Stuck in a Rut: Anesthetic Brain Dynamics in the Young

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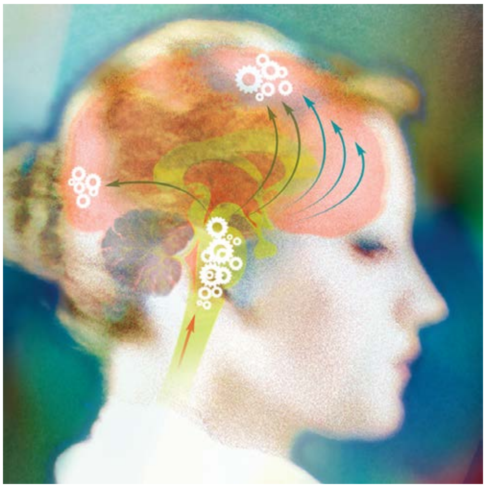
Every human would agree that wakefulness is marked by a succession of experiences—the "stream-of-consciousness." This implies that the state of the brain is continuously changing in some way that parallels this stream of experience. The wakeful brain jumps often between many different patterns. In contrast, when consciousness is reduced by general anesthesia, we might expect the brain to have only a few available configurations, and to be much slower in moving among them. The electroencephalogram (EEG) is an imperfect representation of the oscillations and synchrony between cortical regions, but may capture some aspects of these changing brain configurations.



"General anesthesia had rendered the brains of the young patients functionally 'rigid,' [which] contrasts with a previous study in adults."

In this issue of Anesthesiology, Puglia *et al*. report an evaluation of multichannel EEG functional brain connectivity in older children and teenagers (8 to 16 yr) undergoing general anesthesia and surgery.[1] In this age group, the maturing brain is in the process of undergoing widespread structural changes in brain anatomy, notably, a profound decrease in gray matter. Consonant with previous work, the authors found that general anesthesia increased average functional connectivity between prefrontal and frontal regions, as measured by phase differences of alpha and theta waves. They then went further and examined how functional connectivity evolved over time during the anesthetic. It appears that anesthesia was associated with the presence of very stable and stereotypical patterns of EEG connectivity—over a wide range of hypnotic drug concentrations. Initially the patients transitioned through a high prefrontal delta band connectivity pattern around induction (cluster 3), but then the patients were almost uniformly stuck in one or two almost identical EEG patterns for the whole maintenance phase of anesthesia (clusters 5 and 6). General anesthesia had rendered the brains of the young patients functionally "rigid."

This contrasts with a previous comparable study done in adults by the same research group,[2] which found that patients typically switched every few minutes between five markedly different connectivity patterns during general anesthesia. There is a proviso. The best method of representing the state of the brain is an open question. Of note, during wakefulness, the EEG patterns were largely classified as a single cluster (cluster 1). This is in contradiction to my statements in the opening paragraph and is plausibly the result of using a relatively coarse-grained scalp EEG methodology.

I have purposefully used the verb "switching" because the transitions between brain configurations are usually quite abrupt rather than gradual. As mentioned by the authors in their discussion, the term "metastability" is commonly used to describe these short-lived configurations of coupled brain regions where waves oscillate in phase. What do we mean by the word "stability"? There are technical dynamical systems definitions, but an intuitive definition of a stable system is one that naturally tends to return to what it was previously doing, after it has been nudged by some external force. A pencil balanced on its point is clearly not stable. The idea of metastability—where the system switches between several moderately stable states—has been reviewed by Hudson as pertains to brain dynamics and anesthesia,[3] and is intricately bound up with the concept of "neural inertia."[4] It is intuitive to present this framework diagrammatically as movement of a ball rolling around a landscape. The position of the ball represents the state of the brain (in this case estimated by the spectral functional connectivity patterns). There are certain preferred metastable states—the valleys into which the ball will tend to settle. These could be the seven EEG frequency–connectivity clusters, as defined in the paper by

Image: J. P. Rathmell/A. Johnson, Vivo Visuals Studio.

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Puglia *et al.* The time spent in each state (the valleys) will depend on a combination of how deep the valleys are (their stability) and the level of exogenous stimulus or internal neuronal noise required to shift the brain to a new cluster (*i.e.*, to push the ball up out of its existing valley, from where it can descend into another valley). From this, we can infer that anesthesia induces a single deep (stable) valley in young patients (and/or there is little neuronal noise), but that older patients can inhabit many different valleys, and that these are not very deep (and/or there is a lot of neuronal noise). The neuropharmacologic mechanisms underlying these differences are not known,[5] but this paper is adding to an expanding body of evidence suggesting that the ability of the brain to respond to a γ-aminobutyric acid–mediated hypnotic drug with a strong stable synchronous frontal alpha EEG pattern is a biomarker of a patient with a functionally youthful brain.

These are elegant concepts, but does this knowledge influence the day-to-day practice of delivering general anesthesia for surgery? The most obvious answer is in the vexed question of how we interpret various EEG indices of consciousness or depth of anesthesia. We need to acknowledge that there can be a disconnect between hypnotic drug concentrations and brain states. On the one hand, there are plateaus in drug response, where the *same* brain state occurs over a *range* of hypnotic drug concentrations (as reported in 8- to 16-yr-old brains). On the other hand, the brain may spontaneously move between multiple metastable states—while exposed to *unchanging* general anesthetic drug concentrations (the results of the adult study). Given the existence of these phenomena, we should not be surprised that a single-channel EEG index might not be a fully reliable guide to hypnotic drug dosing. The work by Puglia *et al.* suggests that these monitors might be more reliable in the young. This is consonant with observations that older surgical patients have more irregularity in their intraoperative EEG,[6] and more difficulty in its interpretation. Although it is yet to be proven definitively, if the patient's EEG is stuck in a rut, it may be taken as a sign that a good brain is responding well to an optimal anesthetic.

Competing Interests

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