Integrated Brain Network Architecture Supports Cognitive Task Performance

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Spontaneous fluctuations in neural activity and connectivity are thought to support cognition and behavior. In this issue of *Neuron*, Shine et al. (2016) describe a possible mechanism responsible for fluctuations in the human brain's network architecture that are related to rapid shifts in cognitive state.

The human brain can rapidly shift from a state of quiet reflection to a state of more active problem solving. For example, imagine you are driving home from work. For many people, this is a relatively automated process that requires little cognitive effort. Instead, you might be thinking about your plans for the evening or what you will make for dinner. However, about halfway home, you run into an unexpected road closure. Under these circumstances, you shift from self-reflection to a goal-driven state. This is simply one illustration of a phenomenon that we all experience multiple times a day. How does the brain support these rapid shifts in cognitive state? A paper in this issue of *Neuron* (Shine et al., 2016) provides evidence that the brain traverses through different states over time and that a brain network topology with an emphasis on the integration of information across the brain is associated with better performance on a cognitive task. Furthermore, an increase in pupil diameter accompanies this shift to greater network integration, which may reflect the influence of ascending neuromodulatory signals on this process.

Temporal fluctuations in brain activity and connectivity have been recognized in electrophysiology and electroencephalogram (EEG) for some time, but these phenomena have only recently garnered attention in the fMRI literature (Hutchison et al., 2013). Changes in functional connectivity have generally been associated with attention (Madhyastha et al., 2015), learning (Bassett et al., 2011), and cognition (Cole et al., 2014). The precise nature of the topographic changes in brain network communication, and the mechanisms underlying those changes, is unknown. By creating a novel "cartographic profile" based on graph theoretical measures (Bullmore and Sporns, 2009) and applying k-means clustering, Shine et al. (2016) found that individuals fluctuated between two different states. One state was characterized by a more segregated network structure with greater within-network connectivity. A second state was characterized by a network topography with greater between-network connectivity, which is more conducive to the integration of information across the brain (Figure 1A).

Shine et al. (2016) also performed a similar analysis on data collected while participants were performing a challenging cognitive task (the N-back working memory task). They found that the network topography transitions were correlated with performance of the task and that the cartographic profile of the brain shifted toward integration (Figure 1B). These shifts were largely driven by increased connectivity between the frontoparietal, dorsal attention, cingulo-opercular, and visual networks. Based on these results, Shine et al. (2016) next tested whether or not the network topographic shift toward integration was sensitive to specific task demands. While all tasks were characterized as shifting toward integration, the more challenging tasks showed the largest shift (Figure 1B). Furthermore, individual differences between the degree of network integration and behavioral measures derived from a drift diffusion model were significantly correlated. Together, these data suggest that the brain shifts to a more integrated network structure during the performance of challenging tasks, and the degree of that shift is related to the complexity of a task, as well as how well participants perform the task. These findings are consistent with other studies that have found increases in integration during task performance with fMRI (Kinnison et al., 2012) and relationships between network efficiency and intelligence using fMRI (Santarnecchi et al., 2014) and EEG (Langer et al., 2012) approaches.

A recent study found that high performers on several cognitive tasks possess a task functional connectivity structure that is more similar to resting-state functional connectivity architecture (Schultz and Cole, 2016). This suggests that high-performing individuals have a resting-state functional connectivity pattern that is "preconfigured" to switch into an organization that is beneficial to cognitive task performance. One intriguing possibility of this is due to high-performing individuals spending more time in an integrated (task-oriented) state during rest and therefore having to expend less time and resources to adjust their functional connectivity topography when they enter a goal-driven state. It would be interesting for future studies to examine whether or not individual differences in network preconfiguration can account for the tendency for some individuals to shift into a more integrated network state during task performance. This would suggest a related mechanism underlies these two findings.

If the temporal fluctuations between more segregated and more integrated network topography are related to various measures of behavioral performance on complex tasks, is there a potential mechanism that drives these fluctuations? Shine et al. (2016) hypothesize that ascending neuromodulatory systems related to arousal may provide a mechanism for switching between segregated and integrated network topographies (Figure 1C). Pupil dilation, a surrogate measure for

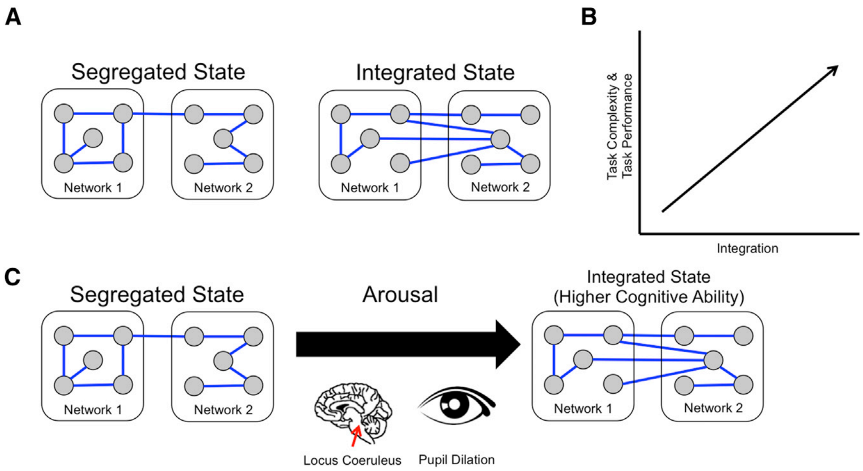

Figure 1. Integrated Brain Network States Are Related to Task Performance and Complexity
(A) An illustration of a segregated and integrated network organization. The gray circles represent nodes in the brain. The blue lines represent connections between nodes. In a segregated state, there is a great deal of intra-network connectivity, but little inter-network connectivity. An integrated state has a greater degree of inter-network connectivity.
(B) The degree of network integration is positively correlated with both task complexity and task performance.
(C) The proposed mechanism of how we switch from a more segregated to a more integrated network organization. Under minimal task demands, the networks are largely segregated. Locus coeruleus activity, a surrogate for arousal, is measured indirectly by pupil dilation. Pupil dilation is significantly correlated with integration.

arousal, was recorded during rest in an independent set of participants. Pupil diameter was correlated with the degree of integration measured in the network. This suggests that ascending neuromodulatory activity reflecting neural gain (Aston-Jones and Cohen, 2005) may be driving the fluctuations between segregated and integrated network architecture.

The results reported by Shine et al. (2016) appear to be robust, as the authors replicated the main findings and used two existing datasets collected with different scanners and scan parameters. However, it may be important for future studies to verify the existence of these two states as recent studies have suggested that resting-state functional connectivity should be considered stationary and that observed non-stationarity is caused by sampling bias, motion, or sleep (Laumann et al., 2016). Shine et al. (2016) did not find that motion was related to any of the outcome measures or that eliminating high-motion frames had any influence on the results. However, it would be important to further investigate the role of motion since another recent study found that a number of cognitive measures were significantly correlated with motion (Siegel et al., 2016).

The results from this study suggest that ascending neuromodulatory signals may be the mechanism that switches the brain between segregated and integrated states. However, the methods used in this study preclude the ability to identify a causal relationship. Future studies using complementary designs and approaches that allow for manipulation of the system are needed to support this interpretation. If neuromodulatory signals indeed form the mechanism responsible for shifting the brain between these two states, this mechanism would present a potential therapeutic target for individuals that struggle with complex cognitive tasks.

These results raise an important question: if the brain is more effective at general task performance in a more integrated state, why isn't the brain always in that state? Is there a benefit to the periods of time when individuals are in a more segregated state? It will be important to determine whether, for instance, the segregated state is more conducive to self-reflection and whether there are any negative consequences to shifting the brain to have a more integrated functional network architecture over long periods of time.

These findings contribute to our growing understanding of how dynamic changes in brain network communication support our ability to switch between different cognitive states. Importantly, Shine et al. (2016) also propose that ascending neuromodulatory signals may serve as a mechanism for how the brain can switch from a more segregated, modular organization during rest to a more integrated organization during the performance of complex tasks. We look forward to future studies that extend these findings to further enhance understanding of the brain network dynamics that underlie the dynamics of cognition.

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