



Published in final edited form as:

*Nat Ment Health*. 2023 November ; 1(11): 827–840. doi:10.1038/s44220-023-00133-w.

## Recent advances in the neuroscience of spontaneous and off-task thought: implications for mental health

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### Abstract

People spend a remarkable 30–50% of awake life thinking about something other than what they are currently doing. These experiences of being “off-task” can be described as spontaneous thought when mental dynamics are relatively flexible. Here we review recent neuroscience developments in this area and consider implications for mental wellbeing and illness. We provide updated overviews of the roles of the default mode network and large-scale network dynamics, and we discuss emerging candidate mechanisms involving hippocampal memory (sharp-wave ripples, replay) and neuromodulatory (noradrenergic and serotonergic) systems. We explore how distinct brain states can be associated with or give rise to adaptive and maladaptive forms of thought linked to distinguishable mental health outcomes. We conclude by outlining new directions in the neuroscience of spontaneous and off-task thought that may clarify mechanisms, lead to personalized biomarkers, and facilitate therapy developments toward the goals of better understanding and improving mental health.

### 1.0: Spontaneous Thought and its links to Mental Health

The last several decades have brought a wealth of research into the neural underpinnings of processes evoked by experimentally-directed tasks. However, typical adults spend much of their waking life entertaining thoughts that extend *beyond* the task at hand (termed “off-task thought”), and/or that emerge *spontaneously*, relatively free from constraints that guide and stabilize cognition. For example, depending on how these types of experiences are sampled,

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Author Contributing Statement

AK completed the initial draft. JWYK, JRAH, KC and SWG contributed to writing, conceptualization and editing.

Code Availability Statement

The code that was used to generate Figure 1 is available at <https://github.com/DynamicBrainMind/NatMentHealth2023>.

Competing Interest Statement

The authors declare no competing interests.

being “off-task” has been estimated to occupy a striking ~30–50% of daily time awake in adults.<sup>1–5</sup>

Having spontaneous and off-task thoughts is a normal, and typically healthy, part of everyday life that can involve reminiscing, reflecting, imagining, fantasizing, problem-solving, or generating creative ideas.<sup>6–8</sup> Yet such experiences—to which an enormous amount of daily time is dedicated—can also take on forms that are negative in character. For example, rather than reminiscing about the past, an individual may repetitively dwell on prior negative experiences; instead of adaptively planning for the future, one may engage in uncontrollable worry or suicidal ideation. With increasing prevalence rates of psychiatric symptoms and illness in recent years,<sup>9</sup> it is likely that dysfunctional manifestations of inner experience have been increasing in frequency. Given that a significant proportion of psychiatric patients are resistant to currently available treatments,<sup>10</sup> there is a need for novel therapies such as neuromodulation to correct disruptive patterns of thought. Thus, understanding neural mechanisms of spontaneous and off-task thought is becoming of increasing societal and clinical importance,<sup>11–13</sup> an urgency mirrored by growing scientific interest (Figure 1).<sup>14–18</sup>

Advances in our understanding of spontaneous thought have linked it to dynamic patterns of brain activity that fluctuate across various time scales.<sup>14,15</sup> The recently proposed Dynamic Framework of Thought (DFT)<sup>14,19</sup> describes spontaneous thought as emerging in the course of interactions across large-scale brain networks such as the Default Mode Network (DMN), with its core and medial temporal lobe (MTL) subcomponents, as well as the salience and frontoparietal-control networks. Mapping the dynamic interactions across large-scale brain networks to the rich varieties of covert, subjective experience presents some unique scientific challenges that have led to novel developments in experimental paradigms. The neural basis of spontaneous thought, along with off-task, have so far largely been investigated with functional neuroimaging,<sup>14,15</sup> but the field is rapidly maturing, incorporating insights from causal experiments (neurostimulation and lesion studies),<sup>20</sup> neurophysiological mechanisms of memory,<sup>16,21</sup> and dynamics of ascending neuromodulator systems.<sup>16,18,22</sup>

In this review, we cover the most recent developments in methodologies and advances in the study of the neural bases of spontaneous and off-task thought with an emphasis on the implications for mental health. We provide an updated overview of the DMN and broader, large-scale networks. Beyond those networks, we discuss candidate mechanisms that involve spontaneous activity in hippocampal memory and ascending neuromodulatory systems. Throughout, we explore how distinct brain states can be associated with and give rise to various forms of healthy and unhealthy thinking patterns. Finally, we outline new directions in the neuroscience of spontaneous and off-task thought that may significantly advance mental health research and clinical practice.

## 2.0: Conceptual and Methodological Considerations

Before reviewing the neural bases of spontaneous and off-task thought, we consider conceptual and methodological issues that provide background for interpretation of

research findings. We cover some definitional issues surrounding the evolving concept of ‘spontaneous thought’, examine the evidence for how the related but distinct construct of off-task thought relates to mental health, and review some of the challenges when it comes to investigating spontaneous thought along with the emerging techniques that are beginning to help us overcome these challenges.

## 2.1: The concept of spontaneous thought is still evolving

The term “spontaneous thought” has become prominent in the scientific literature on a broad range of inner experiences such as mind-wandering and dreaming.<sup>23</sup> Yet notions of what spontaneous thought exactly is and how it is best defined continue to evolve. One important outstanding question remains on whether certain forms of repetitive thought (e.g. rumination and worry) should be viewed as spontaneous thought,<sup>24,25</sup> or as the DFT argues, are better characterized as a distinct mode of thought that unfolds in a highly constrained, inflexible manner.<sup>14</sup> There are also broader philosophical concerns regarding the spontaneity of thought.<sup>26</sup> One proposed way to determine spontaneity is to inquire whether the experiencer could identify a cue or trigger.<sup>27</sup> However, even in a context where a thought is not initiated consciously by an external stimulus or explicit cognitive control, factors that are typically unobserved, such as interoceptive inputs, may trigger experiences.<sup>28</sup> Similar issues have been discussed regarding spontaneity in brain activity.<sup>29</sup>

Beyond considering how mental activity is initiated, it is also important to account for the dynamic processes that ensure the continuity of thought.<sup>30</sup> The DFT<sup>14,19</sup> offers an explicit definition of spontaneous thought that hinges on a crucial distinction that the DFT makes between mental contents and dynamic thought processes. Contents describe *what* someone is thinking about, including dimensions such as relevance to current performance of a task, affective valence (e.g. feels positive or negative), temporal orientation (e.g. past or future-oriented), and sensory imagery (e.g. mentation in the visual or auditory modality). In contrast, dynamics describe how thoughts change from one mental state to another. Within the DFT, spontaneous thought occurs when those dynamics are relatively flexible, and thoughts can change easily and freely (rather than being limited to repetitively recurring content). Conversely, according to the DFT, thought’s spontaneity is reduced when its flow is deliberately constrained (i.e., by cognitive control) or automatically constrained (i.e., by perceptual or affective salience mechanisms that lead to attentional capture). Thus, within the DFT, spontaneous thought is defined based on thought’s dynamics rather than its content, and mind-wandering is defined as a form of spontaneous thought that unfolds relatively freely, with low deliberate and automatic constraints.<sup>14</sup> Dreaming and creative thinking are also defined as forms of spontaneous thought with distinct deliberate and automatic constraint profiles.

Despite the emphasis on thought dynamics within the DFT, the vast majority of empirical investigations have focused on measuring thought contents rather than dynamics.<sup>31</sup> Mind-wandering, specifically, has been frequently operationalized based on thought contents, although recent empirical investigations have begun measuring subjective, dynamic features such as the extent to which thoughts shift around freely.<sup>31,32</sup> Alternatively, thought dynamics

have been characterized by quantifying how experiences change with different durations of time passing.<sup>33</sup>

Acknowledging ongoing philosophical debates and outstanding conceptual issues (see<sup>25,34</sup> for detailed discussions), this article reviews a variety of mental experiences and is inclusive of off-task thoughts, experiences described by the DFT as “spontaneous thought,” and thoughts that arise and unfold in an automatically constrained or habitual manner. All of these classes of thought may be indirectly elicited by environmental cues in everyday life (e.g. by initiating mental associations),<sup>35,36</sup> but they are not, by definition, directly initiated by explicit cues that instruct people to deliberately engage in specific thoughts. Shared features across classes are a focus on inner mental content (as opposed to immediate physical stimuli) and the involuntary nature of thought unfolding. According to the DFT, the category of automatically or habitually constrained thought is of particular interest because it includes phenomena such as rumination and obsessive thought that are of clinical significance.<sup>14</sup> However, automatic constraints on thought and their clinical implications remain relatively understudied. Instead, most empirical investigations have focused on the related but distinct phenomenon of off-task (or task-unrelated) thought, which we turn to in the next section.

## 2.2: On the relationship between off-task thought and mental health

Research has overwhelmingly focused on deleterious cognitive and health effects of thoughts that are unrelated to the task at hand (i.e., off-task thoughts that can be spontaneous or deliberate). Studies suggest that off-task thought impairs cognitive performance in various experimental and real-world settings, including in executive control,<sup>37</sup> sustained attention,<sup>38</sup> memory encoding<sup>39</sup> tasks, in classroom lectures,<sup>40</sup> during reading,<sup>41</sup> and during automobile driving.<sup>42</sup> Off-task thought can lead to perseverative thinking such as rumination and worry,<sup>43,44</sup> lowered mood,<sup>2,45</sup> increased stress,<sup>46</sup> and impaired sleep.<sup>47</sup> Excessive off-task thought—particularly when initiated unintentionally—has been associated with symptoms of depression,<sup>48</sup> obsessive-compulsive disorder,<sup>44</sup> and eating disorders,<sup>49</sup> and attention-deficit/hyperactivity disorder (ADHD)<sup>50</sup> in certain task contexts.<sup>51</sup>

In contrast, positive impacts on mental wellbeing often become apparent when evaluating characteristics beyond the sheer presence of off-task thought, such as what people think about and how thought unfolds.<sup>8</sup> For example, though off-task thoughts are often associated with less positive affect than on-task thoughts, off-task thoughts are still, on average, experienced as mildly pleasant, positive and enjoyable.<sup>52</sup> In some situations, the content of off-task thought may lead to subsequent improvements in mood.<sup>53,54</sup> While negative mood has been associated with thinking about past events,<sup>55–57</sup> people tend to daydream more frequently about the future than the past.<sup>58</sup> This “prospective bias” of thought can be adaptive, for example benefiting problem-solving and creative achievement<sup>6</sup> or advancing social relationships<sup>59</sup> (though positive content in future-oriented off-task thought is reduced in individuals with depression symptoms<sup>60</sup>). Past-related thoughts can also be adaptive, promoting meaningful connections with the current and future self.<sup>61</sup> Engaging in off-task thought may promote insight—moments when one becomes abruptly aware of a solution to a problem, often associated with a pleasurable feeling of reward.<sup>62</sup> Besides thought content,

there is increasing recognition for the mental health relevance of dynamic dimensions. For example, thought described as freely-moving (i.e., unconstrained) has been associated with momentary positive affect.<sup>32,63</sup>

Context is another major factor that determines how off-task thought interacts with mental health.<sup>8,17</sup> For example, the content and dynamics of off-task thought depend on whether a task is high or low demand<sup>64</sup> and whether thoughts are sampled in the laboratory or in the real world.<sup>65</sup> In one study, several patterns of off-task thought were identified based on distinct content, and among these patterns, emotional thoughts showed the least generalizability between laboratory and real-world environments across individuals.<sup>65</sup> Overall, how off-task thought interacts with mental health is highly dependent on factors such as thought content, dynamics, and context. Importantly, there is tremendous variability between—and even within—individuals that is critical to consider when assessing impacts on mental health.

### 2.3: How can spontaneous thought be studied in the brain?

The study of spontaneous thought in the brain faces a unique challenge: How can mental activity that is initiated without any instructive, external trigger—and that is unpredicted even by an experiencer themselves—be measured or quantified, and attributed to brain events? While typical experimental paradigms in cognitive neuroscience employ structured tasks or stimuli to trigger brain responses that are time-locked to external events, distinct approaches are needed to generate insights into the neural basis of spontaneous thought.

Prior to the last two decades, hypotheses about neural mechanisms were largely limited to interpretive comments when authors observed patterns of elevated brain activity during task-free, waking rest, such as the EEG posterior alpha wave (reviewed in<sup>66</sup>).<sup>67,68</sup> However, “resting state” paradigms alone cannot generate direct insights into the brain’s representation of subjective experiences during spontaneous thought, which require that brain activity be directly linked to self-reports of such experiences.<sup>14,15,69</sup> Starting in the 1990’s, positron emission tomography (PET)<sup>68,70</sup> and functional MRI (fMRI)<sup>71,72</sup> studies began to examine relationships between brain activity and self-reported frequency of off-task thought, which participants estimated retrospectively after completing brain scans.

More recently, online *experience-sampling* during neuroimaging has been applied to examine finer temporal dynamics within individuals (Figure 2a)<sup>73</sup> (see also<sup>74</sup> for an earlier EEG example). Here people are intermittently presented with self-report prompts (“thought probes”) asking them to rate or describe their most immediate experience. Thought probes must be designed carefully and with the aim of identifying valid and reliable brain-experience relationships, as it has been shown that the specific phrasing and manner of presentation<sup>4,5,75</sup> as well as the population being studied<sup>76</sup> can influence participant responses. Despite such issues, experience sampling has been used successfully to identify brain-experience relationships in groups of participants on the order of seconds to minutes.<sup>77</sup> Alternative approaches to intermittent experience sampling, such as self-caught reporting of experience may provide temporal insights into the arising of spontaneous thoughts and their neural antecedents (especially in trained individuals such as meditation practitioners).<sup>78,79</sup> Moreover, free association-based thought sampling<sup>80</sup> and think aloud paradigms<sup>81</sup> have also

been used, albeit more rarely, in combination with neuroimaging. In some cases, verbal or auditory cues have been used to elicit involuntary mental associations, thereby manipulating the occurrence of spontaneous thought.<sup>82–84</sup>

Researchers have only recently begun to characterize the brain bases of spontaneous thought's more granular features that have relevance to mental health. Multi-dimensional experience-sampling<sup>17</sup> during neuroimaging has been used to examine thoughts that vary in terms of emotion,<sup>85</sup> self-relevance,<sup>28</sup> level of detail,<sup>86</sup> modality and perceptual features of sensory imagery,<sup>87</sup> and dynamic properties.<sup>88</sup> Recent work has also explored the neural basis of “mind-blanking,” an absence of reportable thought (Box 1).<sup>89,90</sup> Studies involving online experience-sampling with brain activity measures are beginning to emerge in patients diagnosed with ADHD<sup>91,92</sup> and treatment-resistant depression.<sup>93</sup> Correlative neuroimaging findings are being complemented with insights from interventions<sup>94</sup> as well as causal approaches in neuroscience such as transcranial direct current stimulation (tDCS), intracranial electrical stimulation, and lesion studies, providing insight into the emergence of spontaneous thought across a wide range of time scales (Figure 2b). Taken together, the study of spontaneous thought in the brain is quickly expanding in terms of paradigms used, phenomenology explored, clinical populations examined, and neuroscience techniques applied. With these emerging developments, it is timely to examine their potential to yield new insights, given what is currently known about spontaneous thought in the brain.

### 3.0: Recent Neuroscientific Findings with Relevance to Spontaneous Thought and their Links to Mental Health

#### 3.1: Default Mode Network: An Update.

The DMN has by far received the most frequent attention in reference to the neural basis of spontaneous and off-task thought. The DMN has also been studied extensively in relation to mental health and illness. We provide updates on different features of the DMN, including its activation and deactivation profiles, functional connectivity, subsystems, and the effects of perturbation. We describe how these features inform the neural basis of spontaneous thought and the implications for mental health.

**3.1.1: Activation and Deactivation.**—Regions comprising the default mode network—including large portions of the posteromedial, medial prefrontal cortex, and lateral parietal cortex (among others)—were initially largely appreciated for showing relative decreases in blood flow during (external) cognitive tasks compared to passive control conditions.<sup>95</sup> The “default mode” network<sup>96,97</sup> has since been shown to be recruited across a variety of internally-guided processes such as remembering, envisioning the future, and social inference<sup>98</sup>—experiences that are common during spontaneous thought.<sup>68,99</sup> Moreover, the DMN's activity is often anticorrelated with, or fluctuates independently from, networks involved in externally-oriented attention.<sup>100–102</sup> Such observations led to the hypothesis that the DMN could be “the core brain system associated with spontaneous cognition.”<sup>103</sup> Subsequently, fMRI studies with online experience-sampling identified trial-by-trial associations between off-task thought and increased DMN activation (or decreased deactivation), which was replicated across multiple contexts.<sup>73,99,104,105</sup>

The implications of such findings for mental health immediately became a topic of interest. In particular, researchers explored the idea that DMN over-activation underlies an inability to disengage from unwanted, off-task thoughts. For example, in attention and psychotic disorders, it was suggested that an inability to suppress the DMN could give rise to attention lapses, performance variability, and cognitive impairments.<sup>106,107</sup> In disorders of mood and anxiety, DMN hyper-activation was hypothesized to underlie maladaptive rumination and worry.<sup>107</sup> On the other hand, DMN activation may support healthy forms of thought such as creative idea generation and evaluation.<sup>108</sup> Overall, findings highlighted that nuanced interpretations are needed when evaluating DMN activation/deactivation as a potential biomarker or treatment target in mental health contexts. Adding complexity, recent experience-sampling fMRI studies question the notion of a simple one-to-one relationship between DMN activation and off-task thought,<sup>86,109,110</sup> while other paradigms have linked DMN activation to the use of working memory to guide task-related behavior.<sup>111,112</sup> To better clarify the DMN's role, it may be important to consider other network features.

**3.1.2: Functional Connectivity.**—A distinct defining feature of the DMN is correlated spontaneous activity between its different regions.<sup>97</sup> Such “functional connectivity” has been shown to persist during resting states, task performance, and even sleep and unconscious states. As within-network functional connectivity appears to be largely preserved across cognitive states,<sup>113</sup> it may not purely reflect current thoughts.<sup>15</sup> Instead, the strength of correlation within intrinsic networks may be shaped by an intricate combination of factors such as prior life experience, genetic traits, current cognitive state, and other “intrinsic” neuronal processes.<sup>114</sup>

Resting state fMRI studies have reported correlations between individual off-task thought tendencies and DMN functional connectivity strength.<sup>115,116</sup> Moreover, DMN connectivity abnormalities have been extensively reported within various populations in which mental health is impacted.<sup>107,117</sup> Based on the widespread idea that DMN activation signifies off-task thought, authors have sometimes attributed connectivity abnormalities to disruptions in spontaneous thought or rumination that may arise at rest. Interestingly, distinct recurring brain states can be identified at rest,<sup>118</sup> and the occurrence rate of a DMN-activation state was recently associated with individual differences in post-rest retrospective reports of unintentional intrusive thoughts about the past.<sup>119</sup> However, to disentangle state (intra-individual) from trait (inter-individual) relationships, it is critical to examine experiential fluctuations within individuals.

To do so, studies have combined online experience-sampling with intra-individual analyses of pre-thought probe functional connectivity.<sup>92,105,110,115,120</sup> These “dynamic functional connectivity”<sup>121</sup> studies have so far focused almost exclusively on off-task thought. A complex set of findings have emerged, where intra-individual off-task thought has been associated with both increased and decreased within-DMN functional connectivity. Potentially reconciling those findings, recent work revealed both positive and negative correlations with off-task thought depending on the precise DMN subregions involved.<sup>92</sup> Taken together with additional evidence linking DMN connectivity fluctuations with ongoing cognition and behavior, it is becoming clear that DMN dynamics reflect a complex combination of state factors (e.g. experience/thought, arousal and attentional fluctuations)

and traits of individuals.<sup>123,124</sup> However, as resting state functional connectivity studies in clinical populations do not typically include measures of online experience, it has been difficult to directly link alterations of spontaneous thought (or other state factors) to functional connectivity abnormalities. Further investigations that combine resting state paradigms, dynamic functional connectivity approaches, and online multi-dimensional experience-sampling may have an important role in clarifying the role of disrupted spontaneous thought in DMN connectivity abnormalities observed in mental illness.<sup>69,123</sup>

**3.1.3: Subsystems.**—While the DMN as a whole may support a domain-general function, there is a wealth of fMRI evidence for specialized subsystems.<sup>98,125–127</sup> According to one neurocognitive model,<sup>128</sup> a DMN subsystem anchored in dorsomedial prefrontal cortex may support high-level abstract and verbal forms of cognition such as mentalizing and language comprehension (a “mind’s mind” form of thought), whereas a subsystem anchored in the posterior MTL may support more contextually-specific and imagery-based forms of cognition such as episodic memory and episodic future thinking (a “mind’s eye” form of thought). Recent findings illustrate individual-level, precise delineation of DMN subsystems based on intrinsic functional connectivity<sup>129</sup> and activation during deliberate self-generated thoughts with distinct content.<sup>130</sup> A common finding is that subsystems can be distinguished based on coupling with MTL structures including the hippocampus.<sup>131</sup> The MTL-anchored DMN subsystem has also been termed the “posterior-medial memory network”<sup>132</sup> and is consistently implicated in episodic thought about the past and future.

Understanding the specific roles of DMN subsystems in thought content and dynamics is an active area of investigation. Regarding content, it is likely that subsystems are regularly activated spontaneously during the occurrence of similar categories of thought that have been mapped in task-activation studies. For example, a ventromedial prefrontal region that has been implicated in social cognition (based on task-evoked activation) also shows increased activation with off-task thought involving episodic social content (as detected with experience sampling).<sup>133</sup> Indirect support also comes from studies of individual differences showing that functional connectivity of the MTL, but not dorsomedial prefrontal, subsystem is associated with daydreaming frequency<sup>115</sup> and with retrospectively reported thoughts about the past and future.<sup>99</sup> Moreover, greater cortical thickness of MTL regions within DMN has been associated with individual tendencies for higher level of detail in off-task thought (in both laboratory and real-world settings).<sup>65,134</sup> In terms of thought dynamics, it has been hypothesized that the MTL subsystem initiates spontaneous thought during conditions when deliberate constraints are weak.<sup>14</sup> This idea is supported by fMRI findings within mindfulness practitioners, where self-caught spontaneous thoughts were preceded by MTL activation.<sup>78</sup> We further discuss the potential role of the MTL in initiating spontaneous thought in Section 3.3.

How might DMN subsystems shed light on the role of spontaneous thought in mental health? A promising avenue involves characterizing relationships with phenomenological experiences, beyond off-task thought. A recent fMRI study provides insight into the role of the MTL subsystem in the self-relevance and affective valence of spontaneous thought,<sup>80</sup> features known to be important to long-term health.<sup>2,45,135</sup> In a free-association thought sampling paradigm,<sup>136</sup> participants generated conceptual associations that varied



in self-relatedness and negative affectivity. Multivoxel pattern analyses revealed that the self-relevance and affective valence of concepts could be predicted from a variety of brain networks, including key contributions of MTL and other DMN regions.<sup>80</sup> Such findings suggest that DMN subsystems provide insight into the neural bases of spontaneous phenomenological experiences that are closely tied to mental health.

**3.1.4: Effects of Perturbation.**—So far we have reviewed neuroimaging studies that offer correlational evidence. Recently, investigators have begun to explore the possible causal role of the DMN based on lesion studies as well as perturbation with tDCS and invasive stimulation to localized DMN regions (Box 2). Beyond being critical to establishing causal mechanisms of spontaneous thought, these studies have direct implications for neuromodulation therapies for mental health.

Several investigators have applied tDCS to DMN regions and tested the short-term (presumably reversible) effects on frequency of off-task thought.<sup>137–139</sup> However, these studies have so far yielded mixed findings that may depend on the targeted region, stimulation parameters, outcome measure, and other factors.<sup>20</sup> Further research is needed to determine whether non-invasive DMN neuromodulation can reliably alter off-task thought frequency and whether effects may have clinical utility in conditions such as ADHD where off-task thought can occur excessively.<sup>140</sup>

Interestingly, both lesion and tDCS studies provide preliminary converging support for the causal importance of the MTL subsystem in the content of spontaneous thought. Patients with lesions to regions within this subsystem (ventromedial prefrontal cortex<sup>141</sup> and hippocampus<sup>142</sup>) and with neurodegeneration affecting this subsystem<sup>122</sup> report a reduced frequency of spontaneous thoughts about the past and future. In a recent study in healthy adults, tDCS to the posterior inferior parietal lobule, an MTL subsystem region, resulted in reduced frequency of thoughts about the past involving negative affect.<sup>143</sup> Given the associations between past-related thought, negative affect and rumination,<sup>55,56</sup> these findings preliminarily suggest that targeting the MTL subsystem may improve mood via altering the temporal focus of spontaneous thought.

### 3.2: Large-Scale Network Dynamics Beyond the DMN

Despite the field's emphasis on the DMN, it is now widely appreciated that multiple other large-scale brain networks support the diverse content and dynamic qualities of spontaneous and off-task thought. In this section, we provide brief updates on networks beyond DMN, focusing primarily on the frontoparietal control (FPCN) and salience networks. We then highlight select, novel findings that have mapped network dynamics to features of spontaneous thought that are important to mental health.

The FPCN, a network that interacts closely with both the DMN and externally-oriented systems,<sup>144</sup> has repeatedly been implicated in off-task thought.<sup>14,20</sup> The FPCN is hypothesized to impose deliberate constraints and to cooperate with the DMN to control the course of thought.<sup>14,145</sup> Recent tDCS studies have shown both increases and decreases in off-task thought after stimulation of a dorsolateral prefrontal area within the FPCN.<sup>146,147</sup> Despite diverging results that may have depended on task context,<sup>20</sup> these studies hint that

modulation of the FPCN may alter deliberate constraints on thought, which can be beneficial in contexts where it is desirable to increase cognitive control and reduce off-task thought.

The salience network is often engaged when orienting attention toward salient stimuli or mental events<sup>148</sup> and is hypothesized to impose automatic constraints on thought.<sup>14</sup> Cortical areas of the salience network (e.g. anterior insula, mid-cingulate cortex) are tightly associated with subcortical arousal and noradrenergic systems.<sup>149,150</sup> Though the salience network is not usually activated during off-task thought in fMRI studies (though see<sup>79</sup>), future studies are needed to determine its relevance for thought content and dynamics. Resting state fMRI combined with separately conducted experience-sampling in real-world settings have shown that individual tendencies to engage in negative thinking are associated with functional connectivity between the salience network, FPCN and DMN.<sup>151,152</sup> These findings may be consistent with the salience network participating in thoughts with strong automatic constraints and arousal qualities, such as rumination and worry.

Various other large-scale networks appear to be involved in spontaneous thought content and dynamics. Sensory and motor networks have been linked to processes such as internally-generated imagery<sup>87</sup> and perceptual decoupling.<sup>153</sup> Within the context of reading, one study revealed that individuals who had more frequent off-task thoughts displayed reduced resting state functional connectivity between the DMN and early visual regions (potentially supporting perceptual decoupling during reading).<sup>154</sup> The dorsal attention network (DAN) may compete with the DMN to support the movement of attention between spontaneous thought and external stimuli.<sup>14</sup> Experience sampling across multiple task conditions has revealed that areas of the DAN (in parietal cortex) are more activated for on-task relative to off-task thought regardless of context.<sup>64</sup> Subcortical systems that control ascending neuromodulatory signals likely contribute to the regulation and flow of spontaneous thought.<sup>16</sup>

Overall, spontaneous and off-task thoughts involve complex, dynamic orchestration of activity across distinct networks at the whole-brain level. These findings have motivated recent applications of data-driven, predictive modeling analyses<sup>155</sup> that take into account a rich variety of brain network features. In recent work,<sup>92</sup> connectome-based predictive modeling<sup>156</sup> was combined with fMRI and online experience-sampling. In healthy adults, a pattern of whole-brain functional connectivity predicted trial-by-trial off-task thought and involved interactions within and between virtually all intrinsic networks to some degree (Figure 3a). A prominent feature was decreased anticorrelation between the DMN and FPCN during off-task thought, a finding in line with research implicating DMN-FPCN interactions in controlling the course of thought.<sup>145</sup> A second prominent feature was decreased coupling between DMN and sensorimotor regions, a process that may underlie perceptual decoupling.<sup>153</sup> Importantly, the network pattern also predicted off-task thought in adults with ADHD. These patients reported a heightened frequency of off-task thought and over-expressed the network pattern. As excessive off-task thought is strongly associated with adverse clinical outcomes in ADHD,<sup>140</sup> these findings give clues into complex network interactions that could be considered as therapeutic targets.

Most studies examining network dynamics and spontaneous thought have used fMRI, which has limited temporal resolution, indirectly measures brain activity, and is usually limited to short sessions. To overcome these limitations, one study combined experience-sampling with intracranial EEG (iEEG).<sup>157</sup> Patients with semi-chronic, implanted electrodes (within limited cortical and subcortical regions) were asked to rate task-free fluctuations in subjective mood over several days. Based on inter-electrode temporal coherence, multiple intrinsic functional networks were identified involving the amygdala, hippocampus, and salience network regions (e.g. insula, cingulate) (Figure 3b). Self-report mood fluctuations were predicted from the variability of coherence in the beta (13–30 Hz) frequency range within a network involving amygdala-hippocampus coupling.<sup>157</sup> This pattern may be indicative of interactions between the salience network (amygdala<sup>150</sup>) and DMN (hippocampus<sup>131</sup>). These iEEG findings provide strong neurophysiological evidence for the relevance of network dynamics to fluctuations in subjective experience, highlighting the role of synchronized oscillatory patterns that have been more broadly linked to cognition<sup>158</sup> but have been rarely explored in relation to spontaneous and off-task thought. Extending the findings, the iEEG experience-sampling approach was recently applied in treatment-resistant depression for the purpose of identifying a deep brain stimulation target.<sup>93</sup> This novel direction highlights how mapping large-scale network dynamics to spontaneous thought may provide clinical biomarkers to guide treatment.

### 3.3: Hippocampal Sharp-Wave Ripples and Replay

The field has likely focused extensively on large-scale brain networks because their function is readily detected with current human neuroscience methods. However, certain brain events that have been observed in nonhuman animals display properties that may be consistent with the occurrence of spontaneous or off-task thought. One neurophysiological event that is receiving growing attention is the so-called sharp-wave ripple (SWR).<sup>16,21,159</sup> The SWR is an electrophysiological event, generated from highly synchronous neuronal activity, that lasts <150 ms and occurs spontaneously in the hippocampus within the MTL. Information from SWRs is transmitted widely to cortical and subcortical targets. Micro-scale local field potential signals are typically used to detect hippocampal SWRs, but recently, putative SWRs have been documented at coarser spatial scales in the human brain using iEEG<sup>160,161</sup> and magnetoencephalography (MEG).<sup>162</sup>

There are several reasons to suspect that hippocampal SWRs have a mechanistic role in spontaneous thought. First, SWRs are observed selectively during “offline” periods such as wakeful rest (e.g. when animals are remaining still) when external constraints on thought are low.<sup>163</sup> Second, SWRs coincide with extrahippocampal neuronal firing sequences that replay past experiences (reverse replay) or construct potential future scenarios (forward replay).<sup>164</sup> Combinations of these sequences could support unconstrained semantic associations that are characteristic of spontaneous thought.<sup>21</sup> Spontaneous memory reactivations have also been identified in hippocampus and cortex in human resting state fMRI<sup>165</sup> and MEG.<sup>162</sup> Third, hippocampal SWRs<sup>166,167</sup> and replay events<sup>168</sup> occur in concert with activation of the DMN, the large-scale network most frequently associated with spontaneous thought.<sup>169</sup>

Despite these theoretical considerations, a direct link between SWRs and spontaneous thought has not yet been firmly established. While it is possible that SWRs are directly involved in conscious experience, an alternative is that they support preconscious contemplations that influence subsequent experiential phenomena.<sup>163</sup> As SWRs have largely been studied in animal models, it has been difficult to draw conclusions about relationships with mental experience. Notably, intracranial electrical stimulation of the hippocampus and nearby white matter tracts in neurosurgical patients often evokes spontaneous vivid experiences of past events.<sup>133</sup> However, it remains unknown whether such stimulation influences SWRs. A recent iEEG study showed that SWRs increased in frequency prior to spontaneous, conscious recall of previously viewed images,<sup>161</sup> providing correlative evidence for involvement in mental experience.

Several authors have speculated that spontaneous hippocampal SWRs are involved in adaptive forms of thought, such as creative thinking and problem-solving.<sup>21,159</sup> During SWRs, replay-related hippocampal and cortical sequences can generate new combination ‘strings’ of sequences.<sup>162</sup> When conditions promote spontaneous and off-task thought (e.g. rest), the continuous stitching together of different sequence combinations provides a potential basis for abstract thinking, novel ideas, or sudden insights.<sup>159</sup>

On the flip side, SWRs and associated replay may lead to disruptive forms of thought in conditions affecting mental health. An MEG study showed that patients with schizophrenia, relative to control subjects, showed a reduction in spontaneous neural replay and elevated (potentially compensatory) SWR power.<sup>171</sup> Such distortions in resting state brain activity, which may relate to DMN abnormalities in schizophrenia,<sup>107</sup> could be associated with experiences such as disorganized or delusional thinking. Additionally, it has been hypothesized that disrupted SWRs and replay play a role in disrupted thought in depression and anxiety; sustained SWRs that drive forward and reverse replay, respectively, could be the bases of uncontrollable worrying and ruminative thoughts.<sup>172</sup> Overall, SWRs may play key roles in both adaptive and maladaptive thought, and there is need to further characterize these events and their interplay with cortical networks during experience.

### 3.4: Ascending Neuromodulatory Systems.

Ascending neuromodulatory systems—such as the cholinergic, noradrenergic, and serotonergic systems—originate in brainstem or subcortical nuclei and send broad projections to cortical networks. These systems, and their complex interactions with one another, strongly influence the neural phenomena described here (DMN activity, large-scale network dynamics, hippocampal SWRs).<sup>173</sup> Ongoing fluctuations within neuromodulatory systems regulate many aspects of behavior and cognition and have a vital role in mental health. Pharmacological agents that target these systems are regularly used in treatment of mental illness, yet little is known about the role that neuromodulators play in spontaneous and off-task thought. In this section, we discuss two systems where knowledge is beginning to accumulate: the noradrenergic and serotonergic systems. Other systems (e.g. cholinergic, dopaminergic) that have been theoretically implicated in spontaneous thought but require empirical study are beyond the scope of this review (see<sup>16</sup> for an excellent overview).

**3.4.1: Noradrenergic System.**—The noradrenergic system originates in the locus coeruleus, projects diffusely to cortical regions, and has a major role in the regulation of global brain states to control vigilance and arousal. Tonic and phasic fluctuations in noradrenaline levels, respectively, refer to slow and fast changes that mediate separate functions.<sup>174</sup> The size of the pupil is often used as a proxy for noradrenergic activity level, which is supported by neurophysiological and neurostimulation evidence.<sup>175,176</sup> However, this relationship between pupil size and noradrenergic activity is somewhat variable over time.<sup>177</sup> Other systems (e.g. cholinergic) are also associated with pupil size.<sup>176</sup> As such, findings from studies examining pupil size in relation to spontaneous thought should be interpreted as preliminary regarding involvement of the noradrenergic system.

During off-task thought, tonic pupil size was found to be both elevated and reduced in different studies.<sup>120,178,179</sup> These findings have been interpreted with reference to the inverted U-shaped relationship that noradrenergic activity has with task performance: too much (high arousal) or too little (low arousal) activity can impair behavior.<sup>174</sup> One suggested possibility is that low levels of noradrenaline, associated with low arousal and increased SWRs,<sup>173</sup> promote freely-moving and transitory thoughts (mind-wandering, according to the DFT<sup>14</sup>) while high levels promote disjointed thoughts with reduced awareness (that have been referred to as ‘mind blanking’).<sup>16,179</sup> In contrast to tonic pupil size, phasic responses to stimuli have consistently been found to decrease during off-task thought<sup>120,180</sup> (though see<sup>110</sup>). This may reflect disengagement of arousal responses to external stimuli related to perceptual decoupling. However, phasic pupil dilation, which occurs regularly during wakeful rest, could reflect engagement with inner thoughts. A recent iEEG study showed that spontaneous pupil dilations (resembling task-evoked, phasic dilations) were consistently preceded by neuronal population activations in the anterior insula within salience network.<sup>181</sup> A possibility that could be explored is that coupling between the noradrenergic system and salience network may impose automatic constraints during worrying and ruminative thoughts.

Taken together, pupillometric studies tentatively suggest involvement of the noradrenergic system in spontaneous thought. These findings have important implications for the use of stimulant medications that are commonly used to treat mental illness (e.g. ADHD, depression) and include the noradrenergic system as a central target. Further research may clarify how pharmacological manipulation alters spontaneous and off-task thought to impact mental health.

**3.4.2: Serotonergic System.**—The serotonergic system originates in the raphe nuclei and, like the noradrenergic system, projects diffusely to most cortical regions. This system acts on a diverse set of receptor subtypes, enabling precise neuromodulation that depends on the target neuronal population. In psychiatric practice, the serotonergic system has long been a target of pharmacotherapies that aim to improve mood (e.g. selective serotonin reuptake inhibitors). Also acting upon the serotonergic system are psychedelic agents—including psilocybin, lysergic acid diethylamide (LSD), and dimethyltryptamine—that can have profound, short-term effects on subjective experience as well as potentially longer-lasting therapeutic effects for a variety of mental illnesses.<sup>182</sup> There has been a recent resurgence of scientific and clinical interest in psychedelics. Because psychedelics impact

spontaneous thought in an acute and unique manner, we focus here on insights from these agents as a lens into the role of the serotonergic system.

Although psychedelic agents do not act exclusively on the serotonergic system, their agonist action upon the serotonin receptor subclass 5HT<sub>2A</sub> has a key role in generating experiential effects.<sup>183</sup> The psychedelic experience, which may last between ~30 minutes and 12 hours, involves vivid alterations in perception and feelings that take on many variations but often involve hyperassociative and discontinuous thought, visual imagery/hallucination, intense emotion, and an altered or diminished sense of self (“ego dissolution”).<sup>184,185</sup> Given these features, the psychedelic state was recently incorporated into the DFT as a form of spontaneous thought with lower deliberate and automatic constraints than mind-wandering, creative thinking, and dreaming.<sup>c</sup> This characterization situates the psychedelic state as the most unconstrained and least ruminative known version of thought; thus, understanding the role of the serotonergic system in this state provides a potential unique window into neural basis of spontaneous thought.

How psychedelic action at the 5HT<sub>2A</sub> receptor leads to subjective effects remains unclear and an active area of investigation.<sup>186</sup> Recently, resting state neuroimaging has been used to examine the acute effects of psilocybin and LSD. Though multiple neural metrics have been examined and are difficult to compare across studies, one consistent finding is that LSD reduces functional connectivity between the thalamus and sensory cortical regions,<sup>187,188</sup> a phenomenon that may be associated with perceptual decoupling.<sup>153</sup> Psilocybin and LSD have also been shown to decrease functional connectivity within the DMN,<sup>183,185,189</sup> which may be linked to subjective experiences of creative insights.<sup>190</sup> Given the role of the DMN in self-referential thought, this effect has also been attributed to ego dissolution. However, decreased functional connectivity within the salience network<sup>191</sup> and increased coupling between regions rich in 5HT<sub>2A</sub> receptors<sup>192</sup> have also been associated with individual differences in psilocybin-induced ego dissolution. Critically, these resting state studies did not examine intra-individual variability in spontaneous experiences within the psychedelic state. Future studies involving psychedelics, neuroimaging, and experience-sampling may shed light on the mechanistic role of the serotonergic system in functions such as enhancing the spontaneity of thought, reducing rumination, and exerting long-term benefits to mental health.

#### 4.0: Conclusions and Future Directions

In this review, we have highlighted some of the diverse approaches and findings emerging from the quickly growing body of research on the neuroscience of spontaneous and off-task thought. We explored novel findings that build on the well-studied role of the DMN and large-scale network dynamics. We further discussed the potential roles of less-studied phenomena: hippocampal SWRs, memory replay, and neuromodulatory activity in noradrenergic and serotonergic systems. We surveyed how this knowledge may advance our understanding of mental health and lead to clinical applications. In this final section, we spotlight a few methodological directions that may clarify mechanisms, lead to reliable biomarkers, and facilitate development of personalized therapies toward the goals of better understanding and improving mental health.

Studying spontaneous and off-task thoughts and their neural mechanisms presents some unique challenges. Most standard experimental paradigms rely on external perceptual or task-based manipulations that cannot typically be used to elicit and precisely measure these thoughts (though see<sup>82–84</sup> for examples of how such manipulations can indirectly influence involuntary thoughts). The introduction of experience-sampling as a novel technique has led to important advances, and additional new approaches could yield further improvements in our ability to study thought dynamics. Recently, paradigms involving free-flowing descriptions of thoughts have been applied to characterize the dynamic trajectories of conceptual associations.<sup>136,193–195</sup> Moreover, the way that thoughts change over time can be altered in conditions affecting mental health. Semantic network analyses revealed that individuals high in rumination frequently became ‘stuck’ on negative, self-referential topics.<sup>136</sup> The recent integration of descriptive experience-sampling,<sup>196</sup> free association,<sup>80</sup> and think aloud paradigms<sup>81</sup> with fMRI highlight the potential of these approaches to offer further insights into altered neural and thought dynamics affecting mental health.

Innovations are also needed to improve efficiency of discovering brain-experience relationships. Online experience-sampling neuroimaging studies treat experience and brain activity, respectively, as independent and dependent variables. In an alternative, *brain-triggered experience-sampling* paradigm, neural activity is analyzed in real time, and experience-sampling moments are initiated when a pre-specified event of interest (e.g. SWR, DMN activation) occurs. Compared to the standard approach of sampling experience at random intervals, this approach could enhance efficiency because sampling occurs selectively when a pre-hypothesized phenomenological experience is arising.<sup>69</sup> In one application, real-time analysis detected a pre-specified EEG pattern that was predictive of dream contents.<sup>197</sup> It was also suggested that real-time analyses could shed light on whether spontaneous memory reactivations are consciously experienced.<sup>198</sup> In clinical applications employing experience-sampling to identify neuromodulation targets, brain-triggered experience-sampling could reduce the time that a patient needs to be monitored (10 days of iEEG recording in a recent case report<sup>93</sup>).

Finally, it is critical to note that research on the neural basis of spontaneous and off-task thought has almost exclusively focused on groups of individuals. Brain mechanisms giving rise to self-labelled experiences may vary across and even within an individual across contexts. Thus, personally-derived neural markers may allow researchers to test, rather than assume, generalizability across individuals and instances. This issue is critical in the context of mental illness, where thought phenomenology can deviate substantially from the typical pattern. Recent findings illustrate that idiographic, rather than group-level, fMRI predictive models are needed to predict affective valence when spontaneous thoughts have high self-relevance. Moreover, dense, individual-level, online experience-sampling with fMRI recently revealed individual-specific neural patterns predictive of spontaneous sensory imagery.<sup>87</sup> Building on these findings, future studies may derive personalized biomarkers of spontaneous and off-task thought that could aid in guiding brain-based therapies (e.g. neurostimulation, neurofeedback).

These future directions highlight just a few ways in which research on spontaneous and off-task thought may be leveraged to guide assessments and treatments for mental health.

These directions also highlight that the field is still in its infancy, and as such there remains enormous potential for research and clinical practice.

## Acknowledgements

This work was supported by the National Institute of Mental Health of the National Institutes of Health under award numbers R21MH127384 (to AK), R21MH129630 (to AK and SWG) and R01MH125414 (JAH). JWYK was supported by the Natural Sciences and Engineering Research Council Discovery Grant.

## Data Availability Statement

The dataset that was generated for Figure 1 is available at <https://github.com/DynamicBrainMind/NatMentHealth2023>.

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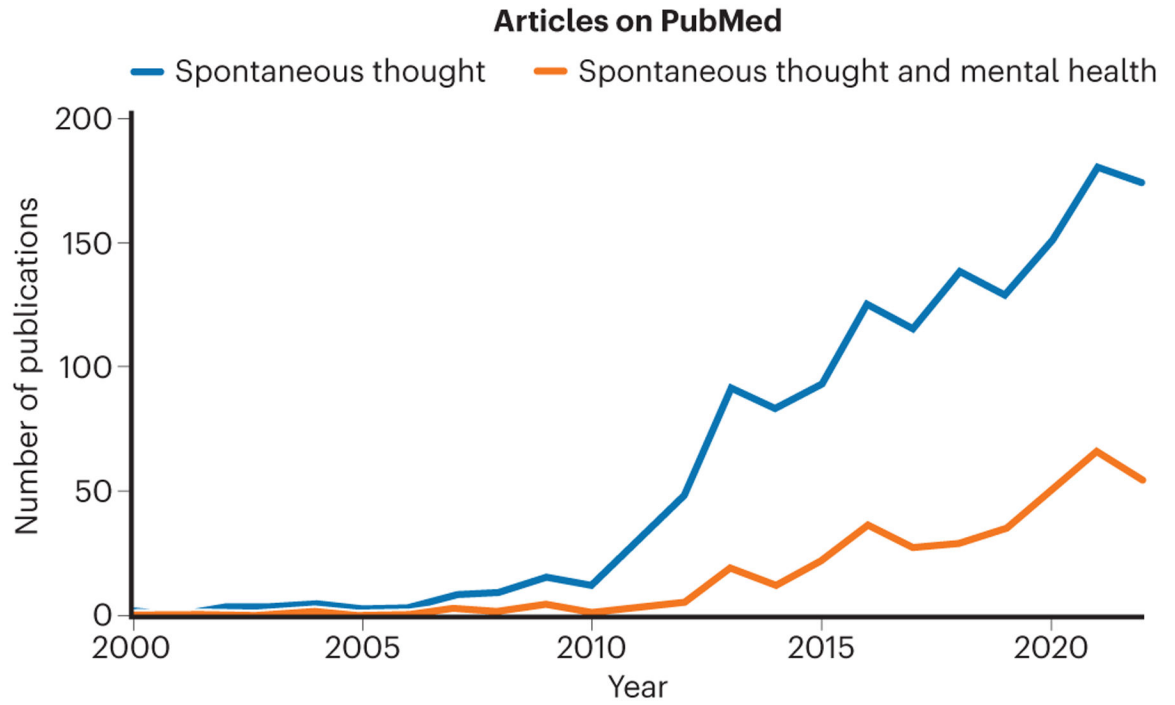
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**Box 1:****Neural basis of mind blanking and implications for mental health.**

When people are disengaged from the immediate environment, they are usually engaged in their own thoughts, but there are also moments of “mind blanking” when no mental contents can be recalled. Though less studied with respect to mental health than mind-wandering and spontaneous thought, studies suggest that mind blanking is elevated in ADHD<sup>199</sup> and impairs cognitive performance in depression.<sup>200</sup> The neural correlates of mind blanking have recently been explored. When people were instructed to intentionally engage in mind blanking, deactivation of the DMN was found (i.e., opposite to the typical pattern for off-task thought).<sup>201</sup> Online experience-sampling with EEG and fMRI have further confirmed that mind blanking has distinct neural correlates compared to mind-wandering or off-task thought.<sup>89,90</sup> These findings should motivate inclusion of mind blanking response options in experience-sampling protocols in mental health contexts. Notably, protocols should carefully distinguish between absence of thought versus absence of all conscious experience, as these distinct features may have been conflated in prior works.<sup>202</sup>

**Box 2:****Intracranial neuromodulation of the DMN and spontaneous thought**

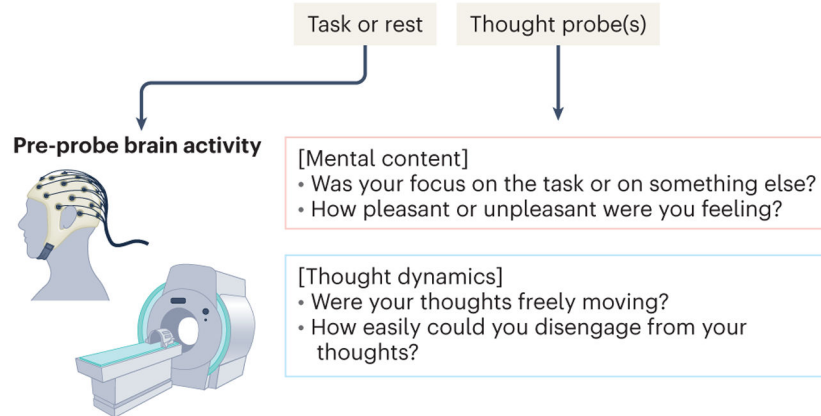
Intracranial electrical stimulation<sup>203</sup> is a neuromodulation technique that offers more focality compared to tDCS and is similar to deep brain stimulation approaches.<sup>204</sup> A short pulse of high-frequency (50–100 Hz) intracranial stimulation, often applied for the clinical purpose of functional mapping in neurosurgical patients, can immediately change subjective experience or behavior. The change may involve a wide range of perceptual, motor, cognitive, and affective effects, including spontaneous vivid experiences of past memories.<sup>205</sup> Recently, intracranial stimulation effects have been functionally mapped to large-scale intrinsic networks. Interestingly, the elicitation rate of changes in subjective experience or behavior was lower in the DMN (~20%) than in any other intrinsic network.<sup>206</sup> This finding may seem surprising, but it is notable that the context of intracranial stimulation is typically comparable to a resting state, when internally-guided cognition may already be high, thus limiting the potential to elicit effects. When DMN stimulation effects are found, they often involve vivid and highly specific phenomenological experiences. In a striking recent example, stimulation of a DMN region within posteromedial cortex caused a patient to report a sense of observing their own thoughts, an experience comparable to self-dissociation in neuropsychiatric illness.<sup>207</sup> Beyond immediate experiential effects, a recent study showed that intracranial DMN stimulation reduced the capacity to generate creative thoughts.<sup>208</sup> Such findings provide preliminary insights into the potential short- and long-term impacts that invasive, deep brain stimulation therapies (e.g. for treatment-resistant psychiatric illness) may have on spontaneous thought patterns and their associated mental health outcomes.



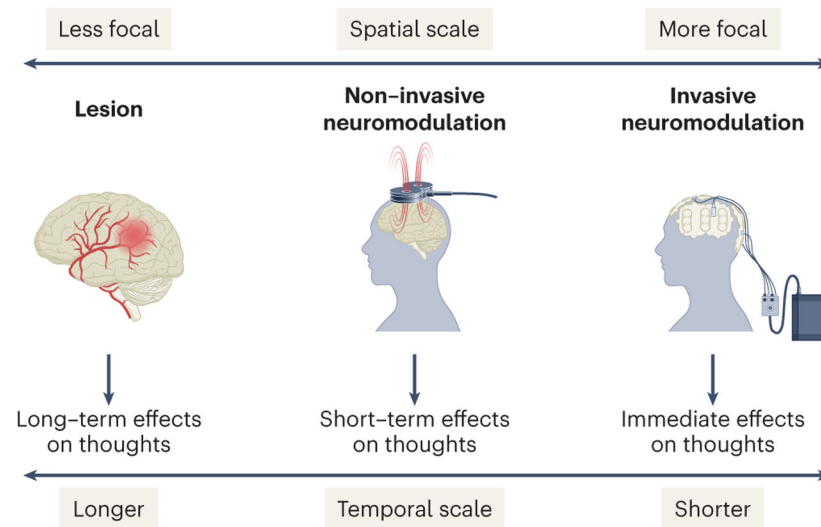
**Figure 1: Number of publications on spontaneous thought and mental health over the last two decades.**

PubMed search query for Spontaneous Thought: (“spontaneous thought” OR “mind wandering” OR “task-unrelated thought” OR “stimulus-independent thought” OR “freely moving thought” OR “self-generated thought”). PubMed search query for Mental Health: (“mental health” OR “positive affect” OR “negative affect” OR “emotion” OR “mood” OR “sadness” OR “happiness” OR “distress” OR “emotional state” OR “depression” OR “anxiety” OR “ADHD” OR “schizophrenia”).

### a Neural correlates of spontaneous and off-task thought

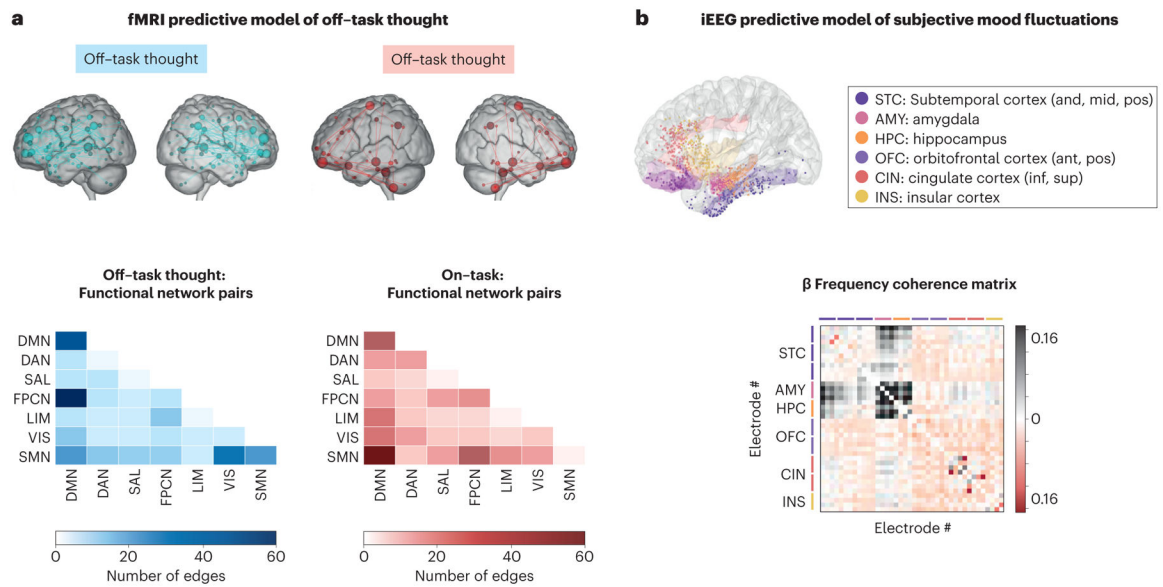


### b Causal brain relationships with spontaneous and off-task thought



**Figure 2: Linking spontaneous thought and off-task thought phenomenology to neural measures with experience sampling.**

(a) Schematic example of the use of online experience sampling to examine neural correlates and predictors of spontaneous thought and off-task thought. (b) Distinct techniques for examining causal brain relationships with spontaneous thought that provide insights at multiple spatial and temporal scales.



**Figure 3: Large-scale brain network predictive models of spontaneous fluctuations in experience sampling ratings.**

(a) (Top) Connectivity features of an fMRI-based functional network model that is predictive of intra-subject off-task thought and on-task attention. (Bottom) The number of edges (pairs of regions) between multiple intrinsic networks that contribute to the model (reproduced with modification from<sup>92</sup>). (b) (Top) Implanted electrode locations and neuroanatomical regions involved in an iEEG-based functional network model that is predictive of subjective mood fluctuations. (Bottom) Connectivity features (beta-frequency coherence matrix) within a subnetwork involving strong amygdala-hippocampus coupling that is predictive of intra-subject mood ratings (reproduced with modification from<sup>157</sup>).