6

How Can Intrusive Thinking Be Measured *in Vivo* and Studied in the Context of Brain Mechanisms?

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Abstract

This chapter reviews different methods that can be used to examine and understand intrusive thought, beginning with behavioral methods. Common among these are self-report and diary measures of the experience, duration, and intensity of intrusive thoughts as well as self-reports of the difficulty in controlling such thoughts. These questionnaires, for the most part, have been tailored to the types of intrusions specific to a given psychiatric syndrome (e.g., flashbacks in posttraumatic stress disorder, thoughts of contamination in obsessive-compulsive disorder), which highlights the need to create a transdiagnostic self-report measure. Another common behavioral paradigm is to investigate intrusions after individuals are exposed to traumatic material, through a symptom provocation paradigm in individuals who have experienced trauma or an analog trauma (e.g., viewing a disturbing movie). Other behavioral paradigms, such as the Think/No-Think paradigm, specifically examine mechanisms of memory retrieval and suppression often thought to be disrupted in posttraumatic stress disorder.

Thereafter, it addresses paradigms for examining the neural mechanisms associated with intrusive thoughts. These approaches primarily couple behavioral techniques or paradigms with functional magnetic resonance imaging or electroencephalographic (EEG/ERP) methods. In addition to providing insights into the neural mechanisms that may underlie intrusive thoughts, these approaches may provide additional information regarding cognitive mechanisms, such as discerning whether memories are being suppressed or replaced. Discussion concludes by examining emerging approaches to the study of intrusive thinking. A main challenge is to find a method to verify that intrusive thoughts have indeed occurred. New paradigms that combine neuroimaging techniques with computational methods drawn from machine learning offer promise, as do techniques which allow intrusive thought processes to be examined as they occur during more naturalistic processing (e.g., watching a film).

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Introduction

The question of how one can measure intrusive thoughts (i.e., thoughts that "pop up" into consciousness in a seemingly uncontrolled manner) is difficult to address, especially in a laboratory setting. It can be challenging to capture and to verify their occurrence by measures other than self-report. Moreover, traditional experimental measures used to explore mental processes (e.g., those that determine reaction time and/or errors) are not applicable. Despite these challenges, a number of approaches, both behavioral and biological, have been employed. In this chapter, I review those methods, discuss some new approaches, and suggest ways that the knowledge from other related arenas of inquiry might be used to inform potential novel approaches to this difficult question.

The need for scientists to have methodological approaches that will enable an understanding of the basic cognitive and neural processes underlying intrusive thinking is apparent when one considers that intrusive thoughts are ubiquitous across a large number of psychiatric disorders. Although intrusive thoughts are generally associated with posttraumatic stress disorder (PTSD) and are captured by the intrusions cluster of diagnostic criteria (American Psychiatric Association 2013), they occur in many psychiatric disorders: depression is characterized by intrusive negative thoughts and memory (Newby and Moulds 2011), anxious apprehension (i.e., worry) by repetitive intrusive concerns about future negative events (e.g., Fox et al. 2015), obsessive-compulsive disorder (OCD) by thoughts of contamination and/or harm to self or others (Bouvard et al. 2017), and schizophrenia by intrusions of semantic and sensory information (Elua et al. 2012). This commonality raises the possibility that intrusive thought across disorders may have a common underlying neural circuitry (Kalivas and Kalivas 2016). What tends to vary somewhat across disorders is the content of those intrusive thoughts (e.g., negative attributions of the self in depression vs. concerns about potential dangerous future outcomes in anxiety). In addition, intrusive thoughts in disorders such as PTSD are generally thought to be more sensorially based and of shorter duration, compared to ruminative thoughts associated with depression and worry, which tend to be more cognitive in nature, of longer duration, and recurrent (Speckens et al. 2007). Nonetheless, what all these types of intrusive thoughts share is that they appear to impinge upon consciousness in a somewhat uncontrolled manner. Hence, my focus here is on methods for examining the complete range of types of intrusive thoughts. To date, however, the majority of the work using methods to examine intrusive thought has focused mainly on individuals with PTSD, OCD, and/or nonclinical populations. Thus, there is a much larger range of individuals with psychiatric disorders to whom such techniques might be applied.

Here, I will consider a number of different ways in which intrusive thoughts have been examined. I begin with a discussion of behavioral paradigms, from

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questionnaires to experimental procedures, that examine how the frequency, nature, and control over intrusive thoughts can be measured. Thereafter, I consider how different brain-based techniques can be used to shed light on the underlying nature and neural bases of intrusive thought and conclude with a discussion of how intrusive thoughts might be verified in ways other than by self-report, specifically looking at emerging techniques that examine or track their representational content.

Behavioral Methods: Measuring the Frequency, Nature, and Control over Intrusive Thoughts

Self-Report and Questionnaires

Foundational work to understand intrusive thought comes from behavioral approaches that rely on self-report, of which there are two main types: The first tries to assess the content and nature of intrusive thoughts, while the second assesses the ability to control or manage thoughts, both those that are intrusive and other thoughts more generally. In addition, there is a third type of self-report that is a hybrid, assessing both the nature and controllability of thoughts. Questionnaires that examine thought content have generally been designed for specific psychiatric diagnoses. A number of these measures and their characteristics are outlined in Table 6.1.

For the most part, these measures appear to have good reliability and validity, so that scores on these scales can be used (or combined) in studies that take an individual differences approach in examining how scores on these measures vary with other metrics of interest. For example, scores on these measures can serve as covariates in brain-based approaches to determine whether the degree of brain activation in particular regions is associated with increasing scores on such measures. This approach is discussed in more detail below (see section, Examining the Neural Systems Related to Intrusive Thoughts).

Importantly, research using these measures indicates that most individuals experience intrusions and that intrusive thoughts occur across a continuum from nonclinical to clinical populations; for example, a similar factor structure is observed in both groups (e.g., Reynolds and Wells 1999). Factors that may distinguish clinical and nonclinical populations include the frequency, importance, and difficulty in managing those intrusions (e.g., Clark et al. 2014a). These findings are notable as they suggest that new and emerging methods used to examine intrusive thoughts in nonclinical populations could be fruitfully employed within psychiatric populations. For example, research with nonclinical populations has attempted to isolate the basic dimensions that underlie repetitive (although not necessarily intrusive) thoughts by asking individuals to rate the nature of their most common thoughts on a number of dimensions,

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Table 6.1 Examples of typical self-report measures of intrusive thoughts and the ability to control thought. Typical self-report measures of intrusive thoughts and the ability to control thought. Example items from these measures are shown in italics.

Name	Construct Measured with Sample Question	Reference
Measures of intrusive thought content:		
OII	Thoughts related to contamination, harm to self and others, and taboo behavior, including frequency and believability: rate frequency of "exposing myself" from 0 "never" to 4 "always"	Purdon and Clark (1993)
RRS-SF	Continuous thoughts typical of depression separate from depressive symptoms, subscales: Brooding—comparison between one's current state and some unachieved standard: *What am I doing to deserve this?* Reflection—repetitive thoughts about problem-solving that might ameliorate negative affect: *Analyze recent events to understand why you are depressed*	Treynor et al. (2003)
Measures of the ability to control thoughts:		
WBSI	Difficulty in controlling thoughts, subscales: Intrusions—the degree of intrusion experiences: *I have thoughts that I cannot stop.* Suppression—tendency/ability to rely on thought suppression as a strategy: *There are things I try not to think about.*	Wegner and Zanakos (1994); 2 factor structure, Schmidt et al. (2009)
PSWQ	The degree to which a person worries: *Once I start worrying, I cannot stop*.	Meyer et al. (1990)
TCQ	Assesses strategies used to control thoughts: *I think about something else*.	Wells and Davies (1994)
IES-R	Measures intrusions after stressful or traumatic events: *I thought about it when I didn't mean to* or *pictures about it popped into my mind.*	Weiss (1997)

including self-relevance, frequency, importance, orientation with regard to goals, orientation with regard to social factors, and level of detail. Using a hierarchical clustering analysis, four major dimensions of thought content emerged: (a) level of construal (degree of temporal and perceptual specificity), (b) degree of personal significance, (c) temporal orientation (future oriented vs. past oriented), and (d) valence (positive, negative). Of relevance to the current discussion, scores on these dimensions are associated with characteristics related to mental health. For instance, higher levels of thoughts characterized by negative valence and high levels of personal significance are associated with higher levels of depression (Andrews-Hanna et al. 2013).

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Table 6.1 (continued)

Name	Construct Measured with Sample Question	Reference
Hybrid measures of both content and control:		
ROII	Includes additional measures of the degree and manner to which obsessive thought can be controlled: rate 0 (never) to 5 (always), e.g., *Say stop to myself*	Purdon and Clark (1994)
ITQ	Frequency, degree of distress, and degree of difficulty controlling intrusive thought: *How disturbing are these thoughts for you? How difficult is it for you to get rid of these disturbing thoughts when they occur?*	Dougall et al. (1999)
EIS	Frequency, unpredictability, unwantedness, interference, and distress caused by the intrusive thoughts after analog trauma: *How often have you found yourself thinking to any degree about the rape scene since seeing the film?*	Salters-Pedneault et al. (2009)
IITIS	Examines thought content and strategies for control via a semi-structured interview, e.g., identify unwanted religious or immoral intrusions	RCIF (2007)

Abbreviations:

ESI: Experience of Intrusions Scale	PSWQ: Penn State Worry Questionnaire
IES-R: Impact of Event Scale-Revised, intrusion subscale	ROII: Revised Obsessive Intrusions Inventory
IITIS: International Intrusive Thought Interview Schedule	RRS-SF: Ruminative Response Scale, short-form
ITQ: Intrusive Thoughts Questionnaire	TCQ: Thought Control Questionnaire
OII: Obsessive Intrusions Inventory	WBSI: White Bear Suppression Inventory

Advantages, Limitations, and Potential Extensions

These types of self-report measures have advantages: they are typically short, easily administered, generally well normed, can be used with both clinical and nonclinical populations, and scores derived from them can be used as covariates in adjunct analyses. In terms of limitations, they require metacognitive abilities related to self-awareness and self-evaluation on the part of the respondent, which may be compromised in individuals with more severe psychiatric disorders. Perhaps most glaringly, however, is the fact that they can be narrow in scope, as most were designed to address a specific psychiatric disorder. As such, they tend to examine the types of processes (e.g., punctate vs. continuous) and specific topics of intrusive thoughts that characterize a given psychiatric disorder.

Hence, a questionnaire on intrusive thoughts and their control is needed that could be used more generally across individuals with a variety of clinical disorders, as well as with individuals who do not meet clinical criteria. There

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are numerous ways to design such a questionnaire, and it might be useful to include the following capabilities:

1. Analyze thought content via the assessment of underlying common factors across psychiatric and nonpsychiatric populations, such as their valence and temporal orientation.
2. Assess the degree to which an individual has difficulty in controlling thoughts as well as those individual differences that protect against intrusive thoughts (e.g., mindfulness) and the mechanisms by which they act (e.g., Emerson et al. 2017).
3. Distinguish intrusive thoughts from mind wandering and task-unrelated thoughts (e.g., Maillet and Schacter 2016).
4. Contain optional subscales that could assess intrusive thoughts specific to a given disorder (e.g., thoughts of contamination in individuals with OCD) as well as differentiate those from thoughts that occur in other psychiatric disorders.

Not only would the creation of such a questionnaire enable a finer assessment of the nature of intrusive thoughts and their control, it might also enable aspects of intrusive thoughts to be linked to specific symptom clusters across psychiatric disorders (e.g., fear).

Next, we take a look at other behavioral and experimental methods for examining intrusive thoughts. They are divided roughly into two types: the first engenders intrusive thoughts whereas the second examines how thoughts (or memory retrieval) can be controlled.

Engendering Intrusive Thoughts

To examine intrusive thoughts in an experimental setting, one approach is to actually engender them. The purpose of this method, often referred to as the *symptom provocation paradigm*, is to provoke intrusive thoughts, often of a traumatic nature (e.g., Brewin and Saunders 2001). Generally, individuals identify specific traumatic events in their lives or categories of stimuli that engender intrusions in a pretest session. Then, within an experimental session, specific pictures or stimuli that are traumatic are shown or individuals are exposed to a category of stimuli associated with trauma, such as combat noise or pictures for veterans (e.g., Daniels and Vermetten 2016).

A related approach, often referred to as *analog trauma*, is designed to induce and engender trauma-related responses (e.g., intrusive memories). This procedure typically involves having individuals watch a film that contains graphic depictions of traumatic events, such as physical or sexual violence (for a review, see Holmes and Bourne 2008). In an extension of this approach, virtual reality can be used to induce an analog trauma (Dibbets 2019). Across both symptom provocation and analog trauma, the degree and nature of thought

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intrusions can then be examined within the context of the laboratory or via a diary of intrusions for some specified time (e.g., one week) after exposure.

As discussed by Visser et al. (2018), a variety of points in memory processing could be disrupted by or associated with intrusive thoughts: from the original attention to and encoding of information to the access and retrieval of memories. Procedures designed to engender intrusive thoughts can be combined (a) to analyze the effects of other variables or manipulations at distinct time points (before, during, or after exposure) and (b) to examine how different processes (e.g., attention/focus, encoding, and recall) influence intrusions. Manipulations implemented before exposure include having individuals recall memories that induce high levels of self-efficacy (Krans et al. 2018) to put the focus on themselves, or playing a distracting video game to place the focus on something else (James et al. 2016b). Manipulations implemented during viewing of the material include varying the cognitive load during the task or instructions that lead to hyperarousal via hyperventilation (Nixon et al. 2007). Manipulations after exposure have included varying instructions on how to deal with the intrusions, such as rumination ("How can I drive again without thinking about what could happen?"), integration so as to distinguish the video from the person's own nontraumatic experiences ("Think about your own driving experiences"), or distraction ("Try to recall as many African countries as you can think of") (e.g., Zetsche et al. 2009; Horsch et al. 2017).

Advantages, Limitations, and Potential Extensions

The advantage of the symptom provocation and analog trauma methods is that they can be implemented relatively easily. They also have face validity, especially for syndromes such as PTSD, which is generally characterized by intrusions linked to a specific event or trauma. These methods can also be used with provocation for particular classes of items that might engender intrusive thoughts, such as those associated with OCD. Although individuals are typically asked to report intrusions, there are other possible means of assessing intrusions. For example, virtual reality approaches have the ability to provide additional information: upon reimmersion into the environment, one can examine the degree to which an individual avoids that portion of the virtual reality space associated with the traumatic scene (e.g., Dibbets 2019). With regard to still photos, one could redisplay portions of a traumatic scene (e.g., a car next to an overpass with a concrete barrier) without the specifically traumatic context (e.g., a bloody person lying in the road by the car) and determine the nature and duration of eye movements to the location of the trauma content. Relatedly, eye movements might be employed to determine when individuals are likely to be more inwardly focused, as has been used for lapses of attention (or mind wandering) during reading (e.g., Reichle et al. 2010). Finally, diary methods for recording intrusions after exposure could be expanded to use digital queries at random times via mobile apps and other smartphone technologies.

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The vast majority of studies that examine intrusive thoughts do so from the perspective of long-term memory formation and retrieval, which is particularly appropriate when intrusive thought is driven by a specific event or circumstance, such as occurs in PTSD. Far less work has focused, however, on mechanisms related to intrusive thoughts, especially those not linked to a specific event, in terms of how they get "stuck" in working memory and current consciousness. Symptom provocation and analog trauma are not well suited to examining the nature of recurrent, ruminative, and cognitively based intrusive patterns of thinking, which are typical in depression or worry (anxious apprehension) but cannot be specifically linked to a particular point in time nor to a particular set of provoking stimuli. For example, depressive intrusive thoughts often focus on how one could "solve" the issues that lead to distress and negative affect. From thinking about social interactions with others to self-reflection on actions taken to an analysis of one's internal mood states, the topical range tends to be larger than, for example, thoughts of contamination in OCD.

Engaging and Examining Thought Suppression Mechanisms

Another method of examining intrusive thoughts is to determine the effects of formally trying to suppress an intrusive thought. In a classic version of this task, individuals are given a period of time (e.g., five minutes) where they are allowed to think of anything that comes to mind (often referred to as the free-thinking condition). Afterward, they are placed in either an expression condition, in which participants are told that they should think about a specific item (e.g., a white bear) for a given period of time (e.g., five minutes), or in a suppression condition, in which they are told to suppress thinking about that item (i.e., the white bear) for an equal amount of time. The participant then indicates by some means, such as ringing a bell or pressing a button, whenever the item comes to mind (Wegner et al. 1987). This results in a paradoxical effect: trying to suppress a thought at first leads to greater subsequent expression than if the idea had initially been expressed and then later suppressed (Wenzlaff and Wegner 2000). Meta-analyses find a small to medium effect of the rebound of thoughts after suppression in both clinical and nonclinical groups (Abramowitz et al. 2001).

From this initial approach, several variations have been employed. In one extension, individuals are asked to identify thoughts, images, or impulses that pop into their mind unexpectedly and in an intrusive manner. The number of intrusions during this free-thinking condition can be compared to a suppression condition as well as other potential manipulations, such as distraction involving thinking about something else (e.g., a past or future weekend with friends) or accepting a thought (e.g., think about the intrusive thoughts coming out of your ears on little signs held by soldiers, who walk them in front and then away from you) (e.g., Najmi et al. 2009).

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Such measures have been used to examine individual differences in clinical symptoms, cognitive abilities, or age. Researchers have examined, for example, whether higher or lower levels of executive function and cognitive control influence the ability to suppress intrusive thoughts successfully in specific populations, such as those with PTSD (Bomyea and Lang 2016), or whether the suppression versus the expression of thoughts is linked to working memory ability (Brewin and Smart 2005). Using a different approach, others have examined whether intrusions vary according to the content (more specific to certain life periods) and age of the participants. In younger individuals, for example, career success or failure might constitute the focus, whereas for older individuals, memory loss (in particular, fear of forgetting friends and family) might be more prevalent (Beadel et al. 2013).

Another experimental method that has been used widely in the laboratory to examine control over thoughts, specifically memory retrieval, is the Think/No-Think paradigm (Anderson and Green 2001). In this classic paradigm, individuals are taught associations between a cue word (e.g., "ordeal") and a target word (e.g., "roach") to a given level of accuracy (e.g., 95%) that will ensure a solid memory trace. In the experimental phase, some cues are presented so that the participant must think about the associated target (Think condition), while other cues are presented so that the participant should *not* think about or allow the associated target into consciousness. Each cue is shown multiple times so that there are numerous opportunities to exert cognitive control over the memory of the target. Then in the test phase, the individual is shown cues for each of the initial pairs, and memory for the associated target is assessed. Memory is typically increased for Think trials and decreased for No-Think trials relative to a baseline of items whose cues were not shown during the experimental phase (which provides an index of forgetting since initial training). Hence, this paradigm is well suited to examine control over retrieval of information from long-term memory, which is highly relevant to disorders in which there is intrusive memory retrieval. Although initial studies used verbal stimuli, similar effects have been observed for visual and emotional stimuli, such as face–scene pairs (Depue et al. 2006). This may be more suited for studying populations where intrusive thoughts take the form of images (e.g., object–scene pairs), such as in PTSD (Catarino et al. 2015).

Advantages, Limitations, and Potential Extensions

These approaches provide methods for examining control over intrusive thoughts as well as the mechanisms (e.g., suppression, distraction) by which such control may be exerted. However, they rely on participant self-report of the occurrence of those intrusive thoughts and a certain amount of metacognitive awareness (i.e., internal monitoring of when those thoughts have occurred). Although not specific to intrusive thoughts, the Think/No-Think paradigm provides a robust and tractable experimental paradigm to examine the control over

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thoughts, especially with regard to memory retrieval. In clinical populations, its use is limited due to the length of the procedure (e.g., 30 minutes to 1 hour) and requirement that individuals learn and retain the pairs. Participants must be able to perform the initial learning and sustain an adequate level of attention and motivation to perform the task. As with the symptom provocation and analog trauma approaches, these methods have clearer linkages to disorders like PTSD and OCD than to the recurrent intrusive thoughts that are characteristic of depression and anxiety.

Neural Systems Related to Intrusive Thoughts

A substantial body of research has focused on examining neural processes that are associated with intrusive thoughts. In general, the main techniques used are magnetic resonance imaging (MRI), typically used to localize brain systems involved with intrusive thoughts, or electroencephalography (EEG), including event-related potentials (ERPs) which provide information about the timing of processes associated with intrusive thoughts. In general, these methods tend to be used in combination with one of the behavioral approaches discussed above.

The utility of such approaches is that they can provide insight into the mechanisms that may be generating intrusive thoughts. For example, although one must be cautious in making reverse inferences from patterns of brain activation (Poldrack 2011), evidence of prefrontal activity when attempting to limit the intrusiveness of thoughts is suggestive of an active control process, whereas evidence of activity in subcortical regions, such as the basal ganglia, would be suggestive of a more automatized process. Likewise, alterations in early ERP components (e.g., P1, N1) are more suggestive of attempts at control over sensory aspects of an intrusive thought, where alterations in later ERPs (e.g., P3 and N4) would be more suggestive of control over information in working memory or of a semantic nature, respectively.

Brain Processes Associated with Intrusive Thoughts

Measures Used to Engender Intrusive Thoughts

The symptom provocation paradigm, especially as it relates to individuals with PTSD, has been migrated into a neuroimaging environment. As with all functional MRI (fMRI) studies, the condition of interest must be contrasted with a baseline of some sort that does not engage the behavioral construct of interest. Often in these studies, brain activation in a symptom provocation condition is compared to baseline condition; this may involve processing information from a nontraumatic memory, emotionally neutral pictures (e.g., civilian or noncombat scenes), or non-emotional information (e.g., white noise or rest). Meta-analyses across such studies of individuals with PTSD (e.g., Sartory et al. 2013) have found that these paradigms reliably isolate a set of brain regions

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that differentially activate during the symptom provocation as compared to comparison conditions. This set of regions includes portions of the default mode network, considered to be involved in internal thought, self-referential processing, and autobiographical memory (Andrews-Hanna et al. 2014), as well as areas that process the emotional significance and valence of information, such as pregenual portions of the anterior cingulate and the amygdala. The involvement of these regions in autobiographical memory and emotion processing provide a piece of converging evidence, not provided by behavioral paradigms alone, that the symptom provocation technique is effective at inducing reexperiencing.

With regard to EEG/ERP methods, some studies (Roh et al. 2017) have examined differences in specific ERP components (e.g., error-related negativity) under symptom provocation as compared to other conditions in individuals with disorders characterized by intrusive thoughts (e.g., in individuals with OCD). Although relatively rare, other studies have examined EEG metrics, such as the hemispheric asymmetry of frontal alpha rhythms (as an index of approach and avoidance behaviors), to symptom provocation (for a review, see Meyer et al. 2015).

Measures Used to Examine the Experience of and Control over Intrusive Thoughts

One can also utilize neuroimaging techniques, in conjunction with behavioral methods that index when an intrusive thought occurs or when control systems are engaged, to limit or otherwise attempt to suppress such thoughts. One approach is to measure brain activation during the time periods in which intrusions occur and compare that to activation during time periods without intrusions. In some paradigms, the participant notes in real time when the intrusion occurs by pressing a button. Brain activation during the intrusive thought is then compared to some baseline, such as the time period right afterward when re-suppression occurs (e.g., Carew et al. 2013). Similarly, in the Think/No-Think task, one can examine neural activation on unsuccessful No-Think trials in which the item to be suppressed intrudes upon consciousness. This activation can be compared to Think trials, in which controlled (rather than intruded) retrieval has occurred (Hellerstedt et al. 2016), or to No-Think trials, in which the item is successfully suppressed (Levy and Anderson 2012). Examining brain activation during intrusions has been done with fMRI, although the fine temporal resolution of EEG/ERPs may be better suited. For example, EEG/ERPs can be used to provide a putative index of how long the intrusion remains in working memory (Hellerstedt et al. 2016) or to identify the onset of the process that is engaged to keep it from coming into working memory (Castiglione et al. 2019).

While some studies look at real-time intrusions, which provide a "state" perspective, other approaches examine this issue from a "trait" perspective.

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Here, individuals are characterized as to the degree to which intrusions are experienced during their daily lives or over longer time periods. For instance, using daily diary entries, Kuhn et al. (2013) examined the average degree to which intrusive thoughts are experienced by an individual over a six-month period and then linked the intrusion rate to patterns of brain activation at rest.

Rather than focusing on intrusions in particular, another approach compares brain activation assessed by fMRI across various conditions, such as free thought, suppression of a given thought, or suppression of all thoughts (e.g., Wyland et al. 2003). Another way is to examine mechanisms that are involved in suppressing thoughts versus replacing thought (e.g., Benoit and Anderson 2012). As detailed below for aspects of working memory, mechanisms of item replacement, specific item suppression, and suppression of all thoughts appear to have partially overlapping but distinct neural mechanisms (Banich et al. 2015). These findings support separate consideration of these potential mechanisms of controlling intrusions.

Another issue that can be fruitfully examined using neural investigations is the degree to which the processes involved in suppression of thoughts are similar to or distinct from other categories of suppression. While a backward inference from brain activation to cognitive processes must be performed with caution, neuroimaging studies nonetheless can provide insights into the specificity of control over memory versus other processes. For example, in the same individuals, Depue et al. (2016) examined the degree to which activation during a memory suppression task (measured by the Think/No-Think task) engendered similar or separate neural mechanisms than either the suppression of emotion or the suppression of motoric responses (all compared to a domain-appropriate nonsuppression baseline). While all three tasks produced activation in right dorsolateral prefrontal cortex, it was the connectivity of this region to domain-specific processing regions (e.g., the amygdala in the case of emotion regulation) that differentiated these three types of suppression. Other studies suggest somewhat overlapping mechanisms of memory and emotional suppression (Gagnepain et al. 2017) as well as memory and motoric suppression (Castiglione et al. 2019).

Advantages, Limitations, and Potential Extensions

The advantage of capturing brain processes associated with both the engendering and controlling of intrusive thoughts is that they can provide more information than a simple behavioral reaction time (i.e., button press) or retrospective report. One must be cautious in inferring the engagement of cognitive processes from patterns of brain activation, even within the context of the broad set of knowledge regarding the neural circuitry underlying memory processes. Nonetheless, these patterns provide insight into what aspects of memory processing are disrupted during intrusive disorders, or whether control mechanisms are intact but mainly engaged at inappropriate times. A disadvantage of

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such approaches is that these neural metrics often require multiple trials for signal averaging; thus, the frequency of intrusions poses a potential limitation. Although they may readily occur, with increasing practice at suppression, they tend to become less frequent (Hellerstedt et al. 2016), which may limit the amount of data that can be collected.

The Multiplicity of Brain Metrics Available

The studies discussed above that used fMRI focused primarily on brain regions that become active during an intrusion or during the attempt to control an intrusion. Additional metrics, however, should be examined to see whether they can provide a distinct window into these processes. For instance, activation within cognitive control (e.g., dorsolateral prefrontal cortex) and memory-related regions (e.g., the hippocampus) has been implicated in suppressing memory retrieval, as has the connectivity between these regions (e.g., Depue et al. 2007; Benoit et al. 2015). Connectivity patterns could be examined using independent component analysis, which reveals groupings of brain regions whose activity follows a similar temporal time course during the suppression of a thought, as compared to other processes, such as visual imagery (Aso et al. 2016).

A variety of electromagnetic techniques can be applied to studying intrusive thoughts. These may focus on specific ERP components, such as the parietal old/new component, which occurs approximately 50–80 ms after stimulus presentation and is thought to be an index of memory retrieval (Rugg and Curran 2007). Such measures could be combined with measures of neural oscillations, recorded from the scalp (e.g., Depue et al. 2013) or via intracranial recordings in patients undergoing surgery for epilepsy (Oehrn et al. 2018), to provide information on the control of such retrieval. Magnetoencephaology has been used to examine downregulation of sensory aspects of long-term memory in the gamma band (70–120 Hz) in traumatized refugees (Waldhauser et al. 2018). Optical imaging methods (e.g., functional near infrared spectroscopy, which provides information on both the location and time course of activation) have been used to examine brain activation in individuals with PTSD during symptom provocation (Gramlich et al. 2017) as well as in individuals high in rumination during stress (Rosenbaum et al. 2018).

All of these methods record or otherwise observe the nature of brain activation associated with memory retrieval or control processes. In contrast, current work that focuses on using brain stimulation techniques (e.g., transcranial magnetic stimulation or transcranial direct current stimulation) to alter intrusive thoughts (i.e., to induce or disrupt them) is still preliminary. In one study, brain stimulation of prefrontal regions and the underlying white matter in three patients about to undergo surgery for epilepsy was found to induce intrusive thoughts. For example, when stimulated one patient reported: "The stimulation induces the disappearance of the word in my mind and replaces

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it with something else" (Popa et al. 2016:3). Another reported that he had "a thought that seems to come from nowhere" (Popa et al. 2016:4). To the best of my knowledge, brain stimulation techniques have not been used to disrupt thought. In addition, such methods may provide other insights into intrusive thoughts. For example, aspects of intrusive memories in PTSD tend to be overgeneralized (Brewin 2011); that is, memories are not clearly differentiated. Transcranial direct current stimulation over lateral occipital cortex during the encoding of a memory leads to interference between memory representations, presumably because of coactivation and less differentiation between those representations (Koolschijn et al. 2019). Hence, such stimulation might potentially be used as a system to model aspects of intrusive thoughts in PTSD.

Advantages, Limitations, and Potential Extensions

Brain-based methods offer a wide variety of tools and a number of different metrics (e.g., brain activity, brain connectivity) that can be used to explore the mechanisms that underlie intrusive thinking. They provide converging evidence for purported mechanisms of intrusive thought and can be used to distinguish potential mechanisms involved in memory control and retrieval of intrusive memories. In addition, brain-based measures offer unique insights. For example, brain-imaging techniques have indicated that memory retrieval can be actively suppressed, as evidenced by a reduction below baseline in activation of hippocampal regions during attempts not to think about specific items (Depue et al. 2007). Recent advances in brain-imaging techniques allow information about intrusive thoughts to be gleaned from nonstructured and more naturalistic stimuli (e.g., a movie) without requiring a specific contrast between conditions (Huk et al. 2018). This opens the possibility for sophisticated computational algorithms to extract over time those critical patterns or signatures of brain activity that are associated with the formation or retrieval of intrusive thoughts.

Individual Differences: Approaches to Brain Anatomy and Function Associated with Intrusive Thought

Another approach is to examine how the functioning of neural systems varies, depending on differences among individuals in the degree of intrusive thoughts and/or the degree to which they can control such thoughts. Some studies examine aspects of the brain that are relatively static (e.g., brain anatomy or the organization of intrinsic resting-state networks) in individuals who experience high levels of intrusive thoughts: PTSD or OCD patients (e.g., Chen et al. 2018a; Gürsel et al. 2018) or individual self-reports from single or extended time periods (e.g., Kühn et al. 2013). While such studies may provide information about variation in potential brain structures involved in intrusive thought (e.g., the hippocampus), they may not provide information specific to intrusive

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thinking. For example, a stress response associated with traumatic events (e.g., increased cortisol and neurotoxicity of hippocampal cells) could cause reduction in hippocampal volume or shape. Moreover, examining brain anatomy and resting-state connectivity may not be ideal for studying intrusive thought, because both are relatively static, whereas intrusive thoughts, by nature, are time limited and dynamic.

Other approaches characterize individuals according to their level and/or controllability of intrusive thought to determine how these factors might affect brain activation. For example, during suppression of recently experienced items, individuals with a higher degree of self-reported difficulty in removing current thoughts from consciousness had higher levels of activation in Broca area; this presumably represents an inclination toward inner speech (Banich et al. 2015). Another recent and potentially profitable approach is to use magnetic resonance spectroscopy (MRS) to examine potential neurochemical mechanisms that may enable certain individuals to block memory retrieval. For example, individuals with higher levels of GABA in the hippocampus, as assessed by MRS, have a greater ability to suppress memory retrieval (e.g., Schmitz et al. 2017). The disadvantage of using MRS methods is that they are quite time consuming (e.g., 25 minutes). In addition, only a few brain regions can be interrogated during a scanning session, and the brain region interrogated is much larger (e.g., at least 3–4 times greater) relative to functional neuroimaging methods.

Advantages, Limitations, and Potential Extensions

Exploring individual differences in the psychological processes involved in intrusive thought has a long and fruitful history, and can be equally well applied for use with neural markers. However, for neuroimaging, an individual differences approach generally requires a larger sample size to detect covariation than is required in studies designed to detect group average patterns of activation (Cremers et al. 2017). Thus, utilizing an individual differences approach requires more time and money.

Future Frontiers for Brain-Imaging Methods

Using Brain-Imaging Methods in a Predictive Manner

There is much interest in determining whether an individual will experience intrusive memories after a distressing event. Prior work has examined whether certain characteristics of an individual and/or the way in which a distressing event is processed are robust predictors of subsequent intrusive thoughts (e.g., Marks et al. 2018). This work has been extended to examine whether measures derived from brain metrics might predict subsequent intrusions. For

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example, ERP measures of the effectiveness of suppression (greater amplitude of a fronto-centrally distributed N2) from the Think/No-Think task can predict subsequent intrusions after analog trauma (Streb et al. 2016). Relatedly, patterns of brain activation derived from machine-learning techniques, during the encoding of material in an analog trauma paradigm, can be used to predict the degree to which an individual will have subsequent intrusive thoughts (Clark et al. 2014b). Although in its infancy, such approaches may have much potential.

Neural Markers versus Self-Report

One important limitation of many of the methods described above is that they rely on self-report to verify an intrusive memory or control over thoughts, and thus do not provide insight into the nature of the representation of that memory. Neurally based measures have been used to try to address this issue.

Autonomic Measures

Autonomic measures have been used in conjunction with the behavioral methods discussed above. The idea is that reexperiencing traumatic events should induce physiological changes and that successful suppression of such thoughts should be associated with reductions in such physiological responses (e.g., May and Johnson 1973). Such measures have also been used in conjunction with an individual differences approach. For example, greater heart rate variability is associated with a better ability to inhibit thoughts, either in a structured thought suppression situation, the Think/No-Think paradigm (Gillie et al. 2014), or in the self-report of intrusive thoughts over specific periods of time (Gillie et al. 2015). Such physiological measures, however, are mainly nonspecific in nature and could reflect arousal, emotional distress, or anxiety, either in a state or trait manner that is unrelated to intrusive thoughts.

Neuroimaging Approaches

Although much work on intrusive thinking has focused on the retrieval of information from long-term memory, by nature, intrusive thoughts involve access to and active representation in working memory (for further discussion, see Visser et al., this volume). Understanding whether a thought is currently in the focus of attention in working memory is an important issue. Initial work suggests that brain-imaging techniques can be applied quite fruitfully to verify that individuals are indeed experiencing specific thoughts and/or manipulating them. In one study (Banich et al. 2015), individuals were shown a picture or heard a brief snippet of a familiar tune (e.g., “Happy Birthday”) for four seconds; immediately afterward they then had to manipulate the item in one of four manners: maintain it, replace it with a different image/tune, specifically

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suppress the item, or clear their mind of all thought. Providing at least some evidence that participants were indeed manipulating their thoughts as instructed, a significant reduction of activity in primary sensory areas (e.g., visual cortex, auditory cortex) was observed averaged across all trials for the two conditions in which a thought needed to be cleared and removed (suppress the item or clear their mind of all thought), compared to when there was an active thought (maintain or replace). In addition, results indicated that while some neural mechanisms were commonly engaged across these operations (e.g., across replacing, suppressing, or clearing an item as compared to maintaining it), there are also specific neural mechanisms that differentiate the suppression of an item from clearing one's mind of all thought (Banich et al. 2015). Thus, neuroimaging may provide a neural marker and confirm specific mental operations performed on a given thought. This may lead us to differentiate the ways in which thoughts can be removed from working memory.

In follow-up work, machine learning was incorporated to expand the questions and issues that can be examined (Kim et al., submitted). Specifically, via a localizer task, a machine-learning classifier was used to distinguish specific categories of items (e.g., places, faces, fruit). These classifiers were then used on a trial-by-trial basis to determine the degree to which removing the thought was successful. If a thought is successfully removed, then the classifier fit should be poor. If the thought is maintained, then the classifier fit should be high. This approach enables us to examine the nature of the mental representation on a trial-by-trial basis and provides a means to determine the level at which such representations are maintained and/or cleared via specific category and subcategory classifiers (e.g., fruit: apples, grapes, pears). For example, one can examine whether clearing the thought of an apple generalizes to other fruit (e.g., grapes and pears). In addition, patterns of brain activation can be examined as a function of classifier fit to determine which brain regions are highly active when the classifier fit is low (indicative of clearing the thought), compared to when the classifier fit is high (indicative of the thought remaining). This, in turn, may provide insight into which brain regions are involved in exerting control over thoughts. While this study did not explicitly track intrusions, such methods could be extended to track the content of intrusive thoughts on a real-time basis by identifying multivariate neural patterns of distinct forms of intrusive content and evaluating the degree to which these patterns manifest on a moment-to-moment basis.

In summary, there are a variety of interesting new directions that might be used to provide novel insights into the nature of intrusive thought. These range from adapting and using paradigms from other areas of cognitive and affective psychology to investigate intrusive thinking, to new approaches and applications from brain-imaging methods that might be used to verify or predict intrusive thought.

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