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REVIEW

THE NEUROBIOLOGY OF SELF-GENERATED THOUGHT FROM CELLS TO SYSTEMS: INTEGRATING EVIDENCE FROM LESION STUDIES, HUMAN INTRACRANIAL ELECTROPHYSIOLOGY, NEUROCHEMISTRY, AND NEUROENDOCRINOLOGY

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Abstract—Investigation of the neural basis of self-generated thought is moving beyond a simple identification with default network activation toward a more comprehensive view recognizing the role of the frontoparietal control network and other areas. A major task ahead is to unravel the functional roles and temporal dynamics of the widely distributed brain regions recruited during self-generated thought. We argue that various other neuroscientific methods – including lesion studies, human intracranial electrophysiology, and manipulation of neurochemistry – have much to contribute to this project. These diverse data have yet to be synthesized with the growing understanding of self-generated thought gained from neuroimaging, however. Here, we highlight several areas of ongoing inquiry and illustrate how evidence from other methodologies corroborates, complements, and clarifies findings from functional neuroimaging. Each methodology has particular strengths: functional neuroimaging reveals much about the variety of brain areas and networks reliably recruited. Lesion studies point to regions critical to generating and consciously experiencing self-generated thought. Human intracranial electrophysiology illuminates how and where in the brain thought is generated and where this activity subsequently spreads. Finally, measurement and manipulation of neurotransmitter and hormone levels can clarify what kind of neurochemical milieu drives or facilitates self-generated cognition. Integrating evidence from multiple complementary modalities will be a critical step on the way to improving our understanding of the neurobiology of functional and dysfunctional forms of self-generated thought.

Key words: self-generated thought, spontaneous thought, mind-wandering, task-unrelated thought, brain lesions, human single-neuron recording.

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INTRODUCTION: INVESTIGATING THE WANDERING BRAIN

One of the most intriguing yet least understood aspects of the human mind is its tendency toward ceaseless activity – a quality famously described by William James as the 'stream of consciousness' (James, 1892). This tendency of the mind to drift from one thought to another has recently sparked interest among cognitive neuroscientists and led to a growing body of neuroscientific investigations of mind-wandering, stimulus-independent thought,

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Abbreviations: DMN, default mode network; ECoG, electrocorticography; fMRI, functional magnetic resonance imaging; iEEG, intracranial electroencephalography; TMS, transcranial magnetic stimulation.

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daydreaming, and task-unrelated thought (Mason et al., 2007; Christoff et al., 2009; Andrews-Hanna et al., 2010; Christoff, 2012; Axelrod et al., 2015). This interest is well warranted, given that these kinds of thought appear to account for as much as 30–50% of our waking thinking (Kane et al., 2007; Killingsworth and Gilbert, 2010). These various forms of undirected cognition represent a subset of a broader collection of processes referred to as ''self-generated thought,'' defined as ''mental contents that are not derived directly from immediate perceptual input'' (Smallwood and Schooler, 2015; Smallwood, 2013). Self-generated thoughts can arise spontaneously or deliberately, and their contents can be task-related or task-unrelated, as long as they arise relatively independently of immediate perceptual inputs. In this respect, emotions, mental imagery, and arguably even interoceptive signals from within the body (e.g., sensations from the stomach) can also be considered self-generated.

From the first-person perspective, self-generated thought involves a staggering variety of phenomenological content, including memory recall, future planning, mentalizing, simulation of hypothetical scenarios, and a wide variety of emotions and imagery from various sensory modalities (reviewed in Andrews-Hanna, 2012; Fox et al., 2013, 2014; Klinger, 2008; Smallwood and Schooler, 2015). Self-generated thought extends well beyond mind-wandering and daydreaming, however: self-generated mental activity is intimately involved in artistic (Ellamil et al., 2012) and scientific creativity (Maquet and Ruby, 2004), insight problem-solving (Kounios and Beeman, 2014), and dreaming (Fox et al., 2013; Domhoff and Fox, 2015). Self-generated thought is also relevant to numerous clinical, neurological, and psychiatric conditions in which typical patterns of thought are altered or exaggerated (Andrews-Hanna et al., 2014), such as depressive rumination (DuPre and Spreng, in press), Alzheimer's disease and dementia (Irish et al., 2012), post-traumatic stress disorder (Ehlers et al., 2004), and attention deficit/hyperactivity disorder (Shaw and Giambra, 1993).

Developing a comprehensive understanding of the neurobiology of self-generated thought is therefore of relevance to many fields of inquiry, from psychology to psychiatry.

Early cognitive neuroscience research recognized and emphasized the importance of the default mode network (DMN) to self-generated thought (Gusnard et al., 2001; Raichle et al., 2001), but this earlier viewpoint is now giving way to a broader but also more nuanced understanding. Our recent quantitative meta-analytic treatment of the neural basis of self-generated thought, for instance, revealed no fewer than a dozen regions that appear to be consistently involved, both within and beyond the DMN (Fox et al., 2015). The most salient activations were found in the default network (including medial and rostromedial prefrontal cortex, posterior cingulate cortex, left ventrolateral prefrontal cortex, and inferior parietal lobule; Fig. 1), which has long been hypothesized to be critical to self-generated cognition in resting states (Gusnard et al., 2001; Raichle et al., 2001). Consistent recruitment was also observed, however, in frontoparietal control network regions (including dorsal anterior cingulate cortex, right anterior inferior parietal lobule, and a cluster bordering right rostrolateral and ventrolateral prefrontal cortices; Fig. 1). There were further activations that fell beyond either network, including in secondary somatosensory cortices, the left insula, medial occipital cortex (lingual gyrus), temporopolar cortex, and medial temporal lobe (Fig. 1). The inherently correlational nature of functional magnetic resonance imaging (fMRI) data, however, as well as its relatively poor temporal resolution, make it difficult to answer deeper questions about which of these brain regions is causally involved in generating thought, or how the origin and subsequent spread of self-generated thought appear at fine timescales on the order of milliseconds (Fox et al., 2015).

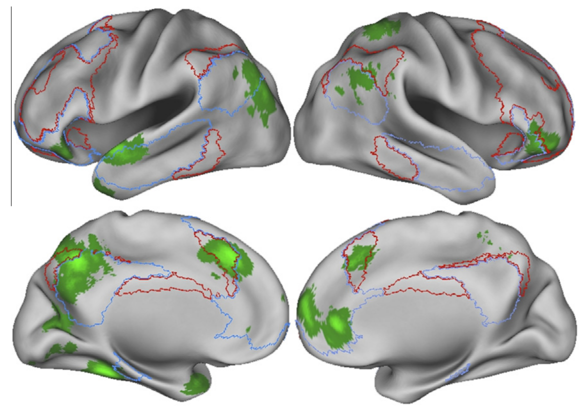

Fig. 1. The breadth of self-generated thought recruitment (green clusters) juxtaposed with the default mode network (blue borders) and frontoparietal control network (red borders).Cortical mapping of significant meta-analytic clusters associated with mind-wandering and related self-generated thought processes (green clusters) juxtaposed with outlines of the default mode network (blue) and the frontoparietal control network (red). Note that self-generated thought activations overlap considerably with both networks, but also include regions beyond both networks (highlighted in Fig. 1). Default mode network and frontoparietal control network masks based on Yeo et al. (2011). Reproduced with permission from Fox et al. (2015). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

In this review we aim to synthesize a diverse body of evidence that can help begin to make sense of the role(s) played by the widely distributed regions identified by functional neuroimaging as important for self-generated thought. A key theme is that different neuroscientific modalities and methods can contribute to this project in unique but complementary ways (Table 1). Investigation of any higher cognitive process necessarily entails certain challenges, but the subjectivity and unpredictability of self-generated thought exacerbate the difficulties of conducting rigorous, well-controlled research, and underscore the importance of using multiple methodologies that can compensate for each other's limitations. Functional neuroimaging has provided an invaluable inroad into the field of self-generated cognition, but understanding the interrelationships and varied roles of the many brain areas implicated in self-generated thought requires a synthesis of evidence from many methodologies. Here,