Biomedical Data Mining

Extended Abstract

Regulation of global brain states: Orienting oscillatory trajectories

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Abstract

Autonomy, the hallmark of advanced living systems, depends on how the brain and extended nervous system are selfregulated to accommodate the multiplicity of tasks and temporal sequencing that comprises cognitive operation. Directed to the good of the whole organism, self-regulation reveals both the need for and existence of global brain mechanisms that modulate local neural events and oversee their spatiotemporal organization. Hence, there is an implicit coupling between global and local scales that characterize large-scale, systemic operation, requiring that oversight mechanisms be regionally distributed for local activation. Existing evidence indicates that mediating control depends on a distribution of oscillatory, electropotential activity, that is, brain dynamical elements that exhibit repetitive and cyclical profiling. There is a broad consensus that oscillations detectable in EEG patterns, for example, can be grouped in frequency bands denoting different brain states. Because of their significance for human health, this paper considers underlying processes that activate and disengage such oscillatory mechanisms, and that is, therefore, responsible for modulating these states. Controlling such oscillatory networks globally is thought to be achieved through modulation of their frequency patterning, which may, for example, include synchronization, desynchronization, or cross-frequency coupling. Synchronization entails oscillatory overlap, which is thought to bind together various feature elements in cognitive representations, like those of emotions and sensory events; desynchronization, by contrast, entails oscillatory disengagement. Accordingly, the capacity for selectively engaging and disengaging oscillator activity is key to directing different brain states, that is, to mediating the orientation of bifurcations to different dynamical elements.

This paper will explore the roles of two processes likely to be critical to inducing regulatory directionality, neural pulsing and neural noise. The two will be considered in the special case of memory circuits, which will be used here as a general model for achieving global brain regulation.

Compared with other mammalian species, human neonates are relatively disadvantaged at birth. While giraffe calves are able to walk within an hour of birth and run within a day, it takes human neonates more than 1 year to walk unaided, and many months thereafter to run. Nonetheless, as children, humans develop uniquely complex cognitive abilities and motor control. Protracted ex utero neurodevelopmental processes continue well into adulthood, and they are characterized in early life by simultaneous apoptosis, synaptogenesis, and myelination of axons. Positron emission tomography (PET) studies indicate that overall brain metabolism rises to twice that of adults in 4- to 5-year-olds, and remains constant at that level until almost 10 years of age, which is thought to indicate the energy demands of these processes. Oligodendrocyte-based development continues into adulthood, with cortical myelination continuing to increase until the third decade of life and white matter volumes peaking in the fifth decade of life. Healthy neurodevelopment ex utero is highly complex, with different processes following regionally specific, often nonlinear, trajectories ranging in time span from years to decades. Characterizing typical developmental trajectories is key if we are to understand why some children develop pathology, such as mental disorders or neurological conditions, while others remain free from illness. While we have a rapidly increasing comprehension of neurodevelopment at a cellular level, a more modest literature offers descriptions of human neurodevelopment derived from in vivo measurements. Understanding at this level is crucial, given that the symptomology of many disorders is reflected in the impairment of complex and uniquely human cognition

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and behavior. Here we characterize typical neurodevelopment using in vivo neurophysiology in a large normative cohort.

Functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) have made advances in our conception of human neurodevelopment. However, fMRI depends on the blood oxygenation level dependent signal, which has a variable lag between neural recruitment and signal change in the order of seconds. Further, recent improvements in fMRI (pre)processing have called many "classic" developmental fMRI findings into question, particularly the many studies that failed to adequately account for head motion–induced artefacts. EEG offers a direct measurement of electrophysiology but because of difficulties in modeling the inhomogeneous and geometrically complex conductivity profile in the head, the spatial resolution is limited.

Therefore, a more promising technique is magnetoencephalography (MEG), which offers a noninvasive and direct measurement of in vivo brain function. Measuring the minute band-limited magnetic fields generated by synchronous postsynaptic potentials in populations of pyramidal neurons, MEG measurements are on the order of milliseconds and, when combined with appropriately implemented spatial filtering informed by anatomical MRI, offer a millimeter spatial resolution. In combination, these features make MEG ideally suited to the characterization of neurodevelopment, both in terms of fundamental electrophysiological features and in terms of functional connectivity between disparate regions.

Neural oscillations, as measured by (M)EEG, are integral to healthy brain function. Oscillations are characterized by their oscillatory power and phase, the latter thought to enable interregional communication. Despite being fundamental to the oscillation, the two measurements are minimally related and provide complementary insights into underlying neurophysiology. Here we investigated how both features change during typical neurodevelopment. Despite many decades of research with both EEG and MEG, a limited literature describes typical neurodevelopment from an electrophysiological perspective. The majority of these investigations used EEG with a small number of electrodes, allowing limited comparisons to MEG. Nonetheless, a consistent finding is that power spectral density (PSD), linked to local processing, decreases with age in the slower frequency bands. There are also some reports of higher frequency PSD decreasing with age, such as alpha and beta frequencies. Whitford and colleagues collected EEG and structural MRI data in 10- to 30-year-old subjects. They found similar curvilinear relations between age and PSD and between age and cortical volume in frontal and parietal lobes. The authors suggested that PSD is related to synaptic pruning, with decreasing PSD in these lobes indicating decreasing synapse numbers. However, this relationship may not hold for all frequency bands, with other reports demonstrating an increase in PSD with age in alpha, beta, and gamma bands.

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