Consciousness, Disorders of

Introductory article

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Disorders of consciousness include coma, stupor, confusion and other abnormal states of acute brief or moderately sustained unconsciousness.

INTRODUCTION

The brain generates the mind, and the healthy, wakeful mind formulates consciousness. The American psychologist William James in 1890 stated, 'Consciousness is the [indispensable] fundamental awareness of the self's internal ego.' He then expanded that self-centered focus to identify the self's greater qualities of memory, attention, intention, chronological time, emotion, learned behavior, and several other less general psychological qualities. At that early time, only philosophical thinking interpreted gross anatomic knowledge in trying to understand how the awake brain might lose conscious functions.

Modern neurological medicine has defined several distinct behavioral pathological states that arise from inherited and acquired brain injuries and lead to disorders of consciousness. Brain injuries that reflect global disorders of consciousness include stupor and coma, the vegetative state, akinetic mutism, absence and partial complex seizures, delirium, and severe dementia. These global disorders, described below, totally disable the capacity of the individual for intentional behaviors. Though different in pattern, 'focal' disorders of consciousness can exist in several serious illnesses. A patient suffering a focal disorder of consciousness can be awake and interact with the environment, and yet exhibit severe alterations in awareness. These disorders uniquely illustrate the constructed nature of conscious experience.

THE FORMULATION OF CONSCIOUSNESS

All people with a healthy brain and body can recognize themselves, their thoughts and their intentional conscious activity. Descriptions may vary in detail, but ask people what they think about the quality called their consciousness and the first reply is likely to be, 'I'm awake and I'm here'. Proof often follows with (for example) 'I'm John Smith!'

An educated person recognizes conscious awareness as a continuously unfolding, automatic sense of being awake, alive, and logically thoughtful. Actually, one's mind is being continuously filled with flowing thoughts, normal language, recent memories, learned motor behavior, or novel discoveries. Even the most educated person, however, sometimes wonders about how the brain automatically experiences normal emotions, how it generates logical thinking, and how it induces the smooth flow of relevant or original thoughts and coordinated deeds.

'Now, how did I come to think about that?' is an often-expressed question, but usually not one that is part of everyday conversation. Nor do we wonder what preceding activities our brain generates when we automatically take our daily walk down the same lane. Even when we 'instinctively' jump out of the way of an unseen, oncoming vehicle, we often fail to realize that our awake, preconscious frontal lobe thought and acted first. Only after we have jumped away from the danger do we become aware of our act and experience an emotional feeling of fright. This example illustrates how we often act or even speak before we consciously think.

The normal brain's cognitive processing systems organize intentional behaviors drawing on a rapidly accessed, vast store of relevant memories. It preconsciously formulates either incoming or spontaneous information in less than a quarter of a second. It is astonishing to realize that the functions of memory, intention, and perception may largely occur before any act or expressed thoughts enter immediate conscious awareness. We may

think it strange that when we hold a conversation, our mind has preconsciously formulated what we are going to say a half-second or more before we actually say it. The Nobel laureate in medicine, Gerald Edelman, recognized this normal, instinctive preconscious formulation of thoughts, words and athletic acts in the ingenious title of his book, *The Remembered Present, A Biological Theory of Consciousness*.

Neuropsychological Dimensions of Consciousness

Consciousness is a time-ordered, egocentric process that interweaves inner and outer perceptions, stored memories, and immediately innovative thoughts. Emotional feelings imbue conscious awareness and sharpen intentional actions. Memory provides not only the ultimate storehouse of explicit conscious knowledge; it also develops the preconscious, implicit brain learning of motor skills and physical practice. Memory qualities and quantities depend on the combination of our innate cognitive talents, our subsequent schooling, our continuously thoughtful appraisal of new objects, and our interpersonal learning from and about people. The goal can be athletic, intellectual, or both. All evidence indicates that the earlier the young begin to learn and continue lifelong studies, the greater will be their future mental and behavioral capacities. Indeed, the longer a person's education and thought-requiring occupation last, the greater the brain's and body's functional longevity.

How this serially time-ordered, organized process of consciousness incorporates outer information with inner attention and immediate evaluation is the subject of intense neuroscientific investigation. Several distinct neuropsychological qualities can be ascribed to distributed networks of brain regions that selectively contribute to organized, wakeful human consciousness. These networks include the brainstem and allied arousal systems which control the sleep–wake cycles of the entire forebrain; prefrontal cortical regions (e.g. anterior cingulate cortex, frontal eye fields) which support continuous attention to self and environment and immediate intention; and posterior cortical regions of the temporal lobes (superior temporal gyrus) and parietal lobes (inferior parietal cortex) which support self-sensory perceptions and instinctive, and automatic awareness of inner and outer spatial relationships. Memory systems of the brain are widely distributed and depend on the integrity of the medial temporal lobe (hippocampus, entorhinal cortex) for initial storage, and on multiple cortical association areas (frontal, parietal, temporal, and occipital) and parts of the thalamus for functions of both storage and retrieval.

Additional neuropsychological qualities include the mind's chronological ordering of events (of unknown localization but disordered by injuries to the thalamus), moods and emotions (contributed by distributed regions of the 'limbic' brain). Learnt symbolic abstractions of verbal (left hemisphere), musical (right hemisphere), and geometric languages (left posterior parietal regions) contribute to humans' singular qualities of normal awareness.

SPECIFIC DISORDERS OF CONSCIOUSNESS

Coma

Coma is a totally unconscious and unarousable brain state resembling sleep, in which the eyes are closed and which lasts 24 h or more, due to any of several major causes. One is the use of sustained therapeutic anesthesia. More frequent causes are direct brain injury or diseases affecting the brain's cerebral hemispheres and arousal systems. Table 1 compares the loss of neuropsychologic

Table 1. Global disorders of consciousness

	Coma	*PVS*	*ASZ*	*AKM*	*HKM*	*CPS*	*DEL*
Arousal	−	+	+	+	+	+	+
Attention	−	−	−	+	+/−	+/−	+/−
Intention	−	−	−	−	+	+/−	+/−
Memory	−	−	−	−	−	−	+/−
Awareness	−	−	−	−/?	+/−	+/−	+/−

AKM, akinetic mutism; ASZ, absence seizures; CPS, complex partial seizures; DEL, delirium; HKM, hyperkinetic mutism; PVS, persistent vegetative state; −, absent; + present (in crude form for attention, AKM, and intention, HKM), +/− incompletely expressed; −/? apparently absent.

components incurred in coma with those of other disorders of consciousness.

Stupor

Stupor is a condition of deep sleep or behaviorally similar unresponsiveness from which the person cannot be aroused except by vigorous and repeated exogenous stimulation. As soon as such stimulation ceases, the person relapses into the unresponsive state. Light stupor is typical in cases of overdoses of soporific drugs or alcohol. Deep stupor more frequently reflects severe pharmacological, metabolic, or traumatic injury to the brain. The term 'semi-coma' is occasionally used in nonmedical writing to describe patients in stupor or persistent vegetative state but is not considered a diagnostic category.

Persistent Vegetative State

The vegetative state is a condition in which physiologically active, systemic organs continue to sustain the life of a body that has become at least temporarily devoid of a conscious brain. In most cases of coma, wakefulness will return spontaneously in a matter of days or weeks; but in some people, despite a wakeful appearance, the mind may be absent for many weeks, months or forever. This tragedy has been named the *persistent vegetative state* (PVS). Such patients express irregularly timed sleep–wake patterns, but all feeding and bodily care must be provided by external sources. The term 'arbitrarily' identifies patients who remain psychologically unconscious for at least a month. They are alive, but totally unaware of self or their environment. The vegetative state presents the fundamental clinical dissociation of arousal from all other components of consciousness (Table 1).

The clinical judgment of unconsciousness in PVS has been supported by the results of positron emission tomography (PET) scan studies that reveal overall cerebral metabolism to be reduced by 50% or more below the normal rate. The observed metabolic levels are equivalent to those found in persons undergoing deep surgical anesthesia. In a study of behavioral and physiological variations in a few patients in the vegetative state, one woman randomly expressed occasional single, understandable words. Her PET studies revealed isolated islands of left frontotemporal cerebral structures that operated at an abnormally low metabolic rate but at nearly twice the rates of the remaining brain. Similar isolated expressions have been encountered in several other vegetative patients. Typically, the patients express easily identifiable, stereotypical, emotional-limbic responses. These emotional expressions probably reflect distinct and isolated limbic mechanisms; their preservation is likely to depend on integrative brainstem structures that lie outside the corticothalamic systems that typically undergo overwhelming injury in PVS patients.

Syncope

Syncope (fainting) consists of brief unconsciousness caused by reduction of systolic arterial blood flow through the brain. Most syncope is benign and occurs in persons younger than 50 years. Termed 'vasogenic', it reflects sudden dilation of the body's cholinergic and sympathetic neurovascular systems, reduces systemic blood pressure and deprives the erect brain's critical oxygen supply. A second type is less frequent and affects older people suffering from postural orthostatic hypotension. A third type affects elderly people with severe cardiac, cardiopulmonary, or systemic atheromatous illness. Such patients rarely regain normal brain function if they fail to gain accurate awareness in more than 4–5 minutes.

Concussion

Concussion is an unconscious state that immediately follows a severe traumatic head injury. Since its ultimate duration cannot be predicted accurately, some surgeons call post-traumatic lack of consciousness 'concussion' for 24 h; after that, the term is changed to 'coma'.

At its least, concussion interrupts the brain's organized thoughts and impairs or blocks its recent memory. Acute severe concussions may suddenly and briefly suppress vegetative brainstem functions, thereby invoking transient breathlessness, slowed heart rate, low blood pressure, and widening of the pupils. Boxing knockouts for 10 s or more vividly exemplify moderate to severe concussion, as the bewildered athlete staggers from the ring and sometimes falls. A few knocked-out boxers will remain unconscious after the count, and a very few may die from acute brain hemorrhage. A measurable group may gradually develop dementia during their early sixth decade. Many drivers or passengers in serious road traffic accidents can suffer brief knockouts of a few seconds, followed by several hours of confused memory and, frequently, light coma or unsteady behavior. Lack of arousal during this time is sometimes regarded as short-term concussion, but brief coma

is a more accurate label to apply until the person awakens.

Confusion

Confusion can be either temporary or permanent. Temporary confusion refers to disturbed memory and an inexact orientation of time, place, or person. Awakening from deep sleep after moderate sedation, suffering the effects of using excessive alcohol or street drugs, or awakening in a strange room, are typical examples. Chronic, waking confusion relates to sustained difficulties in identifying time, date, the environment and the failure to recognize long-known persons. It is also a gentle term for dementia.

Absence and Complex Partial Seizures

Seizures reflect severe impairments of self-aware consciousness, accompanied by unique forms of behavior. Absence seizures typically occur in children and are often noted as 'staring spells'. During the event the eyes typically fix in a forward stare, motion ceases, and movements of the lips or eyelids may be noted. People who undergo frequent absence attacks (once called *petit mal*) may lose extended self-awareness for a matter of hours and sometimes longer. During these states they remain awake and usually continue vaguely purposeful behavior.

Absence seizures originate from the cerebral cortex but involve brainstem and thalamic neuronal networks. People suffering severe complex partial seizures, a different neurological disorder often emanating from the temporal lobes (see below), lose their cognitive memories, but may also express a variety of learned behaviors. Both types of event exhibit attentional and intentional failure, loss of working memory, and perceptual dissociation. In their classic form, absence seizures may be interpreted to represent momentary vegetative states (see Table 1).

Akinetic Mutism

The term 'akinetic mutism' covers different behavioral expressions that relate to damage of several cerebral and subcortical structures. While sometimes confused with the vegetative state, akinetic mutism may resemble a state of constant hypervigilance. Such patients appear attentive and vigilant but remain motionless. The preservation of visual tracking in the form of following persons or moving objects with smooth, roving eye movements can differentiate this condition from the vegetative state. Classic akinetic mutism as listed in Table 1 reflects the recovery of a crude wakeful attentiveness without the apparent recovery of any other neuropsychologic function.

A similar picture, but excluding absence of eye movements, can rarely be a feature of untreated, rigid Parkinson disease. A strong clinical resemblance to this syndrome has been identified in some forms of variant Creutzfeldt–Jakob disease. The hyperattentive form of this disorder is typically seen in patients with large bilateral injuries to the medial and ventral frontal lobes (see below).

Hyperkinetic Mutism

Hyperkinetic mutism is a wakeful, continuous movement disorder accompanied by at least partial loss of global self-awareness. Patients with hyperkinetic mutism exhibit totally unrestrained but coordinated motor activity in the absence of external evidence of awareness of the environment. The patients also demonstrate an inability to develop conditioned responses, and produce no apparent memory of self.

Hyperkinetic mutism is the converse of akinetic mutism, with preserved unconscious expression of frontal intentional mechanisms, loss of sustained directed attention presumably requiring posterior attentional components of the inferior parietal lobe or posterior temporal lobe (see below), and a state of behavioral unawareness despite a whirlwind of activity. In contrast to the akinetic mute state, these people demonstrate minimally expressed intention and attention. The fragment of intention expressed in the meaningless motor activity of the hyperkinetic mute person is a reciprocal of the crude form of attention seen in akinetic mutism. Both examples reveal the fundamentally unconscious nature of such fragmentary neuronal activity.

Similar examples of such unconscious motor activity include the repetitive, uncontrollable production of words in the neurological disorder known as Tourette syndrome.

Delirium

Delirium is generally perceived as an acute or semiacute temporary deficit of attention and working memory. A salient component is temporal disorientation. Delirium may follow acute, moderately severe head injuries, encephalitis, bacterial meningitis, exceptionally high fever, heat stroke, or withdrawal from chronic alcoholism or drug misuse. Delirium in patients less than 45 years old usually

subsides without serious reduction in intelligence, but in alcoholism the person must abandon alcohol completely after the first or second delirious bout or begin to lose intellectual capacities permanently. Elderly people suffering mild dementia often become delirious during acute systemic illness or frequently changed surroundings. Visual hallucinations or impaired perceptions often occur in systemic delirium, whereas auditory hallucinations appear more often, but not solely, in people with schizophrenia.

Dementia

Dementia is characterized by two different conditions. One is a permanent, sometimes fluctuating loss of short-term or long-term memory. It can follow severe brain trauma, a sudden, sustained loss of oxygen to the brain, or surgical removal of the anterior areas of both temporal lobes. The other consists of an insidious, gradual loss of (first) short-term and (later) long-term memory. This process results from degeneration and death of nerve cells in the cerebral cortex.

Focal Unconsciousness: Agnosia, Anosognosia, and Neglect

Agnosia is a term specifically applied to different types of focal losses of awareness. Examples include an inability to see or feel objects as a whole greater than the sum of several parts, and a loss of specific capacities to hear aspects of sounds. A rare bilateral injury to the ventral temporal occipital lobe may produce the loss of perception of motion, leading to an experience of life as if seen constantly through a stroboscope, never in continuous motion.

Anosognosia is a term specifically applied to a loss of awareness and an inability to consciously perceive. Examples of anosognosia include denying that one's hand is one's own and unable to move intentionally. This form of focal unconsciousness is also labeled 'neglect' and is typically applied to a syndrome arising from damage to the right parietal lobe. This normally provides automatic knowledge of the contralateral body as well as the immediate outer space that surrounds it. Neglect increasingly appears to be a disorder of entry of primary sensory information into the appropriate internal context to be integrated into the construction of consciousness. Neglect can be seen following damage to either frontal or posterior (inferior parietal or superior temporal) cortices (see below).

RELEVANCE TO UNDERSTANDING HUMAN CONSCIOUSNESS

Anatomic Relationships

Disorders of consciousness are often generated by selective brain injuries. Specific neuropsychological deficits accompanying these disorders reflect the relatively segregated cerebral neuronal networks that generate human consciousness and complex behavior. Autopsies over almost two centuries and the increasing knowledge of functional anatomy provided by modern brain imaging have greatly added to neuropsychological understanding of conscious or unconscious behavior. Several brain regions are implicated in these disorders, including the two cerebral hemispheres, each of which possesses approximately half of the cerebral cortex, the thalamus, and the basal ganglia. Near the mid-brainstem, they connect with the large cerebellum and the arousal systems that lie within the brainstem. To discover just how this network generates consciousness has become a major scientific effort. (*See* **Cerebellum**; **Basal Ganglia**)

Nonspecific arousal is generated largely in the brainstem and is indispensable to supporting sleep–wake cycling and the wakeful states of consciousness. Cholinergic (pedunculopontine, later dorsal tegmental nuclei), noradrenergic (locus ceruleus), and other neuronal populations located within the upper brainstem, hypothalamus, and basal forebrain have a key role in organizing this large-scale human behavior. By itself, however, arousal is independent of expressed neuropsychological qualities, as is evident in the vegetative state or in 'absence seizures' (see Table 1). Brain mechanisms that govern sleep and its various dreams and perambulations only partially overlap the circuitry of normal wakeful consciousness. The integrity of both distributed cortical and other subcortical structures as is necessary for the expression of integrated cerebral activity to generate consciousness.

Cognitive capacities expressed in the conscious state depend on the moment-to-moment continuity of short-term memory (disordered in delirium) with other neuropsychological components. Short-term or working memory appears to depend strongly on the integrity of the prefrontal and parietal cortices along with subcortical structures. The richness of mental life contained in the storage of long-term memories is a distributed capacity of the association regions of the cerebral cortex and is severely degraded in dementia.

The cortical regions indispensable for conscious behavior are the frontal lobes: these largely govern and express behavior, both immediate and learnt. Their functions provide the executive generator and dictator of consciousness, organizing mood, behavior, and mind. Within the frontal lobes the basal forebrain area has evolved from ancient mammalian brains and occupies most of the undersurface. It participates in generating emotional feelings and social behavior as well as stimulating the person's intentional purposes. The lateral and medial prefrontal areas (including the dorsolateral prefrontal regions, supplementary motor zones, and anterior cingulate cortices) largely influence physical coordination and participate in volitional and cognitive aspects of attention and working memory.

The most posterior regions of the lateral and medial frontal lobe generate and regulate coordinated expressions of logical manipulations, language, intended eye movements and, ultimately, all coordinated, intentional behavior. Examples include skilled athletics, the expression of well-learnt and practiced instrumental music, and other rapidly expressed activity.

Functional generation of self-directed attention and intention are mapped strongly in the ventral-medial frontal lobes and less frequently the posterior thalamus and rostral mesencephalon.

Akinetic mutism reflects the disabling of the ventral-medial and medial frontal and prefrontal networks (including a large contribution from the deep gray-matter structures of the basal ganglia, which interact with the cortex via long-loop connections with the thalamus and underpin much routine learnt behavior), providing volitional drive and self-directed (executive) attention. The crude aspect of attention remaining in this state of impaired consciousness may originate from automatic orienting systems driven by posterior parietal and subcortical structures (thalamus).

The posterior parts of the cerebrum, including the parietal, occipital and temporal lobes, in conjunction with the thalamus, generate the perceived contents of thoughtful consciousness. They receive their direct signals of attention and intention from the frontal lobes and express their immediate demands. The occipital lobes receive inputs of retinal vision, which are processed further within the adjacent temporal lobe. Auditory stimuli are also processed in the temporal lobe. Abstract cognitive icons represent the verbal, musical, mathematical, geometric, and pictorial languages that make up our intellectually conscious knowledge. Most of these particular cognitive qualities and contents are dominantly expressed by the left cerebral hemisphere:

The right inferior parietal lobe and adjacent superiorlateral temporal lobes, however, normally provide a person's dominant preconscious attentive perception and awareness of both the left side of the body and its surrounding environment. Severe acute damage to the right parietal-temporal areas as described in the paragraph on focal unconsciousness may cause total unawareness of the entire left side of the individual's personal universe. Lost is the memory of being able to see, or to remember normal vision; lost is the accurate perception of any existing left-spatial noises; lost is total awareness or memory of the absent hemiworld to the left and, remarkably, the person's ability to recognize his or her own left arm, leg or ear. This remarkable clinical syndrome demonstrates that our conscious experience is instinctual and can be lost in parts.

Evidence from neurological disorders of consciousness demonstrates that subcortical structures are also essential for normal integrative brain function associated with consciousness. Most causes of the global disorders of consciousness reviewed above appear to arise from either large bilateral injury to frontal (e.g. bilateral medial-basal frontal injuries and akinetic mutism) or posterior association cortices (bilateral temporal-parietal association areas and hyperkinetic mutism). In addition, it is known that selective subcortical injuries (generally damage to medial aspects of the thalamus or upper brainstem) may produce identical or very similar disorders. The subcortical injuries that may produce transient coma, vegetative state, akinetic mutism, or conditions resembling hyperkinetic mutism also implicate brainstem and thalamic structures. These include the brainstem arousal systems important for sleep and wake cycling and related brainstem and thalamic substructures that play a part in the complex, large-scale integration of many cerebral networks. The contribution of these deep brain structures may lie in the selective facilitation of activity patterns that allow widely separated brain regions to briefly communicate

Further Reading

Crick F (1964) *The Astonishing Hyphothesis. The Scientific Search for the Soul*. New York, NY: Charles Scribner's Sons.

Edelman GM (1987) *Neural Darwinism, the Theory of Neuronal Group Selection*. New York, NY: Basic Books.

Edelman GM (1989) *The Remembered Present A Biological Theory of Consciousness*. New York, NY: Basic Books.

Edelman GM and Tononi G (2000) *A Universe of Consciousness. How Matter Becomes Imagination*. New York, NY: Basic Books.

Plum F (1991) Coma and related global disturbances of the human conscious state. *Cerebral Cortex* **9**: 359–425. New York, NY: Plenum Press.

Plum F and Posner JB (1982) *Stupor and Coma*, 3rd edn. New York, NY: Oxford University Press.

Wilkinson IMS (1999) *Essential Neurology*, Chap. 11 Unconsciousness, pp. 171–186. London, UK: Blackwell Science.