HHS Public Access

Author manuscript

Epilepsy Behav. Author manuscript; available in PMC 2016 November 25.

Published in final edited form as:

Epilepsy Behav. 2014 August ; 37: 234–235. doi:10.1016/j.yebeh.2014.07.008.

A master switch for consciousness?

Hal Blumenfeld

Yale Departments of Neurology, Neurobiology, and Neurosurgery, 333 Cedar Street, New Haven, CT 06520-8018, USA

Consciousness is big. Most neural theories of consciousness involve distributed large-scale networks throughout the brain. Whether it is the global workspace theory [1], information integration theory [2], or global theories of brain neuroenergetics [3], there is broad agreement that normal consciousness depends on widespread bilateral brain activity. An inevitable consequence of these theories is that impaired consciousness—seen in disorders such as head trauma, vascular disease, infection, or seizures—occurs when there is dysfunction in large distributed brain regions. However, size is not everything. Small lesions critically located in the upper brainstem or medial diencephalon are well known to produce coma [4]. Small in size, these regions, nevertheless, interact widely and are responsible for arousal in the entire thalamocortical grid [5,6]. Thus, turning off the relatively tiny nuclei of the subcortical arousal systems brings down the whole cortex, taking consciousness off line. This deep brain arousal circuit is a master switch for consciousness.

Are there other locations in the brain where a focal change can produce unconsciousness? In focal seizures of the temporal lobe or other localized brain regions, consciousness is often markedly impaired. Patients cannot respond to questions or commands during these focal seizures, and later, there is amnesia for the episodes. Recent investigations have shown that impaired consciousness in focal seizures is associated with widespread changes in brain function outside the local region of seizure discharge. Focal temporal lobe seizures with impaired consciousness exhibit decreased cerebral blood flow, slow wave activity, and enhanced synchrony in widespread regions of the frontoparietal association cortex [7–10]. Focal parietal seizures with impaired consciousness also produce abnormally enhanced long-range cortical synchrony [11]. In the case of temporal lobe seizures, there is growing evidence that seizures inhibit the crucial subcortical arousal systems, which, in turn, causes a deep sleep-like state in the cortex and impaired consciousness [12–15]. Thus, temporal lobe seizures may throw the subcortical consciousness master switch. However, the mechanism for widespread altered cortical function and impaired consciousness in parietal lobe and other focal neocortical seizures remains unknown.

In a recent *Epilepsy & Behavior* article, Koubeissi et al. provide another compelling example of focal changes in a small brain area producing unconsciousness [16]. During cortical mapping of a patient undergoing intracranial EEG and video monitoring, the authors

Tel.: +1 203 785 3865; fax: +1 203 737 2538., hal.blumenfeld@yale.edu.

Conflict of interest

The author has no conflicts of interest to report.

stimulated a single-electrode contact and produced behavioral unresponsiveness and amnesia. The electrode was located in the region of the left extreme capsule adjacent to the anterior dorsal insula and claustrum. The effect was seen in 10 of 10 stimuli at 14 mA, and stimuli consisted of 3- to 10-s 50-Hz brief square wave pulses, using a medial frontal electrode as reference (stimulation between the medial frontal contact and other electrodes produced no behavioral change). During stimulation, the patient stared blankly and did not respond to commands. After the stimulus, the patient immediately returned to baseline with no recall of events during stimulation and no recall of words presented during stimulation. Stimulation also produced arrest of reading; however, the patient could continue repetitive hand or tongue movements for up to 4 s after stimulus onset. Similarly, the patient could repeat words during the first 2 s of stimulation if words were given before the stimulus onset, suggesting that more automatic behaviors were, at least, initially spared. Nonlinear correlation analysis of the intracranial EEG signals demonstrated greater synchrony of frontoparietal electrode contacts during stimuli that produced impaired consciousness compared with lower amplitude stimuli which did not. Seizures were not detected during or after stimulation. The effect was limited to the one electrode, and stimulation of adjacent contacts did not produce these changes.

Assuming the stimulation produced a focal effect on the insula or claustrum, the results suggest the intriguing possibility that focal altered function in this small region can produce widespread changes in frontoparietal synchrony and impaired consciousness. The authors discuss prior work demonstrating an important role for the anterior dorsal insula or the claustrum in self-awareness and higher-order cognitive integration [17,18], suggesting that disruption of this region may interfere with normal consciousness. The findings also fit well with previous work by the senior author Fabienne Picard, demonstrating a potential role for the anterior insula in self-awareness [19], as well as with work by another author Fabrice Bartolomei, elucidating the importance of cortical–cortical synchrony in epileptic unconsciousness [9–11]. They further raise the point that the anterior insula/claustrum is not far from the area tempestas, a critical epilepsy hub identified in prior studies [20,21].

The results in the present patient are fascinating and raise important questions for further study. One key question is whether the left anterior insula/claustrum region is truly a second “master switch” for consciousness or whether stimulation in this region somehow flips the established master switch in subcortical arousal systems. The high level of connectedness of this region certainly supports either possibility. The first order of business, of course, should be to confirm the findings in additional patients. Assuming the anterior insula/claustrum is verified as a potential key hub for consciousness, it is then hoped that future studies will shed more light on the mechanisms for impaired consciousness observed during stimulation of this region. For example, it would be of great interest to determine if the effect is specifically seen in left as opposed to right stimulation. In addition, future work should investigate EEG changes in the hemisphere contralateral to the side of stimulation. Electrode locations for intracranial EEG are decided on clinical grounds, and the present patient only had electrodes on the side of stimulation. However, future patients with bilateral electrodes could provide an opportunity to determine if stimulation on one side produces changes in both hemispheres, since disorders of consciousness usually only occur when bilateral cortical functional changes are present. It would also, of course, be of interest to determine if

this region is critically involved in some (or all) seizures that cause loss of consciousness and to determine if therapeutic neurostimulation or other interventions targeting this region could prevent loss of consciousness during seizures. Another important topic of further study is the frequency range of the observed synchrony during stimulation. The current study investigated broadband (0.5–90 Hz) signals, but it would be of interest to know if a particular range of low- or high-frequency signals dominated the changes in synchrony because this may have relevant mechanistic implications. Another challenge is the nature of electrical stimulation, which can elicit changes either by neuronal activation or by neuronal depression and can also produce local effects on neuronal cell bodies as well as distant effects through stimulation of axonal terminals or fibers of passage [22]. Ideally, local unilateral stimulation of the anterior insula/claustrum will be investigated further in conjunction with functional neuroimaging to more fully identify regions of increased or decreased brain activity, as well as with animal models to reach a complete mechanistic understanding of the observed changes.

In conclusion, Koubeissi and colleagues have taken an important step forward in identifying a new potentially critical hub in the network of consciousness. Whether this represents a second master switch operating independently of the established subcortical arousal circuits or whether stimulation of the anterior insula/claustrum is like a short circuit in the kitchen that shuts off the master switch in the basement, time and future studies will tell. Either way, the results are exciting and bring us closer to solving the ultimate puzzle of how consciousness normally works and is impaired in epilepsy and other disorders.

Acknowledgments

This work was supported by NIH grants R01NS055829, R01NS066974, R21NS083783, P30NS052519, and U01NS045911 and the Betsy and Jonathan Blattmachr Family.

References

1. Baars BJ. Global workspace theory of consciousness: toward a cognitive neurosci-ence of human experience. Prog Brain Res. 2005; 150:45–53. [PubMed: 16186014]
2. Tononi G. Consciousness, information integration, and the brain. Prog Brain Res. 2005; 150:109–26. [PubMed: 16186019]
3. Shulman RG, Hyder F, Rothman DL. Cerebral metabolism and consciousness. C R Biol. 2003; 326:253–73. [PubMed: 12806834]
4. Plum F, Posner JB. The diagnosis of stupor and coma. Contemp Neurol Ser. 1972; 10:1–286. [PubMed: 4664014]
5. Steriade, MM.; McCarley, RW. Brain control of wakefulness and sleep. 2. Springer; 2010.
6. Steriade, M.; Jones, EG.; McCormick, DA. Thalamus. Amsterdam: Elsevier Science; 1997.
7. Blumenfeld H, McNally KA, Vanderhill SD, Paige AL, Chung R, Davis K, et al. Positive and negative network correlations in temporal lobe epilepsy. Cereb Cortex. 2004; 14:892–902. [PubMed: 15084494]
8. Blumenfeld H, Rivera M, McNally KA, Davis K, Spencer DD, Spencer SS. Ictal neocortical slowing in temporal lobe epilepsy. Neurology. 2004; 63:1015–21. [PubMed: 15452292]
9. Arthuis M, Valton L, Regis J, Chauvel P, Wendling F, Naccache L, et al. Impaired consciousness during temporal lobe seizures is related to increased long-distance cortical–subcortical synchronization. Brain. 2009; 132:2091–101. [PubMed: 19416952]

10. Guye M, Regis J, Tamura M, Wendling F, Gonigal AM, Chauvel P, et al. The role of corticothalamic coupling in human temporal lobe epilepsy. Brain. 2006; 129:1917–28. [PubMed: 16760199]
11. Lambert I, Arthuis M, McGonigal A, Wendling F, Bartolomei F. Alteration of global workspace during loss of consciousness: a study of parietal seizures. Epilepsia. 2012; 53(12):2104–10. [PubMed: 23016829]
12. Motelow, JE.; Gummadavelli, A.; Zayyad, Z.; Mishra, AM.; Sachdev, RNS.; Sanganahalli, BG., et al. Brainstem cholinergic and thalamic dysfunction during limbic seizures: possible mechanism for cortical slow oscillations and impaired consciousness. Soc Neurosci Abstracts. 2012. [Online at http://web.sfn.org/]
13. Englot DJ, Yang L, Hamid H, Danielson N, Bai X, Marfeo A, et al. Impaired consciousness in temporal lobe seizures: role of cortical slow activity. Brain. 2010; 133:3764–77. [PubMed: 21081551]
14. Englot DJ, Modi B, Mishra AM, DeSalvo M, Hyder F, Blumenfeld H. Cortical deactivation induced by subcortical network dysfunction in limbic seizures. J Neurosci. 2009; 29:13006–18. [PubMed: 19828814]
15. Blumenfeld H. Impaired consciousness in epilepsy. Lancet Neurol. 2012; 11:814–26. [PubMed: 22898735]
16. Koubeissi MZ, Bartolomei F, Beltagy A, Picard F. Electrical stimulation of a small brain area reversibly disrupts consciousness. Epilepsy Behav. 2014; 37C:32–5. http://dx.doi.org/10.1016/j.yebeh.2014.05.027.
17. Kurth F, Zilles K, Fox PT, Laird AR, Eickhoff SB. A link between the systems: functional differentiation and integration within the human insula revealed by meta-analysis. Brain Struct Funct. 2010; 214:519–34. [PubMed: 20512376]
18. Crick FC, Koch C. What is the function of the claustrum? Philos Trans R Soc Lond B Biol Sci. 2005; 360:1271–9. [PubMed: 16147522]
19. Picard F, Craig AD. Ecstatic epileptic seizures: a potential window on the neural basis for human self-awareness. Epilepsy Behav. 2009; 16:539–46. [PubMed: 19836310]
20. Piredda S, Gale K. A crucial epileptogenic site in the deep prepiriform cortex. Nature. 1985; 317:623–5. [PubMed: 4058572]
21. Laufs H, Richardson MP, Salek-Haddadi A, Vollmar C, Duncan JS, Gale K, et al. Converging PET and fMRI evidence for a common area involved in human focal epilepsies. Neurology. 2011; 77:904–10. [PubMed: 21849655]
22. Vitek JL. Mechanisms of deep brain stimulation: excitation or inhibition. Mov Disord. 2002; 17(Suppl 3):S69–72. [PubMed: 11948757]