Unveiling the Mind's Mystery: Exploring the Neurological Basis of Consciousness and its Impact on Human Health

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Abstract

Viewed as one of the biggest mysteries in science, consciousness was once overlooked as a research topic and is now an expanding field in neuroscience. Currently, there is no set definition for consciousness, and its biological underpinnings are not fully understood. Disorders of consciousness, where appropriate levels of consciousness are not achieved for a given period, can have a significant impact on quality of life. To recognize the implications of consciousness, it is important to understand the neurological basis of consciousness disorders. Today, research is limited to patients that suffer from long-term states of unconsciousness. However, scientists have been able to form a framework for the biological circuits involved in consciousness. It has been determined that consciousness is regulated through the integration of neural circuits between several parts of the brain. Many theories associated with the neural circuits that allow the human body to sustain consciousness exist: the Global Neuronal Workspace Theory, Information Integration Theory, and Temporospatial Theory of Consciousness. External factors can also lead to disorders of consciousness. While researchers have developed a clearer picture of the biological underpinnings of consciousness, treatments and recovery from disorders of consciousness remains challenging. As such, further work is needed to improve patient outcomes in disorders of consciousness. Here, we will define the areas of the brain related to consciousness, discuss the biological systems involved in conscious systems, and discuss disorders of consciousness and their current treatments. Finally, we will discuss new approaches to treatments and how they can improve patient outcomes.

Introduction

Consciousness is a biological phenomenon that lies at the very core of human health and function. Despite being an integral part of our everyday lives, consciousness is one of the most perplexing concepts in human understanding that is understudied relative to other physiological features of the human body. To fully recognize the implications of consciousness, it is important to further understand its neurological basis. Scientists have been able to form the beginnings of a framework for the biological circuits involved in consciousness (Koch et al., 2016; Michel et al., 2019). While researchers have started to develop a clearer picture about consciousness, recovering from consciousness impairments, a state where consciousness has been affected by damage to the brain, remains challenging. For example, it was found that only 25% of patients recovered and regained their communication abilities after being in a minimally conscious state, the less severe consciousness impairment (Steppacher et al., 2013). As such, further research is needed to improve patient outcomes in disorders of consciousness.

Consciousness requires both wakefulness and awareness (Lee et al., 2022). Wakefulness refers to the ability to have basic reflexes, such as pupil dilation, deep tendon reflexes, and pathologic reflexes, which is determined clinically through pupil dilation in response to a light stimulus (Di Perri et al., 2014). Awareness refers to a more intricate set of processes that allow people to incorporate information, understand it, and pursue it (Bekinschtein et al., 2015). Impairments in consciousness, or disorders of consciousness (DoC) are defined as alterations in wakefulness and/or awareness (Edlow, Claassen, et al., 2021). These alterations can be caused by both internal or external damage to the brain. The most severe damages result in prolonged DoC. Each year, about 5 out of 100,000 people will enter a long period, more than 4 weeks, of unconsciousness (Wade, 2018) while 4,200 persons will experience the vegetative state, a type of DoC, in the United States annually (Jennett, 2002). Along with these incident rates, the cost of lifetime care, the cost of keeping them alive week over week with no chance of waking up, for those with extended periods of DoC is at least $1,000,000 (Brain, 1999). The increasing number of cases of DoCcauses significant human suffering and also imposes substantial financial burdens on society (Brain, 1999). DoC vary in terms of the degree of consciousness loss and the cognitive and emotional abilities that may or may not be retained in individuals affected by them. In recent years, there has been significant progress in our understanding of these disorders, however, there is still uncertainty regarding the criteria for diagnosis and the standards of care.

Researchers have acknowledged the importance of consciousness research, and have proposed many theories surrounding the different levels of consciousness (Bayne et al., 2016; Overgaard & Overgaard, 2010). While the various states of consciousness have been well researched, diagnosis and treatment of DoC remains complicated. More than 40% of patients with DoC are misdiagnosed (Porcaro et al., 2022). Along with this, there are no known treatments to cure the root causes of consciousness disorders or to restore a person to consciousness.

Considering the statistics and the current challenges involved in diagnosing and treating DoCs, it is evident that further research to understand the intricate biological aspects of consciousness is needed. This review discusses the current understanding of the basis of consciousness, and how that information can be used to improve treatments and diagnosis, to better patient outcomes from disorders of consciousness.

Areas of the Brain Associated with Consciousness

Consciousness is an active neurological process that comprises many different parts of the brain. Modern neuroscience has sought to explain consciousness through the use of Neural Correlates of Consciousness (NCCs). A NCC is defined as being a precise pattern of brain activity that accompanies a specific consciousness experience, such as feeling and understanding sensory input. Most of our current knowledge of these particular patterns of brain activity has been determined using animal models (X. Zhao & Bhattacharyya, 2018). Many biological similarities, anatomically, psychologically, and genetically, have made the mouse the easiest model to study the biological underpinnings of consciousness, out of the models that are easily accessible (Bryda, 2013). In a study that determined the relationship between the brain of a mouse and a human, it was found that there is a positive correlation between both brains (Beauchamp et al., 2022).

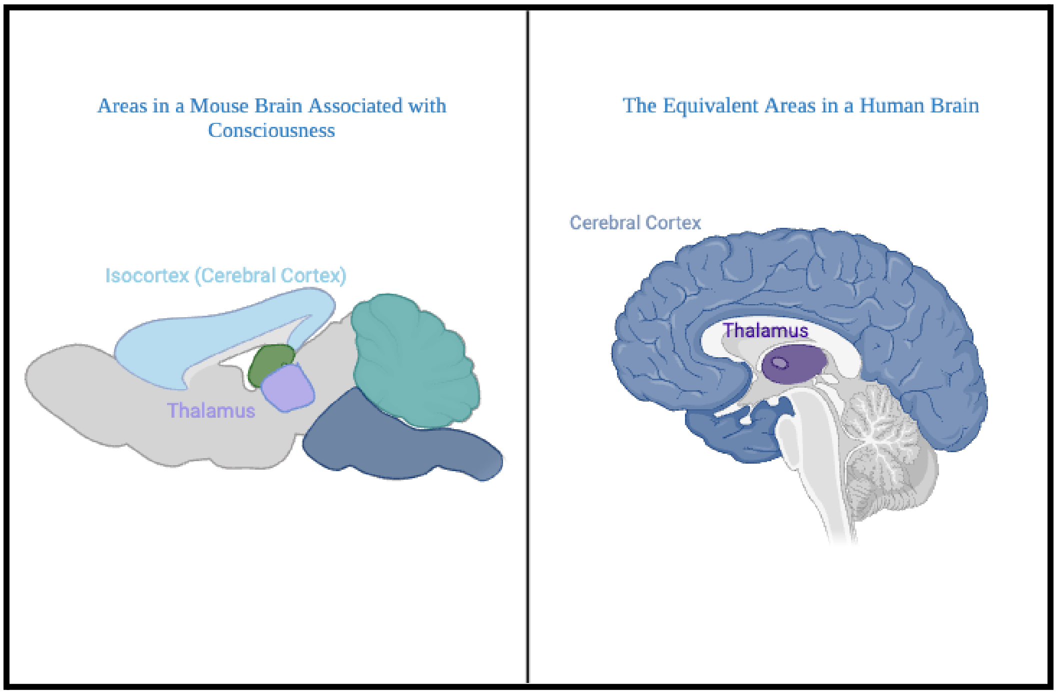

Figure I: Areas in a Mouse Brain Associated with Consciousness and the Equivalent Areas in the Human Brain. A side-by-side comparison of the areas of the mouse brain associated with consciousness (shown on the left) and the equivalent parts of the human brain associated with consciousness (shown on the right). As shown in the figure, the thalamus is located around the center in both organisms, while the cerebral cortex/isocortex makes up the topmost area. This figure was created using BioRender.com.

Due to their similarities, researchers have started to use the mouse brain as a model for the human brain, to better understand neurological underpinnings and structures in human consciousness (Reimann & Niendorf, 2020). Using this model, researchers have determined that in mice, the isocortex and the thalamus are important to consciousness (Kitazono et al., 2023), and the equivalent areas in the human brain are the cerebral cortex and the thalamus (Figure I).

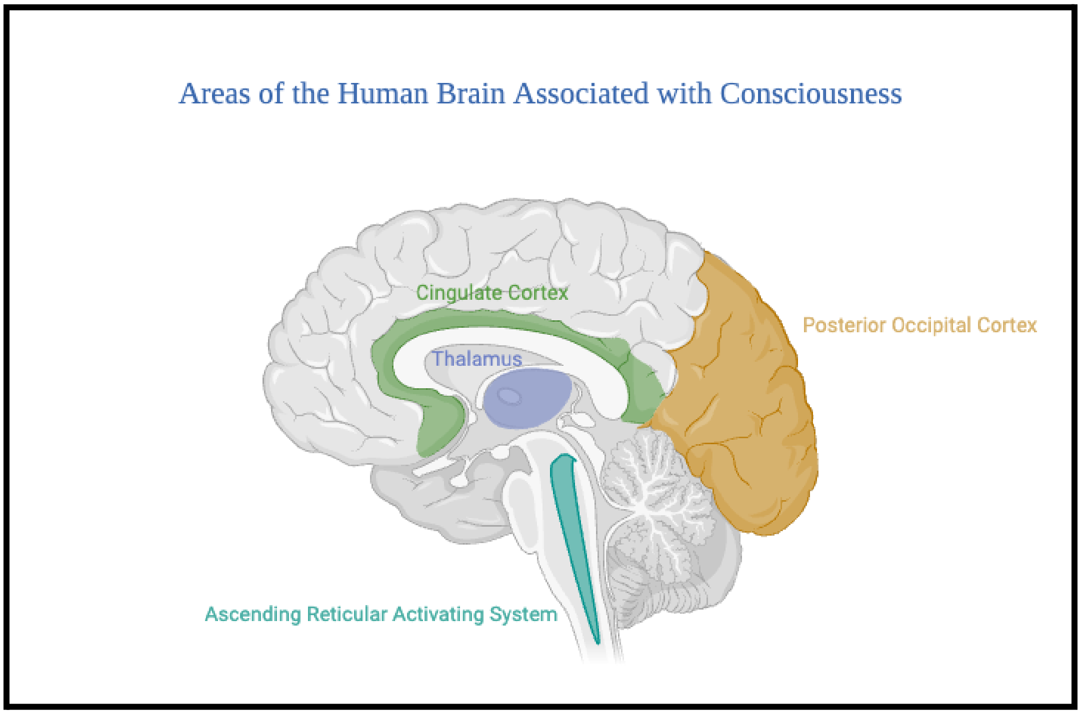

Figure II: Areas of the Human Brain associated with Consciousness. A diagram displaying the locations of some of the larger regions of the brain that are responsible for consciousness in humans (cingulate cortex, posterior occipital cortex, thalamus, ascending reticular activating system). This figure was created using BioRender.com.

The cerebral cortex is the outer layer of the brain's surface and is located on top of the cerebrum. The cerebral cortex, specifically the posterior occipital lobe and the claustrum, plays a role in the production of consciousness (T. Zhao et al., 2019). The posterior occipital lobe is responsible for the activation of the brain (Stephan et al., 2003). Usually, lesions are uncommon in the posterior cortex (Cavanna & Trimble, 2006), but traumatic lesions of the posterior cortex callosum, responsible for connecting large portions of the posterior cortex, are found in 98% of patients who remain in VS for more than 1 year (Kampfl et al., 1998). Others have produced similar results, as they found that lesions in the posterior occipital cortex may lead to comas (Bianchi & Sims, 2008). The claustrum is a sheet of neurons that lies under the cortex, towards the center of the brain. While the exact function of the claustrum is not clearly defined, the claustrum may be related to consciousness because it provides a connection between the frontal cortices and posterior sensory cortices (White & Mathur, 2018). This connection is vital to consciousness because in one study, it was shown that scientists were able to control a woman's consciousness by stimulating her claustrum with electricity (Koubeissi et al., 2014). Along with the posterior occipital cortex and the claustrum, the cingulate cortex, located at the bottom of the cortex (Figure II), also plays a significant role in impaired consciousness. For example, it was revealed that in healthy patients, the posterior cingulate cortex plays an essential role in the network with connections that brought information in (afferent connections) and sent information out (efferent connections), a pattern that was disrupted in patients with disorders of consciousness (Crone et al., 2015).

The thalamus, located towards the center of the brain (Figure II), is composed of several nuclei that have different functions, ranging from sensory to motor, including consciousness (Torrico & Munakomi, 2022). One of these nuclei, the paraventricular nucleus, located in the hypothalamus (the region under the thalamus), has been shown to promote sleep and increase arousal (Kirouac, 2015). Through the use of *in vivo* fiber photometry, a technique used to analyze the dynamics of population neurons, and multi-channel electrophysiological recordings, the total measurements of electrical activity across a cell membrane, in mice, researchers discovered that the paraventricular thalamus (PVT) neurons showed very high activity while the mice were awake, and that low PVT activity led to decreased wakefulness (Ren et al., 2018). This study could indicate that PVT is the most important nucleus in the thalamus that controls consciousness.

The neurons of the ascending reticular activating system (ARAS), located in the upper brain stem, have been shown to play a large role in the function of consciousness through awareness (Englot et al., 2017). Studies have indicated a close relationship between consciousness at the onset of traumatic brain injury (TBI) and injuries of the lower dorsal and upper ARAS (Jang & Kwon, 2020). This result indicates that injuries in the lower dorsal and upper ARAS region may cause unconsciousness after TBI. Brain imaging Technology, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), has given researchers an idea of the areas of the brain that contribute to consciousness and has also revealed the neural functions and activities within these structures that play a significant role in contributing to our consciousness.

Neural Contributions to Consciousness

To provide a better scientific explanation on the neural contributions to consciousness, scientists have started to examine brain activity. Neural signaling can occur in the form of an action potential, which is defined as a change in electrical potential transmitted between neurons that form a neural circuit (Wu, 2018). However, there are many electrical properties that could be related to consciousness, such as spike rate, the average of all the spikes emitted by a single neuron in a given time period, and blood oxygen level dependent signals (BOLD), important as it measures the amount of oxygenated hemoglobin in areas of the brain, which explains blood flow and function, used in functional magnetic resonance imaging (fMRI). Therefore, neuroscientists and researchers are not interested in just a singular neuron, rather a whole group of neurons and their interactions. Higher order properties, like the local field potentials generated by populations of neurons, are also considered in studying consciousness (Wu, 2018). Still, finding correlates in neuronal signaling is not enough to fully understand the biological basis of consciousness. In order to fully understand consciousness, we must identify the minimal neural mechanisms, a combination of neurons or brain regions, that in a specific state, lead to a corresponding state of consciousness.

One of the current theories surrounding the neuroanatomical basis of consciousness is the global neuronal workspace (GNW) theory (Sébastien Maillé & Michael Lynn, 2020). The initial version of this theory, the global workspace, states that conscious thinking occurs when information from different parts of the brain is widely shared and accessible to different parts of the brain, allowing us to become aware of it (Baars, 1993). The updated version of this theory, the GNW hypothesis, suggests that a particular network of cells, termed the GNW neurons, communicates with various brain regions to select and broadcast information, playing a key role in conscious processing and awareness (Dehaene et al., 1998). Activation of the GNW neurons occurs in a non-linear pattern called “ignition”, which can be triggered by stimuli, cognitive tasks, or sometimes spontaneously during rest (Dehaene et al., 2003). Overall, the GNW acts as a distributed network that involves several areas of the brain that communicate extensively with each other to allow for information distribution (Mashour et al., 2020). The GNW hypothesis has given scientists an explanation for how consciousness works in the brain, involving many communication networks and coordinated activity among different brain regions. Other theories include the information integration theory (IIT), which characterizes the subjective nature of consciousness and the physical systems necessary for consciousness, (Tononi et al., 2016) and the temporospatial theory of consciousness (TTC) which focuses on the brain’s spontaneous activity and the features of consciousness(Northoff & Huang, 2017).

Like the GNW theory, the synchronization of oscillatory neural responses, the rhythmic and repetitive electrical activity generated to respond to stimuli, has also been linked to awareness. In one study, scientists looked into the electrophysiological properties of conscious perception (awareness) in human subjects, and it was determined that the precise synchronization of neural oscillations in higher frequency ranges (gamma, beta) is crucial for integrating information across brain regions, and bringing together different aspects of conscious perception(Singer, 2009). Overall, when neural oscillations are synchronized, the different aspects of conscious perception function together, therefore allowing normal awareness, and therefore, consciousness.

Along with these internal frameworks related to consciousness, there are some external factors that can also lead to disorders/impairments of consciousness.

Role of Blood Glucose Metabolism in Consciousness

Some of the proposed theories for the framework of consciousness fail to recognize the energetic-metabolic basis of the mechanisms needed for consciousness (Pepperell, 2018). The brain is generally very active and uses glucose for energy. Glucose is used to create neurotransmitters, which allow neurons to communicate with each other. Neurons and other brain cells called astrocytes are used in the cycle to ensure that neurotransmitters are available (Kim et al., 2019). Researchers have determined that a drop in overall energy use, or glucose use, is responsible for the loss of consciousness. Measuring the glucose metabolism use could potentially allow physicians to determine if a patient is conscious or not(Shulman et al., 2009). In a series of studies, a total of 278 patients, 107 with unresponsive wakefulness syndrome

(UWS), 154 with minimally conscious state (MCS), and 17 with an unspecified disorder of consciousness were chosen. When the data from these studies were analyzed, it was found that patients with DoC had lower levels of glucose metabolism in specific regions of their brains (Arianna Sala et al., 2021). Additionally, studies have also found that when consciousness levels increase, blood glucose use roughly doubles (Hyder et al., 2013), which indicates that the level of use of blood glucose is directly related to the consciousness level and the shifts between different states of consciousness (Chen & Zhang, 2021).

Traumatic Brain Injury

Another external event that can cause loss of consciousness is Traumatic Brain Injury (TBI). TBI happens when the brain gets damaged due to an external force, like injury to the head (Mckee & Daneshvar, 2015). The direct impact that causes TBI can cause the brain to hit the skull internally, causing a disruption in neural activity, which leads to unconsciousness (Mckee & Daneshvar, 2015). When the patient faces fast acceleration or deceleration, different parts of the brain can move at different speeds due to their varying densities, causing shearing forces within the brain that damage neural connections (Blyth & Bazarian, 2010). After the direct impact of TBI, the brain can face chemical imbalances, inflammation and swelling, or blood flow changes in the brain which can affect the brain's ability to maintain consciousness. Traditionally, the Glasgow Coma Score (GCS) has been used to classify TBI as mild, moderate, or severe (Mena et al., 2011). New classification schemes have classified TBI through its effect on consciousness. Signs of TBI include immediate loss of consciousness, decreased consciousness, or a change in consciousness, as well as memory loss, neurological problems, or brain lesions (Blyth & Bazarian, 2010). One study, looking at adults with TBI that resulted in a loss of consciousness, determined that about one in five adults had a brain injury that led to loss of consciousness (John D Corrigan et al., 2018). Different levels of TBI can also lead to different stages/disorders of consciousness, as severe TBIs and a greater number of TBIs are more closely associated with DoC than fewer, more milder TBIs (Blyth & Bazarian, 2010).

Major Classes of Impairment/Disorders of Consciousness

The major classes of impairment of consciousness, also known as Disorders of Consciousness (DoC), are defined as being a prolonged state of unconsciousness or an altered state of consciousness, where a patient does not experience full consciousness through both wakefulness and awareness. These DoC are categorized into coma, vegetative state (VS), or minimally conscious state (MCS) depending on the levels of wakefulness and awareness (Eapen et al., 2017).

The most common disorder that follows TBI is a coma. Comatose patients are characterized by having no signs of being awake and no signs of being aware as they lie with their eyes closed and don't respond to their environment (Plum & Posner, 1982). The pathophysiological processes involved with comas include the dysfunction of corticothalamic loops resulting from brain cells that aren't working properly, that are not connecting well, or that cause a loss of alertness from the upper part of the brain, specifically, the cerebral cortex (Goldfine & Schiff, 2011). Comas may last for less than two to four weeks, during which time a person may wake up or progress into a vegetative state (VS) or minimally conscious state (MCS). A patient in the VS is characterized as being awake but shows no signs of awareness and is able to regulate their heartbeat and breathing without assistance (Jennett, 2002). There are two types of VS : a continuing VS and a permanent VS. An individual is considered to be in a continuing VS if they have been in the condition longer than four weeks, and an individual is considered to be in a permanent VS when it has been more than 6 months if caused by a non-traumatic brain injury, or more than 12 months if caused by a traumatic brain injury ("Medical Aspects of the Persistent Vegetative State," 1994). The pathophysiological basis, which describes the physical processes concerning disease or injury, of VS is similar to that of comas, except it includes more activity in the upper brainstem (Goldfine & Schiff, 2011).

An individual may enter MCS after being in a coma or VS, and the MCS is not usually considered permanent until it has lasted several months and there have been no signs of improvement. In MCS, an individual shows clear but minimal or inconsistent awareness, where a patient may experience consciousness for certain periods of time and switch to states of unconsciousness (Goldfine & Schiff, 2011). The pathophysiologies of MCS are diverse, although they typically diffuse injury to white matter and/or the thalamus, with varying degrees of cortical injury (Goldfine & Schiff, 2011).

Methods for Diagnosis and Treatment of Disorders of Consciousness

With the increasing instances of DoC, the diagnosis and treatment of DoC has become an increasingly important topic in research. One study revealed that 41% of cases of minimally conscious state were mistakenly diagnosed as a vegetative state, which has a much lower likelihood of recovery (Evers, 2016; J.T. Giacino et al., 2002). The results from this study underscore the importance of developing improved diagnostic tools to address this issue. Current diagnosis techniques mainly compose of functional neuro-imaging technologies, including functional magnetic resonance imaging (fMRI), positron emission tomography (PET), electroencephalography (EEG), and others (Crosson et al., 2010). Currently, fMRI is widely used and considered one of the most promising tools for studying DoCs, as it has been successful in identifying patterns of brain activity that indicate a certain level of awareness in individuals with DoCs. The misdiagnosis rate could potentially be decreased using sensitive valid scales such as the Coma Recovery Scale Revised, behavioral tools to assess both cognition and pain, and by continuing to use neuroimaging and electrophysiology for future diagnosis (Schnakers, 2020). These techniques have allowed physicians to identify the preserved brain networks in patients who appear unresponsive, offering hope for more accurate diagnosis.

Certain studies have found that electroencephalogram (EEG) may be a better technique as compared to the more popular fMRI. This finding was specifically proven by a study that determined that 44% of patients who seemed unresponsive to commands actually showed awareness when tested with EEG, meaning that their actual level of awareness was different than what physicians initially thought (Pan et al., 2020). EEG is also a more cost-effective and more accessible method when compared to fMRI, and is currently considered the best way to find low level consciousness in non-responsive patients (Owen, 2020). Along with EEG, another potential method of diagnosis includes Brain-Computer Interface technology. Using Brain-Computer Interface paradigms that do not require patients to move, may improve diagnosis by increasing diagnostic accuracy and predicting patient outcomes (Spataro et al., 2022).

As with the diagnosis of DoC, the available treatment options for patients with DoC are currently limited. The primary approach to therapy involves early and intensive neurorehabilitation, which combines physical, occupational, speech/language, and neuropsychological therapies (McNamee et al., 2012; Nakase-Richardson et al., 2012). This comprehensive neurorehabilitation has shown to improve long-term functional recovery in patients with DoC (Edlow, Sanz, et al., 2021). Additionally, pharmacologic stimulant therapies are utilized during the rehabilitation process to promote the recovery of consciousness (Thibaut et al., 2019). Currently, Amantadine is the only therapy that allows for a faster recovery of consciousness (Edlow, Claassen, et al., 2021). Due to the lack of therapies and treatments that can be used to relieve patients from DoC, further research is required in clinical settings.

Conclusion

Consciousness plays a vital role in human health, one that has not been fully understood. Consciousness and the two components of consciousness, wakefulness and awareness, lie in different parts of the brain. Researchers have analyzed the brain structure and function of the mouse brain, to recognize analogous structures that lie in the human brain. These studies have given us an idea of the areas of the brain involved in the function of consciousness, including the thalamus, the reticular activating system, and certain portions of the cortex. Through meticulous research, scientists have identified key regions and neural networks that contribute to the phenomenon of consciousness. The discovery of NCCs combined with the global neuronal workspace theory and oscillatory neural synchronization, have shed light on the underlying mechanisms that give rise to our awareness and wakefulness.

As our knowledge of consciousness deepens, so does our understanding of the challenges that arise when consciousness is impaired. DoCs, encompassing states like coma, VS, MCS, pose complex dilemmas for diagnosis and treatment. Misdiagnosis rates underscore the need for refined diagnostic tools, where methods like EEG and Brain-Computer Interfaces hold promise in improving patient diagnosis. The lack of treatment methods emphasizes the further research that is required in clinical settings, to ultimately better patient outcomes.

Facing these challenges, the study of consciousness is at a very crucial point. Deciphering the neural processes that generate consciousness can not only revolutionize our understanding of the human mind, but also potentially alleviate the suffering of individuals with DoC. As ongoing investigations strive to refine diagnostic techniques, explore therapy and treatment options, and unlock the mysteries of neural circuits, the hope for improved patient outcomes in DoCs becomes an ever more attainable reality. As scientists keep exploring consciousness to enhance human well-being, collaboration between neuroscience, medicine, and technology remains essential. As we understand more about the neurological underpinnings of consciousness and DoCs, we can bridge the gap between the conscious and unconscious mind and provide a brighter outlook for those affected by DoCs.

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