Eur. Phys. J. Spec. Top.
https://doi.org/10.1140/epjs/s11734-026-02367-y

THE EUROPEAN PHYSICAL JOURNAL SPECIAL TOPICS

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Review

Bridging scales in some brain diseases that may result in impaired consciousness: clinical biomarkers, circuit dynamics, and network neuroscience

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Received 16 March 2026 / Accepted 27 April 2026

Abstract This review provides a thorough examination of recent developments in neurological and psychiatric disorders and systematic understanding of applications and methodology applied. Our main methods include meta-analysis, search queries with the keywords and network-based approach. Our analysis reveals that terms related to the temporal lobe frequently co-occur with EEG methods and studies involving auditory processing and epilepsy. The prefrontal cortex is commonly investigated using EEG, PET, and DTI, underscoring its role in cognition, consciousness, and neural connectivity. The brainstem shows strong co-occurrence with CT and angiography, particularly in the context of stroke and vascular pathology. The structured and organized presentation of information, along with the accompanying visualizations and diagrams, makes it a valuable resource for scientists and researchers working in the domains of intensive care medicine and rehabilitation.

Abbreviations

AI	Artificial intelligence
BOLD	Blood-oxygen-level-dependent
DoC	Disorders of consciousness
DL	Deep learning
DMN	Default mode network
ECN	Executive control network
FC	Functional connectivity
fMRI	Functional magnetic resonance imaging
MCS	Minimal consciousness state
ML	Machine learning
PTSD	Post-traumatic stress disorder
SN	Salience network
TCD	Transcranial Doppler
UWS	Unresponsive wakefulness syndrome

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Published online: 03 June 2026

1 Introduction

Disorders of consciousness (DoC) represent a spectrum of conditions resulting from severe brain injuries, characterized by varying degrees of impaired awareness. This spectrum includes coma, a state of persistent eye closure, absence of sleep–wake cycles, and unresponsiveness to both spontaneous and external stimuli, typically observed in the acute phase following brain injury [1–3]. Patients may then transition to the unresponsive wakefulness syndrome (UWS) [4], also referred to as the vegetative state (VS) [5], where they exhibit spontaneous eye opening and reflexive behaviors but show no signs of awareness of themselves or their surroundings. The term UWS is increasingly favored by experts to avoid the negative connotations associated with "vegetative" and to highlight the potential for covert consciousness. Diagnosis of UWS is based on the absence of sustained, reproducible, purposeful, or voluntary behavioral responses to external stimuli or internal needs [6, 7]. A subsequent stage is the minimally conscious state (MCS), where patients demonstrate intermittent and reproducible behavioral responses indicative of some awareness, for example, localized reactions to pain, visual tracking, execution of simple commands [8–10]. MCS can be further categorized into MCS+, indicating higher-level behavioral responses like command following or communication, and MCS-, indicating lower-level responses like visual pursuit. Finally, emergence from MCS marks further recovery of consciousness the appearance of purposeful speech activity [11, 12].

Network neuroscience [13–16] has become increasingly vital in understanding the complex neural mechanisms underlying consciousness and its disruption in DoC [17–20]. Rather than attributing consciousness to specific brain regions, it is now understood as an emergent property of integrated activity across distributed brain networks. DoC can be conceptualized as a disconnection syndrome, characterized by disrupted communication pathways, particularly within thalamocortical [21–23] and cortico-cortical circuits [24, 25]. By examining the interactions between different brain regions, network neuroscience provides a framework for identifying the specific neural networks critical for consciousness, such as the default mode network (DMN), salience network (SN), and executive control network (ECN) [26–28].

Functional magnetic resonance imaging (fMRI) connectomes have emerged as a powerful tool for mapping these functional brain connections in individuals with DoC. fMRI allows for the non-invasive measurement of brain activity by detecting changes in blood flow, specifically the blood-oxygen-level-dependent (BOLD) signal. These BOLD signal fluctuations across different brain regions can be analyzed to construct connectomes, which represent the pattern of functional connections, offering insights into the organization and disruptions of brain networks in DoC. Resting-state fMRI (rs-fMRI) is particularly valuable in this context, as it measures spontaneous brain activity in the absence of specific tasks, making it suitable for patients with limited ability to participate actively [29].

The evolution in terminology from "vegetative state" to "unresponsive wakefulness syndrome" reflects a growing recognition within the scientific community of the potential for residual cognitive function in these patients and aims to mitigate the negative perceptions associated with the former term. This shift underscores the dynamic nature of the field and highlights how language can influence both societal and clinical perspectives on DoC. Furthermore, the conceptualization of DoC as a "disconnection syndrome" provides a unifying theoretical framework for understanding the diverse clinical presentations observed across the spectrum [30, 31]. This perspective suggests that the primary underlying mechanism involves a breakdown in the effective communication between different brain regions, rather than localized damage to specific areas. While the Coma Recovery Scale-Revised (CRS-R) [32] remains the established "gold standard" for clinical assessment of consciousness , its reliance on observable behavioral responses inherently limits its ability to detect covert consciousness. This limitation underscores the critical need for complementary neuroimaging techniques, such as fMRI, to provide a more comprehensive and accurate assessment of the level of awareness in patients with DoC.

Recent reviews often provide valuable insights into specific neuroimaging techniques or conditions; however, they frequently fall short in offering a truly integrated and comprehensive meta-analysis across a wide spectrum of modalities and their diverse applications. Our meta-review directly addresses this gap by systematically unpacking the preferential use of various neuroimaging tools from the widely adopted MRI, USG, and CT, to specialized techniques like Angiography, DTI, EEG, MEG, PET, and MRS—within the context of distinct neurological conditions and specific brain regions. We move beyond general descriptions to explain why certain modalities—such as those most researched for encephalopathy—are dominant and what their inherent advantages are.

This meta-review aims to systematically analyze the scientific literature on DoC from the past 30 years to identify overarching trends, methodological disparities, and underexplored intersections between key domains. By employing a structured search strategy across PubMed, we interrogated the interplay of diagnostic modalities, clinical applications, neuroanatomical correlates, and therapeutic interventions. Through co-occurrence network analysis, we reveal patterns in research priorities, such as the dominance of certain technologies over others or the paucity of studies linking specific brain regions to treatment outcomes. Our work addresses critical gaps by

– Interest Mapping: Charting in research focus across three decades to highlight evolving paradigms.
– Interdisciplinary Synthesis: Bridging siloed discussions on neuroimaging, clinical subpopulations, and therapies.

– Methodological Critique: Identifying biases in study design, such as underrepresentation of longitudinal or multimodal approaches.

By contextualizing these findings, this review not only clarifies the current landscape but also provides a roadmap for future research to address unresolved scientific and clinical challenges in DoC.

2 Materials and methods

As part of the methodology implementation, published articles were retrieved from scientific databases for the last 30 years using PubMed search engine (https://pubmed.ncbi.nlm.nih.gov, accessed on 20 May 2025). The following terms were used in the construction of search queries to conduct an analytical review of the current scientific and technical, regulatory, methodological literature addressing the scientific and technical problem of FC for the DoC: "Functional connectivity" keyword was mandatory part of the query, while terms for the modality (e.g., "EEG"), and application (e.g., "coma"), brain region, or treatment were combined pairwise as shown in Table 1.

At the initial stage of our review, we have identified and highlighted the following key issues that we wish to address:

– Which types of methods and modalities are popular;
– Most common applications among the DoC;
– Brain areas associated with DoC;
– Stimulation and treatment techniques most commonly tried in the consciousness research.

During the research phase, we carefully reviewed papers that met the criteria of having one of the search queries or equivalent restatements in their title, abstract, or key words. Additionally, we excluded papers with the types "Book", "Chapter", and "Monograph" from our final sample using PubMed search filters. Following the collection of the number of relevant papers found for each query, we chose the most significant results and features, and then performed a more specific review to identify the causes behind these findings on the basis of specific examples.

We created a keyword co-occurrence network which used information gathered from around 1500 papers found in PubMed by using a search query using VOSviewer version 1.6.20 (Center for Science and Technology Studies, Leiden University, The Netherlands) [33]. This network provides a visual representation of the frequency with which certain terms appeared together in the studies analyzed, offering a clearer understanding of the overarching trends and connections that exist within the field. The methodology of VOSviewer visualization technique is provided in details in [34]. We have previously used a similar network-based approach to analyze AI methods in biomedical research [35].

Table 1 List of the used keywords

Methods and modalities	Application	Brain region	Treatment
Electroencephalography	Aneurysm	Auditory cortex	Acoustic stimulation
Angiography	Brain concussion	Basal ganglia	Anti-inflammatory agents
Computed tomography	Coma	Brain stem	Deep brain stimulation
Diffusion tensor imaging/tractography	Encephalopathy	Cerebellum	Electric stimulation therapy
Magnetic resonance spectroscopy	Hypoxia/anoxia	Occipital lobe	Transcranial direct current stimulation
Magnetoencephalography	Hemorrhagic stroke	Parietal lobe	Transcranial magnetic stimulation
Positron emission tomography	Ischemic stroke	Prefrontal cortex	
Ultrasonography	Minimally conscious state	Temporal lobe	
	Unresponsive wakefulness syndrome	Thalamus	
	Vegetative state	Visual cortex	
	Traumatic brain injury		

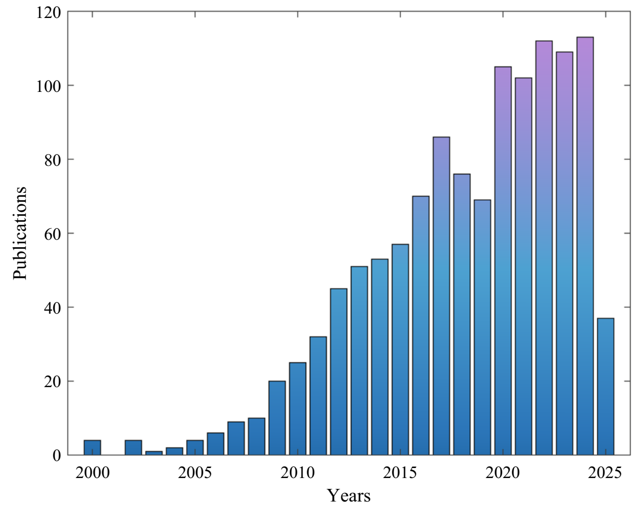


Fig. 1 Amount of relevant publications (including keywords on consciousness disorders and "functional connectivity" over years

By employing network visualization techniques, it became possible for us to detect clusters or communities within the keyword co-occurrence network by assigning a color code to each item based on the cluster to which it belongs. In our research, we utilized the VOSviewer algorithm which employs a modularity function to identify these groups [36]. The extracted clusters offer further information and insights regarding the relationship between keywords within the field being studied (Fig. 1).

3 Review

3.1 Results and findings

The VOSviewer identified three big (> 20 items) clusters, which can be easily interpreted based on the keywords they contain (Figs. 2 and 3).

Cluster 1 focuses on the clinical assessment, diagnosis, prognosis, and treatment outcomes of consciousness disorders. This cluster encompasses a variety of diagnostic tools and methodologies, such as MRI, diffusion tensor imaging (DTI), PET scans, and the Glasgow Coma Scale [37], which are essential for assessing brain injuries, coma, and other consciousness disorders. Biomarkers and the study of white matter integrity, as shown by diffusion MRI, are crucial for understanding the underlying pathology and predicting recovery of function. Machine learning appears in this cluster, indicating the use of advanced computational methods to improve diagnosis and prognostication. The inclusion of terms like "arousal," "oxygen," "neural pathways," and "signal transduction" reflects the physiological and cellular mechanisms involved in consciousness and recovery. PTSD and stress disorders suggest an interest in the psychological consequences of brain injuries. Overall, this cluster is heavily clinically oriented, focusing on assessment, prognosis, and treatment outcomes.

Cluster 2 is focused on the neural mechanisms underlying cognitive functions and awareness, also methods of their assessment and stimulation. This cluster includes keywords related to basic neuroscience, such as action potentials, neurons, interneurons, neural inhibition, and neuronal plasticity. Brain regions like the hippocampus, motor cortex, prefrontal cortex, and the olfactory bulb are mentioned, highlighting the importance of specific brain areas in cognition, memory, and sensory processing.

Techniques such as electric stimulation, transcranial stimulation (tDCS and TMS), photic stimulation, and functional neuroimaging are central to this cluster, indicating a focus on understanding and modulating brain activity. Terms like "awareness," "cognition," "memory," and "visual perception" indicate a strong emphasis on higher-order brain functions. Epilepsy is included, likely due to its impact on neural activity and cognitive functions. Overall, this cluster focuses on the fundamental neural processes and brain regions that contribute to cognitive functions and awareness.

Cluster 3 revolves around different states of consciousness, brain networks, and the neural correlates of consciousness. This cluster includes keywords like consciousness, unconsciousness, wakefulness, sleep, and attention, signifying a focus on various states of awareness. Brain regions mentioned include the cerebral cortex, frontal lobe, parietal lobe, thalamus, and cingulate gyrus, which are all crucial for regulating consciousness and attention.

The default mode network (DMN) and the connectome are also included, reflecting an interest in large-scale brain networks associated with consciousness and self-referential thought. EEG is a significant keyword in this cluster,

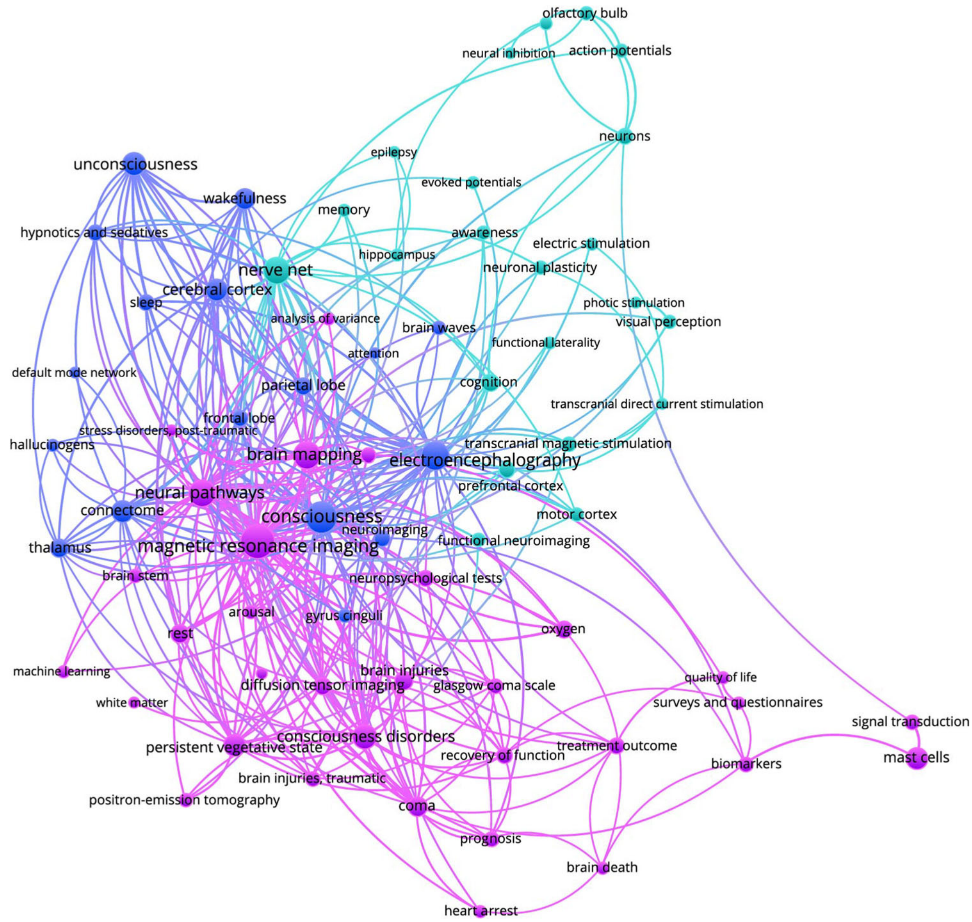


Fig. 2 The co-occurrence network constructed using VOSviewer. The size of the nodes are determined by the weight of the corresponding item that indicate the importance of the item, and the color is determined by the cluster to which the item belongs

as it is a primary method for studying brain waves and different states of consciousness. The presence of terms like hallucinogens and hypnotics/sedatives suggests research into how substances affect consciousness. Neuroimaging is also mentioned, indicating the use of imaging techniques to study brain activity related to consciousness. Overall, this cluster is focused on understanding the neural basis of different consciousness states and the brain networks involved.

In summary,

- Cluster 1: Clinical assessment and prognosis—focuses on the diagnosis, prognosis, and treatment of consciousness disorders using clinical tools and biomarkers.
- Cluster 2: Neural mechanisms and stimulation techniques—centers on the neural mechanisms and brain regions involved in cognitive functions, awareness, and basic neuroscience research.
- Cluster 3: Consciousness states and brain networks—revolves around the study of various consciousness states, large-scale brain networks, and the neural correlates of consciousness.

To further analyze the co-occurrence trends in the publications, we looked into pairwise combinations of the keywords (Table 1) most prevalent in the database output.

3.1.1 Modalities and applications

Let us first look at the combination of the keywords Modalities and Applications (Fig. 4).

Looking at the first row, MRI has high numbers across many conditions, especially encephalopathy (8621), traumatic brain injury (722), and vegetative state (1685). This reflects MRI's versatility in detecting structural abnormalities, functional connectivity, and metabolic changes in chronic and acute neurological disorders [38–40].

Encephalopathy is a major focus. Encephalopathy has the highest co-occurrence counts across almost all modalities (MRI: 8621, USG: 6009, PET: 949), likely due to its broad definition (encompassing metabolic, toxic, and hypoxic brain disorders) including due to the global aging of the population and the need for multimodal diagnostic approaches [41–45].

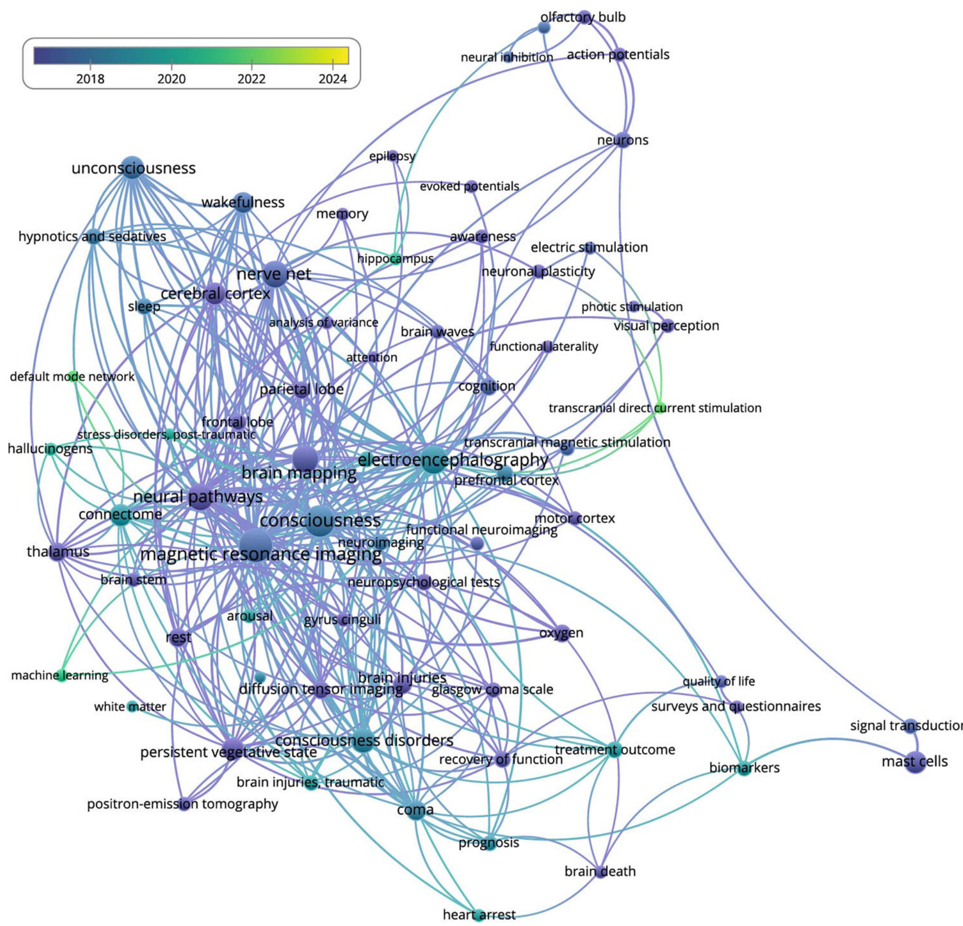
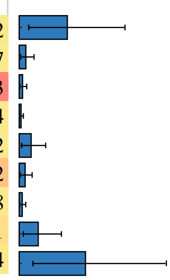


Fig. 3 The co-occurrence network constructed using VOSviewer. The size of the nodes are determined by the weight of the corresponding item that indicate the importance of the item, and the color is determined by the publishing activity per year (blue color denotes nodes with the majority of publications of 2014 year, and yellow denotes nodes where corresponding publications are from 2023 to 2025)

	An	BC	Coma	En	Hx	HS	IS	MCS	UWS	VS	TBI
MRI	114	263	227	8621	86	25	360	111	51	1685	722
EEG	2	27	147	2582	54	3	51	107	60	387	107
AnG	193	1	4	223	17	7	30	0	0	87	3
CT	156	13	13	631	32	5	32	16	0	174	34
DTI	2	67	38	1609	21	5	81	19	6	166	202
MRS	1	11	6	239	16	1	12	1	1	40	22
MEG	3	21	9	464	0	0	2	6	3	71	48
PET	7	8	38	949	15	2	12	39	16	118	31
USG	327	203	138	6009	109	23	244	83	38	1288	444



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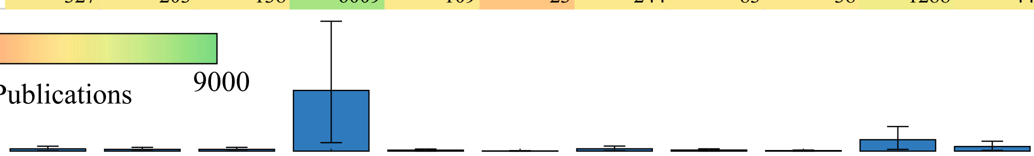


Fig. 4 Amount of publications by Modality/Application keywords (magnetic resonance imaging (MRI), electroencephalography (EEG), angiography (AnG), computed tomography (CT), diffusion tensor imaging or tractography (DTI), magnetic resonance spectroscopy (MRS), magnetoencephalography (MEG), positron emission tomography (PET), ultrasonography (USG), aneurysm (An), brain concussion (BC), coma, encephalopathy (En), hypoxia/anoxia (Hx), hemorrhagic stroke (HS), ischemic stroke (IS), minimally conscious state (MCS), unresponsive wakefulness syndrome (UWS), vegetative state (VS), traumatic brain injury (TBI)). The blue histograms provide an overview of the average number of publications related to each technique or application, respectively

USG as a fairly simple and accessible to perform in the conditions of almost any hospital shows high associations, particularly with encephalopathy (6009) and TBI (444). Possible explanations: use in neonatal/pediatric encephalopathy [46, 47] and the transcranial Doppler for cerebral blood flow monitoring in TBI or stroke [48–50].

Condition-specific techniques

- Aneurysm: strongly linked to angiography and CT—tools critical for vascular imaging and acute hemorrhage detection.
- Traumatic brain injury: DTI and MRI dominate, highlighting their role in assessing axonal injury and structural damage.
- Vegetative State/Unresponsive Wakefulness: EEG and MRI are prominent, reflecting their use in consciousness evaluation and neuroimaging.
- Ischemic stroke: MRI and USG lead, due to MRI's sensitivity to ischemia and carotid ultrasonography for stenosis detection.

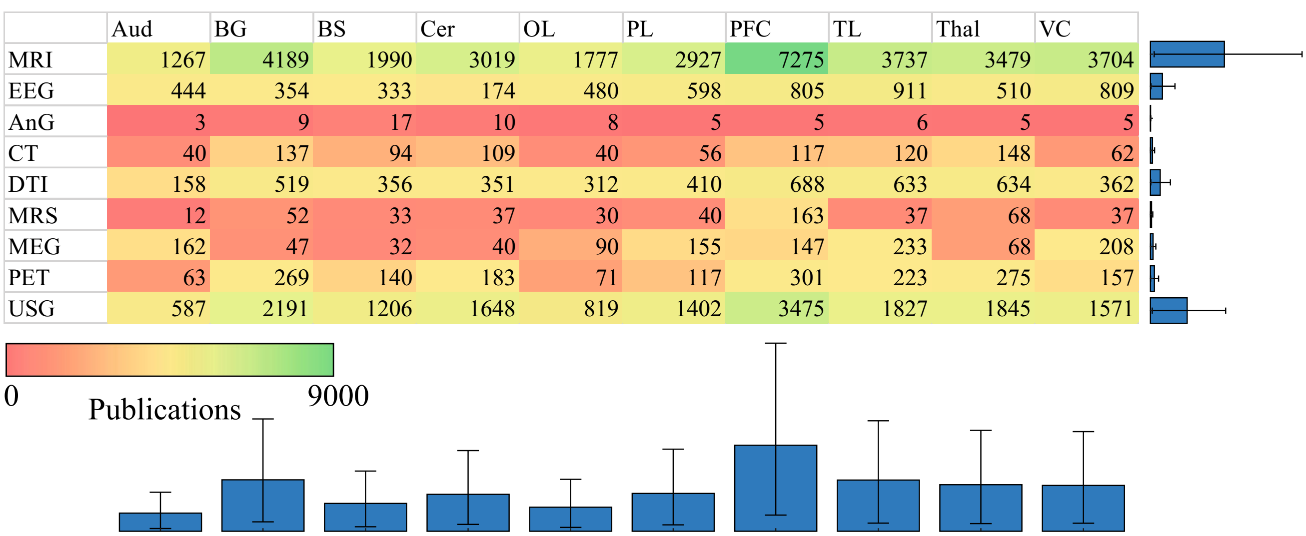
MEG and MRS have low overall counts, suggesting specialized/research-oriented applications (e.g., metabolic profiling with MRS in encephalopathy [51]). PET is a method of mapping metabolic activity [52–54].

Trends to be observed: CT and angiography dominate in acute settings (aneurysm, stroke), while MRI, DTI, and EEG are preferred for chronic/functional assessments (coma, vegetative states). USG and CT may be overrepresented in low-resource settings or emergency departments, while PET and MEG's lower counts may reflect cost/availability limitations. High MRI/DTI use in TBI aligns with modern focus on white matter integrity and connectomics. EEG's role in coma/vegetative states underscores its importance in neurophysiological monitoring.

3.1.2 Modalities and brain areas

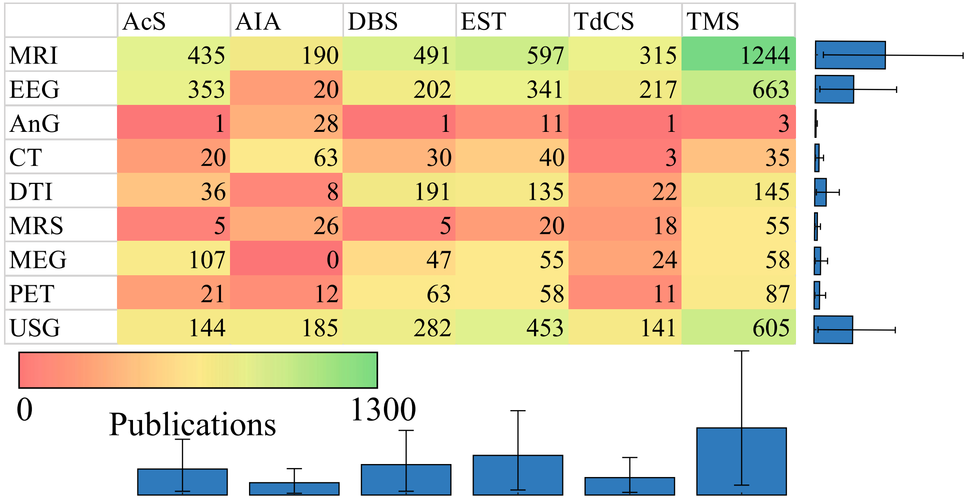
As we can see from Fig. 5, MRI is the most widely associated technique across all brain regions, with the highest counts in: prefrontal cortex (7275), thalamus (3479), basal ganglia (4189), and visual cortex (3704). That reflects MRI's versatility in structural and functional imaging, particularly for regions critical to cognition (prefrontal cortex) [55–57], sensorimotor integration (basal ganglia) [58–60], and sensory processing (visual cortex) [61, 62]. Furthermore, MRI, unlike almost all neuroimaging methods, allows to precisely map deep brain structures, such as, for example, the thalamus.

EEG shows strong associations with the temporal lobe and prefrontal cortex, aligning with its use first and foremost, for the diagnosis of epilepsy, and in studying auditory processing [63–68], memory (temporal lobe) [69–71], and executive functions/neuropsychiatric disorders (prefrontal cortex) [72–74]. USG has unexpectedly high counts for prefrontal cortex (3475) and basal ganglia (2191). Likely explained by neonatal/pediatric brain



	Aud	BG	BS	Cer	OL	PL	PFC	TL	Thal	VC
MRI	1267	4189	1990	3019	1777	2927	7275	3737	3479	3704
EEG	444	354	333	174	480	598	805	911	510	809
AnG	3	9	17	10	8	5	5	6	5	5
CT	40	137	94	109	40	56	117	120	148	62
DTI	158	519	356	351	312	410	688	633	634	362
MRS	12	52	33	37	30	40	163	37	68	37
MEG	162	47	32	40	90	155	147	233	68	208
PET	63	269	140	183	71	117	301	223	275	157
USG	587	2191	1206	1648	819	1402	3475	1827	1845	1571

Fig. 5 Amount of publications by Modality/brain areas keywords (magnetic resonance imaging (MRI), electroencephalography (EEG), angiography (AnG), computed tomography (CT), diffusion tensor imaging or tractography (DTI), magnetic resonance spectroscopy (MRS), magnetoencephalography (MEG), positron emission tomography (PET), ultrasonography (USG), auditory cortex (Aud), basal ganglia (BG), brain stem (BS), cerebellum (Cer), occipital lobe (OL), parietal lobe (PL), prefrontal cortex (PFC), temporal lobe (TL), thalamus (Thal), visual cortex(VC)). The blue histograms provide an overview of the average number of publications related to each technique or application, respectively



	AcS	AIA	DBS	EST	TdCS	TMS
MRI	435	190	491	597	315	1244
EEG	353	20	202	341	217	663
AnG	1	28	1	11	1	3
CT	20	63	30	40	3	35
DTI	36	8	191	135	22	145
MRS	5	26	5	20	18	55
MEG	107	0	47	55	24	58
PET	21	12	63	58	11	87
USG	144	185	282	453	141	605

Fig. 6 Amount of publications by Modality/treatment keywords (magnetic resonance imaging (MRI), electroencephalography (EEG), angiography (AnG), computed tomography (CT), diffusion tensor imaging or tractography (DTI), magnetic resonance spectroscopy (MRS), magnetoencephalography (MEG), positron emission tomography (PET), ultrasonography (USG), acoustic stimulation (AcS), anti-inflammatory agents (AIA), deep brain stimulation (DBS), electric stimulation therapy (EST), transcranial direct current stimulation (TdCS), transcranial magnetic stimulation (TMS)). The blue histograms provide an overview of the average number of publications related to each technique or application

imaging, DTI peaks in prefrontal cortex, thalamus, and parietal lobe, emphasizing its role in mapping connectivity between hubs involved in cognition, sensory integration, and attention [74–76]. PET is most linked to prefrontal cortex and basal ganglia, likely due to its use in studying dopamine pathways (basal ganglia in Parkinson's) and glucose metabolism in neurodegenerative diseases (prefrontal cortex in Alzheimer's) [77, 78]. MEG: strongest for temporal lobe and visual cortex, reflecting its sensitivity to auditory/visual-evoked responses [79–81]. MRS: highest in prefrontal cortex, used to study metabolic changes in psychiatric/neurodegenerative disorders [82, 83]. Angiography (AnG) and CT: minimal associations, as they focus on vascular anatomy or acute pathology.

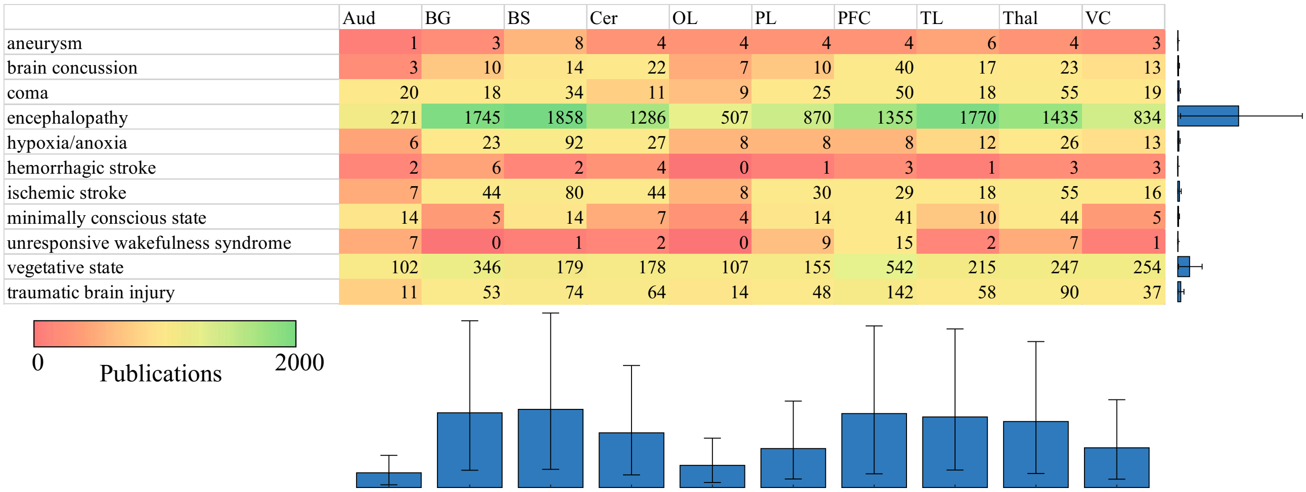
3.1.3 Modalities and treatments

As we can see from Fig. 6, MRI is the most widely associated technique across all interventions, especially with transcranial magnetic stimulation (TMS: 1244) and deep brain stimulation (DBS: 491). This reflects MRI's role in target localization (e.g., DBS electrode placement) and monitoring neuroplasticity post-TMS. USG shows surprisingly high co-occurrence with TMS (605) and electric stimulation therapy (453), likely due to use in real-time monitoring of cerebral blood flow during stimulation and neonatal applications.

EEG pairs strongly with TMS and electric stimulation therapy, highlighting its use in assessing real-time brain activity changes during/after stimulation [83–89]. TMS dominates across most modalities (MRI: 1244; USG: 605; EEG: 663), reflecting its broad research applications in depression, stroke recovery, and cognitive neuroscience. MEG correlates strongly with acoustic stimulation, aligning with its sensitivity to auditory-evoked responses. MRS has limited associations but peaks with TMS, likely probing metabolic changes (e.g., GABA/glutamate shifts [90]). Angiography has minimal connections, with the exception of anti-inflammatory drugs (28), since it is used as an independent diagnostic method in routine clinical practice. USG and electric stimulation therapy: ultrasound is used as a method of monitoring the electrostimulation intervention in situ, and possibly include methods for monitoring the effectiveness of neuromodulation therapy. MEG and acoustic stimulation outlier: they stand out from the general picture, reflecting mostly scientific research of auditory perception as a biomarker in various neurological pathologies [91–93].

3.1.4 Applications and brain areas

As we can see from Fig. 7, encephalopathy dominates the table with exceptionally high values across all regions (e.g., 1858 in brain stem, 1770 in temporal lobe). This is due to the fact that it represents a diffuse lesion of the brain matter, due to its systemic nature (for example, of metabolic, toxic or infectious origin, affecting multiple areas). Vegetative state and traumatic brain injury (TBI) also show high co-occurrences, particularly with the prefrontal cortex, aligning with their associations with executive dysfunction and consciousness disorders.



	Aud	BG	BS	Cer	OL	PL	PFC	TL	Thal	VC
aneurysm	1	3	8	4	4	4	4	6	4	3
brain concussion	3	10	14	22	7	10	40	17	23	13
coma	20	18	34	11	9	25	50	18	55	19
encephalopathy	271	1745	1858	1286	507	870	1355	1770	1435	834
hypoxia/anoxia	6	23	92	27	8	8	8	12	26	13
hemorrhagic stroke	2	6	2	4	0	1	3	1	3	3
ischemic stroke	7	44	80	44	8	30	29	18	55	16
minimally conscious state	14	5	14	7	4	14	41	10	44	5
unresponsive wakefulness syndrome	7	0	1	2	0	9	15	2	7	1
vegetative state	102	346	179	178	107	155	542	215	247	254
traumatic brain injury	11	53	74	64	14	48	142	58	90	37

Fig. 7 Amount of publications by Application/brain areas keywords [auditory cortex (Aud), basal ganglia (BG), brain stem (BS), cerebellum (Cer), occipital lobe (OL), parietal lobe (PL), prefrontal cortex (PFC), temporal lobe (TL), thalamus (Thal), visual cortex (VC)]. The blue histograms provide an overview of the average number of publications related to each technique or application, respectively

Prefrontal cortex: Highly linked to coma (50), vegetative state, TBI, and minimally conscious state, reflecting its role in higher-order cognition and consciousness. Thalamus is strongly associated with coma, ischemic stroke, and encephalopathy, consistent with its role as a sensory/motor relay hub and modulator of consciousness [94–96]. Brain stem is prominent in encephalopathy (1858) and coma (34), likely due to its critical role in vital functions (e.g., breathing, arousal). Basal ganglia shows high co-occurrence with encephalopathy (1745) and ischemic stroke, possibly reflecting motor and cognitive dysfunction in these conditions (e.g., Parkinson's disease). Visual cortex: Notably linked to vegetative state, possibly due to preserved visual reflexes or studies on residual sensory processing in unconscious states.

Condition-specific patterns:

- Coma: strong ties to the thalamus and brain stem, underscoring their roles in arousal and consciousness [97].
- Ischemic stroke: high values in basal ganglia and thalamus, regions commonly affected by vascular events [98–100].
- Hypoxia/anoxia: most associated with the brain stem, which is highly sensitive to oxygen deprivation [101].
- Hemorrhagic stroke: low overall co-occurrence, potentially due to its focal nature (e.g., basal ganglia, thalamus) being less frequently studied in multi-regional analyses.
- Unresponsive wakefulness syndrome (UWS): minimal co-occurrence with most regions except the prefrontal cortex, suggesting limited research focus or specificity to frontal networks.

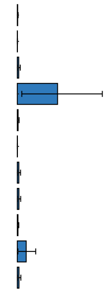
The data emphasize the prefrontal cortex, thalamus, and brain stem as hubs for consciousness-related disorders, while encephalopathy serves as a catch-all term for diffuse brain involvement. Conditions like ischemic stroke and TBI show region-specific patterns aligning with their pathophysiology.

3.1.5 Applications and treatments

As we can see from Fig. 8, encephalopathy dominates the table with extremely high co-occurrence across most interventions—electric stimulation therapy (792) and deep brain stimulation (597) are most prominent, reflecting the high and increasing prevalence of this pathology and, accordingly, the need to study effective correction of the condition, including neuromodulation methods [102]. Vegetative state and coma also show strong links to transcranial magnetic stimulation (TMS) and electric stimulation therapy, aligning with research on restoring consciousness [87, 103–107].

TMS is the most frequent for ischemic stroke, TBI, coma, and encephalopathy. This reflects its non-invasive role in motor recovery (stroke/TBI) and consciousness recovery methods. Electric stimulation therapy shows strongest links to encephalopathy and vegetative state, possibly for seizure control or arousal modulation [108, 109]. Anti-inflammatory agents demonstrate highest values for encephalopathy and aneurysm, indicating research into neuroinflammation in systemic brain dysfunction or post-hemorrhage management [110–112]. Deep brain

	AcS	AIA	DBS	EST	TdCS	TMS
aneurysm	0	17	0	5	0	1
brain concussion	1	0	0	0	0	5
coma	10	4	12	15	15	30
encephalopathy	132	230	597	792	157	543
hypoxia/anoxia	3	33	2	5	1	5
hemorrhagic stroke	0	1	0	1	0	3
ischemic stroke	2	17	4	28	10	32
minimally conscious state	12	4	11	27	16	28
unresponsive wakefulness syndrome	8	1	2	6	8	17
vegetative state	78	105	57	145	44	112
traumatic brain injury	5	10	19	22	10	36



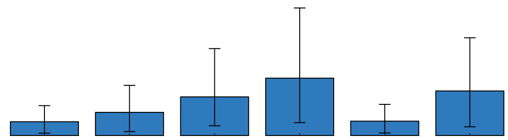


Fig. 8 Amount of publications by Application/treatment keywords (acoustic stimulation (AcS), anti-inflammatory agents (AIA), deep brain stimulation (DBS), electric stimulation therapy (EST), transcranial direct current stimulation (TdCS), transcranial magnetic stimulation (TMS)). The blue histograms provide an overview of the average number of publications related to each technique or application, respectively

stimulation is primarily tied to encephalopathy and coma, suggesting experimental use in severe neurological disorders (e.g., epilepsy, central autonomic dysregulation) [56, 113].

3.1.6 Brain areas and treatments

As we can see from Fig. 9, TMS (689) and tDCS (247) are most prominent in the prefrontal cortex, reflecting its role in cognitive/psychiatric research (e.g., depression, executive function) [114–118]. Auditory cortex is unsurprisingly strongly linked to acoustic stimulation (742), as expected for auditory processing studies. Basal ganglia has highest co-occurrence with DBS and electric stimulation, aligning with its role as a target in movement disorders (e.g., Parkinson's disease) [119–123]. Thalamus is strongly tied to DBS, likely targeting epilepsy [124], tremor [125], or chronic pain [126]. Visual cortex has high values with TMS and electric stimulation, which is explained by the wide representation of studies on the effect of TMS on visual function and the potential usefulness of such an effect for the treatment of certain conditions [127, 128].

Intervention-specific trends

- Transcranial magnetic stimulation is the most frequent for prefrontal cortex, parietal lobe, and visual cortex, emphasizing non-invasive modulation of cortical functions (executive functions, vision, sensory integration).
- Deep brain stimulation is focused on basal ganglia and thalamus, reflecting its use in motor symptoms, epilepsia and DoCs.
- Transcranial direct current stimulation has the strongest link to prefrontal cortex, targeting cognitive enhancement or mental health.
- Acoustic stimulation is almost exclusive to auditory cortex and temporal lobe, tied to auditory processing and speech studies.

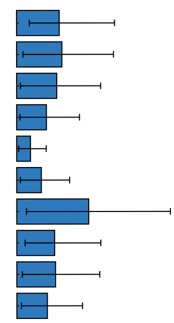
In general, we can see that non-invasive methods (TMS/tDCS): dominant in cortical regions for cognitive, sensory, and psychiatric applications and invasive methods (DBS): reserved for subcortical targets in movement/seizure disorders and anti-inflammatory research are focused on neurodegeneration but may expand to neurovascular or autoimmune conditions.

4 Discussion

Our comprehensive meta-analysis of neuroimaging and electrophysiological techniques has helped to discover several main trends in their application across various neurological conditions and specific brain regions and conditions.

MRI's versatility in imaging different tissues, angiography's role in vascular conditions: the key advantages of MRI include its superior image quality, exceptional detail of soft tissues, and the complete absence of ionizing radiation, rendering it a safer option for repeated imaging procedures. However, its disadvantages encompass higher costs, longer scan durations, the generation of significant noise during operation [129].

	AcS	AIA	DBS	EST	TdCS	TMS
auditory cortex	742	11	34	32	31	114
basal ganglia	114	83	395	295	25	112
brain stem	267	41	184	195	63	157
cerebellum	52	26	145	157	71	222
occipital lobe	81	9	31	34	29	128
parietal lobe	95	9	53	88	63	249
prefrontal cortex	125	82	187	297	247	689
temporal lobe	517	19	61	76	37	146
thalamus	159	24	322	260	26	85
visual cortex	233	18	51	63	63	262



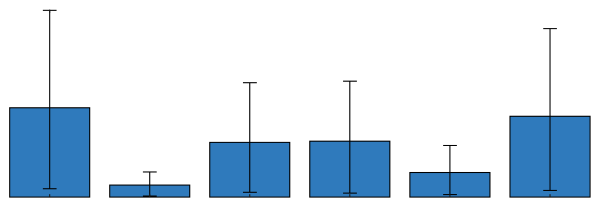


Fig. 9 Amount of publications by brain areas/treatment keywords (acoustic stimulation (AcS), anti-inflammatory agents (AIA), deep brain stimulation (DBS), electric stimulation therapy (EST), transcranial direct current stimulation (TdCS), transcranial magnetic stimulation (TMS)). The blue histograms provide an overview of the average number of publications related to each technique or application, respectively

Ultrasonography's high numbers might need more context; it is used in specific populations like neonates or for non-brain applications related to these conditions as well as the prevalence of vascular pathology in the modern world. Ultrasound utilizes high-frequency sound waves to produce real-time images of brain structures and evaluate blood flow. Transcranial Doppler (TCD) specifically assesses blood flow in the major cerebral arteries. Ultrasound is recognized for its safety, non-invasiveness, and painless nature, making it a relatively inexpensive, quick, and easily accessible modality, often available as a portable device [130].

Looking at EEG, the highest co-occurrence is with the temporal lobe and prefrontal cortex shows an interesting detail. EEG measures electrical activity, so the temporal lobe might be related to auditory processing or memory, which are often studied using EEG, and also with the fact that EEG is the main method of diagnosing epilepsy, among which temporal epilepsy is the most common. The temporal lobe is critically involved in temporal lobe epilepsy, the most common type of focal epilepsy, where seizures frequently originate. EEG can detect characteristic sharp spikes and waves in this region [131].

Angiography has very low numbers across all regions. The highest is brain stem. That is expected because angiography is mainly for vascular imaging, so unless the study is on blood vessels in specific regions, it is less common. Common regional co-occurrences include areas near the Circle of Willis and other cerebral arteries, which are frequent sites for brain aneurysms. For brainstem vascular anatomy, vertebral arteries travel along the brainstem, and the basilar artery runs along the pons, making angiography vital for assessing issues in these critical areas. Thus, we can speculate that in studies of the consciousness, it is reflecting brain stem strokes or aneurysms [132–134].

CT scans are moderately prominent, highest values in basal ganglia, thalamus, and brain stem. The basal ganglia and thalamus are common sites for strokes and TBI, so that could explain the numbers, as CT scans are highly effective for the rapid diagnosis of acute stroke, particularly for differentiating hemorrhagic stroke, where blood appears brighter, from ischemic stroke, which is critical for immediate treatment decisions. It can swiftly detect acute conditions such as brain hemorrhages and fractures. Furthermore, CT offers accurate detection of calcifications and metallic foreign bodies within the brain. Its speed makes it the preferred choice in cases of trauma and other acute neurological emergencies [135].

MEG shows higher numbers in temporal lobe and visual cortex. MEG is good for temporal resolution, so auditory processing in the temporal lobe and visual processing in the visual cortex would be areas of focus. A common clinical application of MEG is presurgical mapping for epilepsy and brain tumors. It is used to localize epileptic discharges and map eloquent cortex, which includes motor, somatosensory, and language areas, with the goal of preserving essential brain regions during surgical procedures [136–138].

DTI, which is for white matter tracts, shows high numbers in prefrontal cortex, thalamus, and parietal lobe. These regions are involved in connectivity, so DTI's use in studying neural pathways makes sense. Prefrontal cortex connections are crucial for various functions, hence the high count. DTI offers enhanced sensitivity in detecting subtle white matter abnormalities, making it particularly valuable in the context of traumatic brain injury (TBI) and concussion. It can identify diffuse axonal injury, which may not be visible on conventional MRI. This capability is crucial for tailoring rehabilitation programs and informing decisions regarding an athlete's return to high-impact sports following a concussion. Beyond TBI, DTI metrics, such as Fractional Anisotropy (FA) and Mean Diffusivity (MD), serve as biomarkers reflecting white matter integrity. These metrics are utilized in the study of various neurodegenerative and neurodevelopmental disorders, including amyotrophic lateral sclerosis, multiple sclerosis, Parkinson's disease, Alzheimer's dementia, epilepsy, and ischemic stroke [139–141].

PET scans are highest in prefrontal cortex and basal ganglia. PET is used for metabolic activity, so studies on dopamine in the basal ganglia (like Parkinson's) or glucose metabolism in the prefrontal cortex (Alzheimer's—using fluorodeoxyglucose) is common. The advantages of PET include its ability to provide functional information about brain metabolism and neurochemistry, allowing for the early detection of pathological processes even before structural changes become apparent. It is highly sensitive for detecting functional brain changes. However, its limitations include high cost, the use of radioactive tracers, and generally lower spatial resolution compared to MRI [142].

MRS can measure metabolites, so perhaps used to study neurochemical changes post-TMS or in inflammation. In terms of regional co-occurrences, MRS provides a "chemical profile" or "spectroscopic fingerprint" of specific metabolites within defined voxels in the brain, allowing for highly localized biochemical analysis [143].

The selection of a neuroimaging modality is a complex decision influenced by several factors, including diagnostic capabilities, accessibility, cost-effectiveness, and patient-specific considerations such as radiation exposure, the presence of metallic implants, and the patient's ability to cooperate during the procedure. Each technique offers a unique window into the brain, presenting distinct strengths and limitations that necessitate careful consideration in clinical practice [139]. While the bibliometric trends presented above offer a valuable map of how neuroimaging and electrophysiological techniques are applied across brain regions and conditions, a deeper consideration of circuit dynamics is essential to understanding the functional relevance of these patterns. Circuit dynamics refer to the temporal and spatial interplay of neural activity within and between distributed brain networks, which underpin both normal cognitive processes and pathological states. Our analysis reveals that certain modalities are uniquely positioned to capture distinct aspects of these dynamics. For instance, EEG and MEG, with their millisecond-level temporal resolution, are indispensable for characterizing oscillatory activity and synchrony within cortical-subcortical loops, particularly in conditions like epilepsy where disrupted circuit dynamics are central to pathophysiology.

Together, these findings highlight the differential application of imaging modalities based on both anatomical targets and clinical questions, offering insight into the evolving landscape of neuroimaging research.

It is essential to emphasize that our research has certain limitations. First, we acknowledge that we were unable to carry out a thorough assessment of each paper in relation to its respective field of interest, given the large sample size obtained from the PubMed database. Due to the sheer number of papers involved, it was impractical to manually review each one individually. While we made every effort to ensure thoroughness and accuracy in our review, some elements may have been overlooked. We attempted to address this challenge by applying several filters and inclusion criteria to generate relevant keywords for use in our search. While this method does not guarantee the complete exclusion of unsuitable papers from the final sample, there is a possibility that a few irrelevant articles may have been included. However, we can confidently state that the number of such papers is likely to be relatively small, and their inclusion did not significantly impact our overall results as a consequence of the rigorous screening process and the utilization of stringent filters and inclusion criteria.

5 Conclusions

Therefore, the main points would be that MRI is the most widely used across most conditions, followed by USG and CT. Encephalopathy is the most researched condition. Specialized techniques include angiography for aneurysms, DTI for TBI and concussion, and EEG for monitoring states like coma and vegetative states.

Region-specific imaging trends:

- Temporal lobe: high EEG and MEG co-occurrence, indicating auditory and epileptic studies.
- Prefrontal cortex: frequently studied with EEG, PET, and DTI, reflecting its involvement in cognition, consciousness, and connectivity.
- Brainstem: high co-occurrence with CT and angiography, corresponding to stroke and vascular pathology.

Non-invasive methods (TMS/tDCS): dominant in cortical regions for cognitive, sensory, and psychiatric applications with a slight prevalence of TMS.

Our findings provide a valuable snapshot of current research practices and underscore the distinct yet complementary roles of various neuroimaging and electrophysiological tools in investigating the complexities of the human brain.

This paper features a well-organized and straightforward way of presenting information, making it especially beneficial for specialists in the fields of disorder of consciousness research, treatments and brain areas. It offers a clear overview of the various options available, detailing their advantages and drawbacks, thus serving as an informative guide or reference material for professionals seeking to utilize and apply distinct methods and techniques in their professional work.

Acknowledgements This work had received budgetary funding.

Availability of data and materials The data presented in this study are available on request from the corresponding author.

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