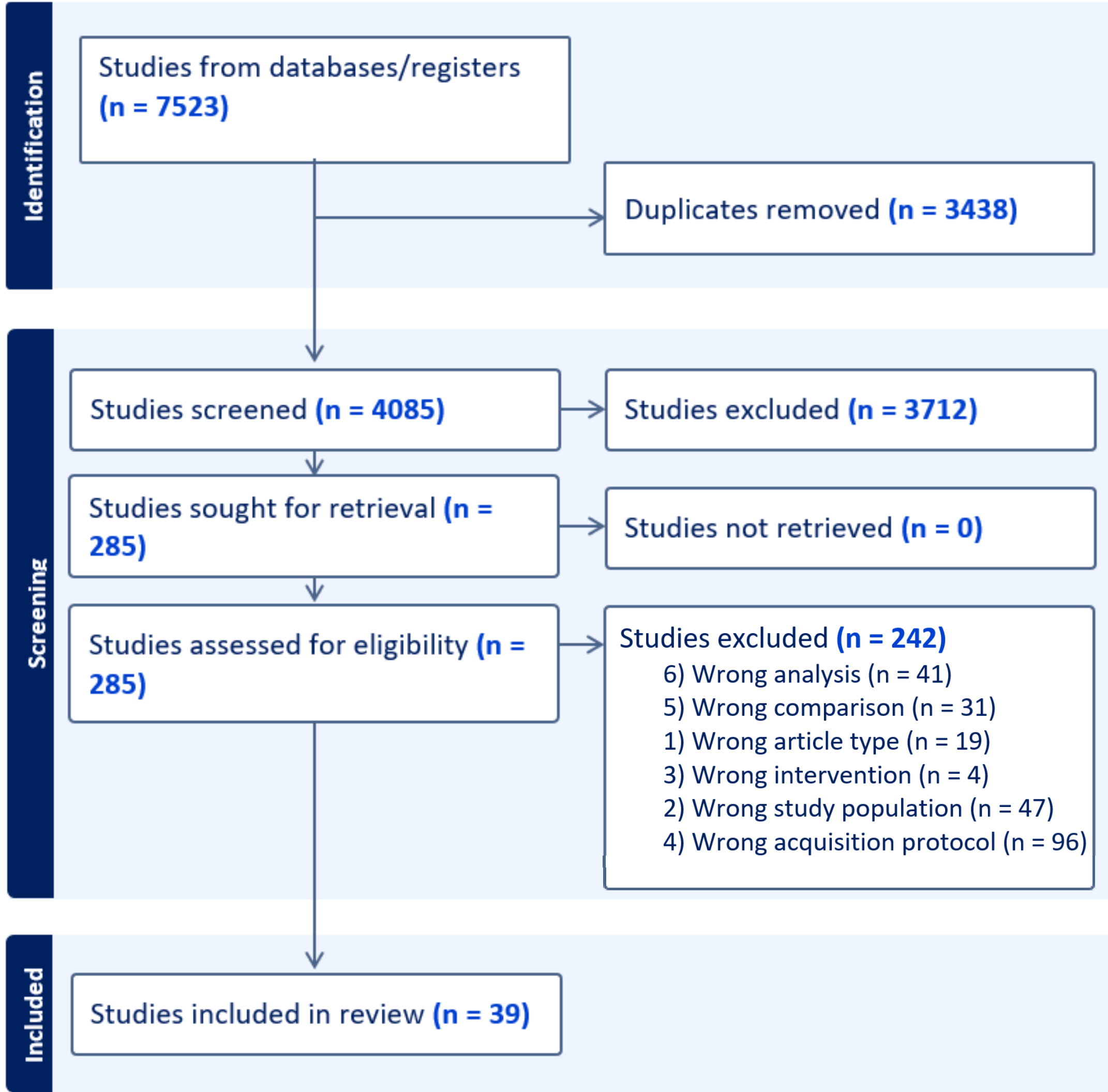


Figure 3. PRISMA flow diagram

		delta			theta			alpha			beta			gamma			broadband			
power																				
	relative power	12	4	4	12	4	4	12	4	4	12	3	3	12	3	3				
	absolute power	2	2	2	3	3	3	3	3	3	2	2	2	2	2	2				effect size
connectivity																				
	dwPLI	6	3	3	6	3	3	6	3	3	6	3	3	5	3	3				1.3
graph theory																				
	participation coefficient	2	1	1	2	1	1	2	1	1	2	1	1	2	1	1	1	1	1	
	σ -participation coefficient	5	3	3	5	3	3	5	3	3	5	3	3	5	3	3				0.8
	centrality	2			2			1			1			1						
	characteristic path length	4	2	2	4	2	2	3	2	2	3	2	2	3	2	2				
	global efficiency	4	1	1	4	1	1	3	1	1	3	1	1	3	1	1				
	clustering coefficient	7	4	4	7	4	4	6	4	4	6	4	4	6	4	4	1	1	1	
	modularity	4	2	2	4	2	2	3	2	2	3	2	2	3	2	2				0.3
complexity																				
	LZW complexity	1			1			1												
	approximate entropy																2	2		
	cross-ApEn																1			
		UWS - MCS	UWS - HC	MCS - HC																

Figure 4. Schematic representation of the results of the meta-analysis. Results are shown per type of EEG measure (row) and per band (column), for each comparison (UWS vs. MCS, UWS vs. HC, MCS vs. HC). Each cell contains the number of studies based on which the effect size for a given measure and band is computed. Color of each cell indicates the size of the effect. White background in a cell denotes lack of a significant effect.

Discussion

- Many metrics used in few studies: difficult to combine results
Power and connectivity most prevalent
- Availability of results: not commonly explicitly reported
- Lack of standardization: methodological differences between studies
Montage setups, preprocessing steps, computation of measures
- Still robust differences across group comparisons
Delta and alpha, theta up to lesser extent

References Poldrack, R.A. (2017), ‘Scanning the horizon: towards transparent and reproducible neuroimaging research’, Nat Rev Neurosci, vol. 18, pp. 115–126 Schnakers, C. (2020), ‘Update on diagnosis in disorders of consciousness’, Expert Review of Neurotherapeutics, vol. 20, no. 10, pp. 997-1004