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Review article

Brain correlates of hypnosis: A systematic review and meta-analytic exploration

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ABSTRACT

Imaging of the living human brain elucidates the neural dynamics of hypnosis; however, few reliable brain patterns emerge across studies. Here, we methodically assess neuroimaging assays of hypnosis to uncover common neural configurations using a twofold approach. First, we systematically review research on the neural correlates of hypnotic phenomena; then, we meta-analyze these collective data seeking specific activation and deactivation patterns that typify hypnosis. Anchored around the role of top-down control processes, our comprehensive examination focuses on the involvement of intrinsic brain networks known to support cognitive control and self-referential cognition, including the executive, salience, and default networks. We discuss how these neural dynamics may relate to contemporary theories of hypnosis and show that hypnosis correlates with activation of the lingual gyrus—a brain region involved in higher-order visual processing and mental imagery. Our findings help to better understand the neurobiological substrates comprising the appellation hypnosis.

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1. Introduction

The term “hypnosis” encompasses a wide spectrum of phenomena that center on response to suggestion (Nash and Barnier, 2008; Yapko, 2015). Hypnosis can modulate perceptual, cognitive, ideomotor, or emotional processes and often results in changes of observable behavior and subjective experience (Kihlstrom, 2008). The following factors predominantly influence hypnotic responses: (i) inter-individual variability in hypnotic susceptibility; (ii) the ritual of hypnotic induction; and (iii) the specific hypnotic suggestions (Fig. 1; Mazzoni et al., 2013; Oakley and Halligan, 2010). Accordingly, researchers investigating the neural correlates of hypnosis tend to focus on these three dimensions (Casale et al., 2012; Kihlstrom, 2013; Oakley and Halligan, 2009, 2013). This approach has yielded substantial, albeit limited, insights concerning the brain mechanisms of hypnotic phenomena (Raz, 2011a). Rather than converge towards a common neural signature, neuroimaging accounts of hypnosis have reported an extensive variety of brain patterns (Landry and Raz, 2015, 2016).

The current body of findings concerning the neural correlates of hypnosis is marked by inconsistency. For example, whereas some studies of hypnosis report increased activity in the ACC (e.g., Egner et al., 2005; Rainville et al., 1999b), other studies show the opposite effect (e.g., Deeley et al., 2012; McGeown et al., 2009; Raz et al., 2005). This trend holds true for many other brain regions implicated in hypnosis (Burgmer et al., 2013; Cojan et al., 2009; Egner et al., 2005; Faymonville et al., 2000; Halligan et al., 2000; Raij et al., 2009). Several factors may account for the discrepancies across neuroimaging investigations of hypnosis. To begin with, methodological differences stemming from both experimental and hypnotic techniques, including the absence of standard procedures for administering hypnosis, likely explain at least part of this variability (Mazzoni et al., 2013). Differences across experimental contexts also impede our ability to generalize findings. For example, hypnotic modulation of the pain neuromatrix during noxious stimulation indexes an interaction between nociception and hypnosis, not the influence of hypnosis alone, which challenges generalization beyond these experimental conditions. Furthermore, the tendency for researchers to hone in on specific brain regions, rather than look at activity across the whole brain, narrows possible comparisons across studies. Although we agree that science thrives on hypothesis-driven research, the prevalent trend to restrict the scope of analysis to pre-determined regions of interest hinders our ability to discern overarching relationships across findings.

Crucially, different suggestions engage different brain areas (Landry and Raz, 2015, 2016). Consider, for example, that whereas highly hypnotically susceptible individuals (HHSIs) showed increased ACC activity on the Stroop task following a hypnotic induction (Egner et al., 2005), such individuals displayed the opposite pattern following a post-hypnotic “alexia” suggestion to see the Stroop words as gibberish from a foreign language (Raz et al., 2005). Thus, while both studies employed a similar experimental task, their distinct use of suggestion yielded disparate neural effects (Egner and Raz, 2007). Finally, hypnotized individuals likely resort to a wide variety of cognitive strategies when responding to suggestions (Cardeña, 2014). In other words, similar hypnotic responses may arise from different cognitive processes (e.g., Derbyshire et al., 2016). Insofar as different cognitive strategies correspond to distinct neural patterns, identifying a unitary signature for hypnosis may well represent an elusive goal (Lynn et al., 2015).

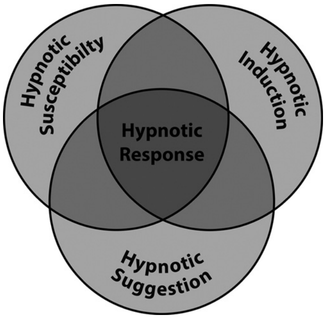

Fig. 1. Central components of hypnotic response: Hypnotic susceptibility, the induction procedure and the hypnotic suggestions.

In spite of these limitations, the available body of neuroimaging findings provides a substantial basis for a comprehensive review. Here we aim to integrate imaging findings concerning hypnosis into a holistic neurobiological framework. To this end, we (1) systematically review neural patterns that emerge throughout investigations of hypnotic susceptibility, induction, and suggestion; and (2) calculate overlapping trends across neuroimaging studies of hypnosis using activation likelihood estimation meta-analysis (ALE; Eickhoff et al., 2012, 2009; Fox et al., 2014; Turkeltaub et al., 2012). Our synthesis strives to inform theoretical models of hypnosis as a function of central components of the hypnotic response, namely inter-individual differences, the induction procedure, as well as the type and content of the suggestion (see Fig. 1; Mazzoni et al., 2013). In particular, we discuss findings in light of a leading conceptual framework concerning the neural mechanisms of hypnosis—an overarching model we refer to as the “top-down” view of hypnosis. We also consider theories that attempt to explain hypnosis by addressing the altered feelings of agency that typify hypnotic responses (Barnier et al., 2008; Weitzenhoffer, 1980). We survey findings through the lens of brain connectomics—an increasingly influential framework that links large-scale connectivity networks to perceptual, cognitive, motor and affective systems (Bullmore and Sporns, 2009; Sporns, 2010, 2011, 2012, 2013a, 2013b, 2014). Collectively, our systematic appraisal and quantitative meta-analysis serve to reconcile discrepancies into a cogent synthesis and yield novel hypotheses for future work addressing the neural mechanisms of hypnosis.

2. Top-down theories and the frontal brain

Theories of hypnosis often emphasize top-down mental processes such as attention, executive control, and cognitive monitoring (Barnier et al., 2008; Crawford, 1994; Dienes and Perner, 2007; Egner and Raz, 2007; Gruzelier, 2006; Jamieson and Woody, 2007; Lynn et al., 2008; Raz, 2011b; Woody and Sadler, 2008). Many such viewpoints propose that hypnotic phenomena follow from a distinct plane of absorption that helps hypnotized individuals focus on mental objects in a manner that propels various cognitive alterations (Barber, 1960; Crawford, 1994; Raz, 2005; Spiegel, 2003; Tellegen and Atkinson, 1974). Some researchers further argue that hypnotic response and related phenomenologies – especially the hallmark sense of automaticity (i.e., the feeling that hypnotic responses happen “of their own”) – stem from changes in functional connections between cognitive control networks and other higher-order mental processes (Dienes and Perner, 2007; Jamieson and Sheehan, 2004; Jamieson and Woody, 2007; Woody and Bowers, 1994; Woody and Farvolden, 1998). Other theorists explain such feelings of automaticity by underlining the role of top-down socio-psychological factors, such as personal attitudes and response expectancies (Kirsch et al., 1999; Wickless and Kirsch, 1989). Thus, although hypnosis commands a vast theoretical landscape, many influential theories place top-down processes at center stage and predict the involvement of corresponding neural systems (Barabasz and Barabasz, 2008; Barnier et al., 2008; Crawford, 1994; Egner and Raz, 2007; Kihlstrom, 2013; Woody and Bowers, 1994; Woody and Farvolden, 1998; Woody and Sadler, 2008).

The frontal brain features prominently in top-down theories of hypnosis (Gruzelier, 2006). Such theories frequently emphasize frontal networks that control and regulate top-down processes (Corbetta et al., 2008; Corbetta and Shulman, 2002; Fox et al., 2006; Goulden et al., 2014; Menon and Uddin, 2010; Raz and Buhle, 2006; Sridharan et al., 2008). As we detail below, various reports link hypnosis to structural and functional changes in regions of the central executive network (CEN) and salience network (SN), two large-scale intrinsic brain systems key to higher-order cognition. These findings include altered activity in the anterior cingulate cortex (ACC) and anterior insula—two important frontal nodes of the SN—as well as changes in the dorsolateral prefrontal cortex (DLFPC), the main frontal component of the CEN (for review, see Casale et al., 2012; Kihlstrom, 2013; Landry and Raz, 2015; Oakley and Halligan, 2013). Below we review how the corpus of the available evidence supports the top-down view of hypnosis, underlining the involvement of neurocognitive systems that typically index attention and executive control. We further discuss the potential of these brain patterns as putative neural markers of hypnosis (Raz and Lifshitz, 2016).

Beyond top-down theories, another prominent group of perspectives emphasizes a correlation between hypnosis and deactivation in the medial prefrontal cortex (mPFC) (Deeley et al., 2012; McGeown et al., 2009). The mPFC is the main frontal node of the default network (DN; Buckner et al., 2008; Raichle, 2015) – a densely-connected intrinsic brain network associated with internal attention, autobiographical thought, social cognition, and mind-wandering (Christoff et al., 2009; Mason et al., 2007). Rather than highlight the role of top-down attention, these accounts draw attention to how hypnosis modulates a brain network governing automatic self-generated thoughts. Some researchers therefore conceptualize the frontal marker of hypnosis as a reduction in mind-wandering (Lynn et al., 2015).

In sum, two distinct neural profiles prevail: On the one hand, hypnosis appears to engage frontal regions of the CEN and SN — two networks associated with attention, executive control, and cognitive monitoring; on the other hand, hypnosis seems to correspond to deactivation in the anterior part of the DN — a network associated with social cognition, internal attention, and self-related thought. Both of these neural patterns emerge as important pieces in the puzzle of relating hypnosis to the brain. We will return to these patterns again and again throughout our exposition as we examine the neural correlates of hypnotic susceptibility, induction, and suggestion.

2.1. The hallmark of hypnosis: altered sense of agency

When producing hypnotic responses, HHSIs usually report feeling that their behaviors occur in an involuntary and effortless manner (Polito et al., 2013; Polito et al., 2014). Many theorists consider this altered sense of agency to be the defining feature of hypnosis and even refer to it as the “classic” suggestion effect, resulting in the development of theoretical conceptions based on the primacy of this phenomenological characteristic (Hilgard, 1965; Kihlstrom, 1985, 2008; Lynn, 1997; Weitzenhoffer, 1974, 1980; Woody and McConkey, 2003).

Inspired by the work of Pierre Janet (1901, 1907) and early models of cognitive control (e.g., Norman and Shallice, 1986), (neo)dissociation theorists propose that alterations in agency follow from a disconnection between executive and supervisory processes (Bowers, 1992; Hilgard, 1973, 1977, 1991, 1992; Woody and Bowers, 1994; Woody and Farvolden, 1998). Recent installments of this view postulate more specifically a functional breakdown of connectivity between executive control and cognitive monitoring systems (Jamieson and Woody, 2007; Woody and Sadler, 2008). In this respect, dissociated control theory draws on prevailing models of agency in cognitive neuroscience. Under normal waking circumstances, the sense of ownership over action seems to arise from sensory and executive feedback loops to monitoring systems, resulting in the emergence of second-order mental representations that we experience as a sense of agency (Blakemore et al., 2002; David et al., 2008; Haggard and Chambon, 2012). Dissociation theorists posit that hypnosis weakens these retroactive connections, thereby allowing suggestions to bypass monitoring processes and act directly on executive systems. In the absence of supervision, the control of movements and perceptions may well feel involuntary and effortless.

The classic Stroop effect — where individuals are slower to name the ink color of an incongruent color word (e.g., the word “red” inked in blue) compared to a congruent color word (e.g., the word “blue” inked in blue) — provides insight into the relationship between control and monitoring processes. Incongruent Stroop trials require executive and monitoring processes to inhibit the automatic reading response and name the appropriate ink color (MacLeod, 1991). Such incongruent trials typically trigger activation of the DLPFC and ACC — main hubs of the executive/control and salience/monitoring networks, respectively (e.g., MacDonald et al., 2000). Taking advantage of this paradigm, Egner et al. (2005) tested dissociated control theory by examining how cognitive conflict modulates the response of these neural systems following a hypnotic induction. Whereas incongruent Stroop trials led to

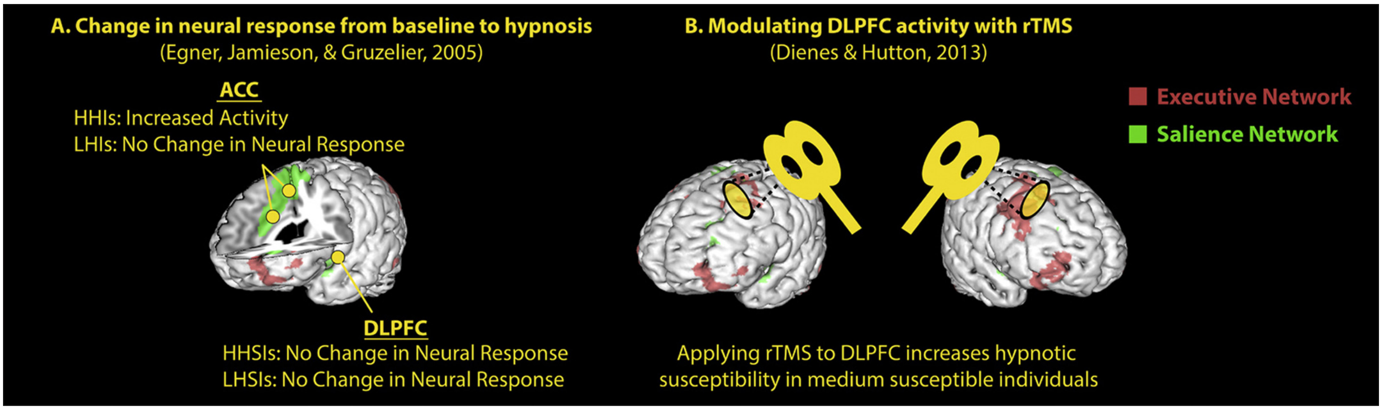

Fig. 2. A. Modulation of neural patterns in the Anterior Cingulate Cortex (ACC) and Dorsolateral Prefrontal Cortex (DLPFC) from baseline to hypnosis, across high and low hypnotic susceptibility individuals, in the Stroop task. These results come from Egner et al. (2005). B. Modulation of Dorsolateral Prefrontal Cortex (DLPFC) via repetitive transcranial magnetic stimulation (rTMS). These results come from Dienes et al. (2009). Central Executive Network and Salience Network come from Shirer et al. (2012).

comparable patterns of activity in the DLPFC for high and low susceptible individuals across baseline and hypnosis, such trials yielded increased ACC activity for HHSIs compared to LHSIs in hypnosis (see Fig. 2). These researchers interpreted their findings as support for the dissociated control theory. In particular, they reasoned that increased ACC/monitoring activity in the absence of corresponding DLPFC/control activity for HHSIs under hypnosis indexes a breakdown of communication between executive and monitoring systems. Moreover, parallel electrophysiological recordings at both sites revealed reduced functional connectivity between them (Egner et al., 2005). Other reports found related changes in oscillatory patterns using electroencephalography (e.g., Jamieson and Burgess, 2014; Terhune et al., 2011a).

While such studies may herald a meaningful advance for the field, other findings seem to challenge the predictions of dissociated control theory. In particular, the theorized disconnection between control and monitoring systems would likely disrupt connectivity patterns between the CEN and SN — a prediction that contradicts current evidence showing increased connectivity between these networks following induction (Jiang et al., 2016). Furthermore, the DLPFC cluster, putatively indexing executive control in the study by Egner et al. (2005), actually sits beyond the canonical CEN, potentially deflating an account centering on executive control (see Fig. 2). As per the predictions of dissociated control theories, future studies should better specify alterations in neural activity in relation to changes in the phenomenology of agency (Polito et al., 2014).

Despite a growing body of findings on the neural correlates of agency in hypnosis (Blakemore et al., 2003; Deeley et al., 2014, 2013; Walsh et al., 2015), few studies have probed differences between spontaneous hypnotic alterations in agency versus alterations that follow from the specific suggestions of the operator. One neurophenomenological investigation found little evidence for the spontaneous emergence of loss of control following a neutral hypnotic induction procedure (i.e, an induction that limits explicit references to what hypnosis should feel like, such as suggestions for greater attentiveness, absorption, or relaxation Cardeña et al., 2013). Thus, while suggestions targeting feelings of control over ideomotor actions modulate agency-related neural patterns (e.g., Walsh et al., 2015), evidence remains ambiguous as to whether hypnosis spontaneously alters the neural correlates of agency. Using fully balanced factorial designs to tease apart the influence of induction and suggestion will allow us to better grasp contrasting findings across paradigms.

Beyond the dissociated control model of hypnosis, early (neo)dissociation perspectives gave rise to a related yet distinct account — the COLD control theory of hypnotic responding. This theory focuses on the relationship between executive control and conscious awareness, rather than between executive control and unconscious cognitive monitoring, as in the dissociated control account. Building on higher-order theories of consciousness (Gennaro, 2004; Lau and Rosenthal, 2011; Rosenthal, 1980, 2005) and recent advances concerning the mechanisms of metacognition (Fleming et al., 2012), COLD control theory contends that hypnosis largely reflects unconscious executive control (Dienes and Perner, 2007). According to this view, hypnotic phenomena arise from the interference of meta-representations of response selection and implementation, resulting in erroneous higher-order appraisals of intents for thoughts and actions (Dienes, 2012). In sum, while the executive system operates aptly in response to suggestions, incorrect metacognitive representations explain why hypnotized individuals feel a lack of ownership over their cognitions and behaviors (Lush et al., 2016).

Because COLD control theory grounds itself in prevalent models of consciousness and metacognition, its hypotheses derive largely from advances in these fields. Mounting evidence links metacognition with the DLPFC (Fleming and Dolan, 2012a, 2012b; Fleming et al., 2012, 2014, 2010; Lau and Passingham, 2006; Rahnev et al., 2016; Rounis et al., 2010). In accordance with this literature, Dienes and Hutton (2013) examined the causal role of the DLPFC in hypnosis using repeated transcranial magnetic stimulation (rTMS; see Fig. 2). Supporting their COLD control hypothesis, they found that transient disruptions of DLPFC activity increased hypnotic responsiveness for medium susceptible individuals. This finding intimates that impairing metacognitive abilities may facilitate hypnosis. However, while this seminal study corroborates the centrality of the DLPFC in hypnotic phenomena (Parris, 2016), COLD control theory still requires further confirmation. As a case in point, a wide range of higher-order cognitive functions implicate the DLPFC – from working memory to cognitive control and decision making – thus broadening the scope of possible interpretations in the absence of concurrent behavioral measures (Terhune, 2012). Advancing the fields of volitional control, metacognition and hypnosis will provide researchers with the means to further explore this theoretical view (Lush et al., 2016).

Dissociated and COLD control theories are two of the most dominant models in the science of hypnosis. Both theories advance the field by drawing from reliable experimental paradigms and making testable predictions (e.g., Dienes, 2012; Jaffer and Jamieson, 2012). And yet, these theories tend to focus narrowly on the classic suggestion effect – the disruption of agency – thus limiting their epistemic range. It is unlikely that a single mechanism will explain the entire realm of hypnotic phenomena (Terhune, 2015). Hypnosis is a complex ritual that involves absorption, embodied relaxation, alterations of self, and changes in agency. Each of these alone does not equal hypnosis. Thus, to provide a more holistic account of the mechanisms of hypnosis, in the following sections we relate existing theoretical models to the broader domain of hypnotic responding.

3. Hypnotic susceptibility

Research efforts to understand hypnotic phenomena typically contrast responses across levels of hypnotic susceptibility (Laurence et al., 2008). Specifically, researchers tend to boost experimental effects by comparing extreme ends of the susceptibility spectrum or by focusing on changes from baseline for HHSIs only (Barnier et al., 2014; Heap et al., 2004). And yet, only about 20–30% of individuals score either high or low in hypnotic susceptibility (Piccione et al., 1989; Register and Kihlstrom, 1986), a shortcoming that hampers the generalizability of these results to the remaining 70–80% of the population. Studies with hypnotic virtuosos represent a conspicuous example of this limitation, as this rare group of individuals includes only those capable of producing extreme and dramatic responses unachievable even by most HHSIs, let alone the rest of the population. Moreover, comparing effects from opposing ends of an indicator variable such as hypnotic susceptibility – as opposed to studying the entire spectrum – merely underlines a relative difference and hardly anchors hypnosis findings into prevailing models of cognitive neuroscience (Lynn et al., 2007). In spite of these caveats, neuroscientific explorations of hypnotic susceptibility provide crucial evidence for building a reliable science of hypnosis. Researchers typically identify HHSIs by their ability to shape their own behavior and subjective experience in accordance with hypnotic suggestions (Barnier et al., 2014; Heap et al., 2004). In addition to responding more strongly to suggestions, HHSIs also experience a wider range of unusual experiences during hypnosis compared to less hypnotically susceptible individuals (LHSIs; Cardeña et al., 2013; Pekala and Kumar, 2007).

Grounded in the comparison of high versus low susceptible individuals, several studies have examined the neural correlates of hypnotic susceptibility (see Table 1 and Fig. 3). Structural assays

Table 1
Neuroimaging studies that investigated structural and functional neural correlates of hypnotic susceptibility.

Study	Imaging technique	Sample Size/Population	Experiment	Results
Structural Neuroimaging				
Horton et al. (2004)	*MRI*	N = 18 LHSIs and HHSIs who can suppress pain perception	MRI data acquisition	Increased white matter volume in corpus callosum for HHSIs
Huber et al. (2014)	*MRI*	N = 37 LHSIs and HHSIs	MRI data acquisition	Increased grey matter volume in Superior Frontal Gyrus and decreased grey matter volume in Insula for HHSIs
McGeown et al. (2015)	*MRI*	N = 29 High, medium and low susceptible individuals	MRI data acquisition	Increased grey matter volume in Superior and Mid-Temporal, as well as Mid-Occipital gyri for HHSIs
Functional Neuroimaging – Resting State				
Hoeft et al. (2012)	*fMRI*	N = 24 LHSIs and HHSIs	Resting State data acquisition	Increased functional connectivity between the DLPFC and ACC
Huber et al. (2014)	*fMRI*	N = 37 LHSIs and HHSIs	Resting State data acquisition	Decreased connectivity between Thalamus and right Fronto-Parietal Network; increased connectivity between Posterior Cingulate Cortex and Precuneus with left Fronto-Parietal Network; increased connectivity between Inferior Parietal Lobule and Central Executive Network
Functional Neuroimaging – Baseline Attention				
Cojan et al. (2015)	*fMRI*	N = 32 LHSIs and HHSIs	Flanker Task	Increased neural activity in Inferior Frontal Gyrus, ACC and Superior Parietal Lobule during task performance
Egner et al. (2005)	*fMRI*	N = 22 LHSIs and HHSIs	Stroop Task (Baseline Condition)	No difference in neural response during task performance between LHSIs and HHSIsfor DLPFC and ACC
Lifshitz and Raz (2015)	*fMRI*	N = 16 LHSIs and HHSIs	Stroop Task	Increased neural activity in Pulvinar and Fusiform Gyrus
Functional Neuroimaging – Placebo response				
Huber et al. (2013)	*fMRI*	N = 28 High, medium and low susceptible individuals	Placebo analgesia	Hypnotic susceptibility positively related to DLPFC activity during anticipation phase, and negatively related to activity in thalamus, caudate, precuneus and posterior temporal gyri.

reveal anatomical differences in a range of frontal sites (Huber et al., 2014; McGeown et al., 2015), including a larger anterior corpus callosum for HHSIs (Horton et al., 2004). This bundle of white-matter fibers tracts facilitates the coordination of activity between hemispheres (Bloom and Hynd, 2005). Thus, volumetric differences in the anterior portions of the corpus callosum may potentially translate into distinctive patterns of frontal neural activity among HHSIs. In addition to these structural findings, functional studies also partially support the top-down view of hypnosis (see Fig. 3; Cojan et al., 2015; Hoeft et al., 2012; Huber et al., 2014). One of these reports notably demonstrates distinct cross-network interactions involving the executive and salience systems when comparing HHSIs and LHSIs (Hoeft et al., 2012). Baseline differences in these large-scale attention systems may provide a basis for the special feats of cognitive regulation available to HHSIs in the context of hypnosis (Rainville and Price, 2003). Neurophysiological investigations similarly report distinct frontal oscillatory patterns as a function of hypnotic susceptibility (Vanhaudenhuyse et al., 2014). Differences in structural neural correlates of hypnotic susceptibility therefore appear to underlie differences in functional activity. One finding however disputes this interpretation by showing that increased DLPFC-ACC functional connectivity among HHSIs hardly corresponds to structural differences (Hoeft et al., 2012). While this study found evidence for greater coupling between the executive and salience networks, it revealed a lack of congruent structural variation. In addition, a neuropsychological investigation found limited support for the idea that frontal dysfunction increased hypnotic susceptibility (Kihlstrom et al., 2013). Nevertheless, the collective body of results intimates that structural and functional differences in the frontal brain shape, at least in part, hypnotic susceptibility.

Some researchers propose that hypnotic susceptibility corresponds largely to differences in top-down regulation, such that HHSIs have a special ability to exert control, in the form of inhibition and facilitation, over cognitive processes (Crawford and Gruzelier, 1992; Gruzelier, 1998, 2006; Kallio et al., 2001). Various studies have tested this hypothesis by examining attention skills at baseline across the susceptibility spectrum. While inconsistency plagues behavioral results (Aiktns and Ray, 2001; Castellani et al., 2007; Crawford et al., 1993; David and Brown, 2002; Dienes et al., 2009; Dixon et al., 1990; Dixon and Laurence, 1992; Egner et al., 2005; Egner and Raz, 2007; Iani et al., 2009, 2006; Kaiser et al., 1997; Kallio et al., 2001; Raz et al., 2005, 2003, 2002; Rubichi et al., 2005; Sheehan et al., 1988; Varga et al., 2011), neuroimaging assays report differences in attention-related baseline brain activity as a function of hypnotic susceptibility (Cojan et al., 2015; Lifshitz and Raz, 2015). However, these neural differences hardly correlate with enhanced task performance; thus, they likely reflect variations in information processing and cognitive style, as opposed to improved proficiency of attentional control *per se*. Supporting this interpretation, a neuroimaging study comparing analgesia placebo responses between HHSIs and LHSIs showed differences in DLPFC activity but no behavioral differences between groups (Huber et al., 2013). These results highlight how distinct neural patterns associated with top-down regulation and processing style can lead to similar behavioral effects. Thus, instead of framing hypnotic susceptibility in terms of task performance or control capacity, researchers may gain

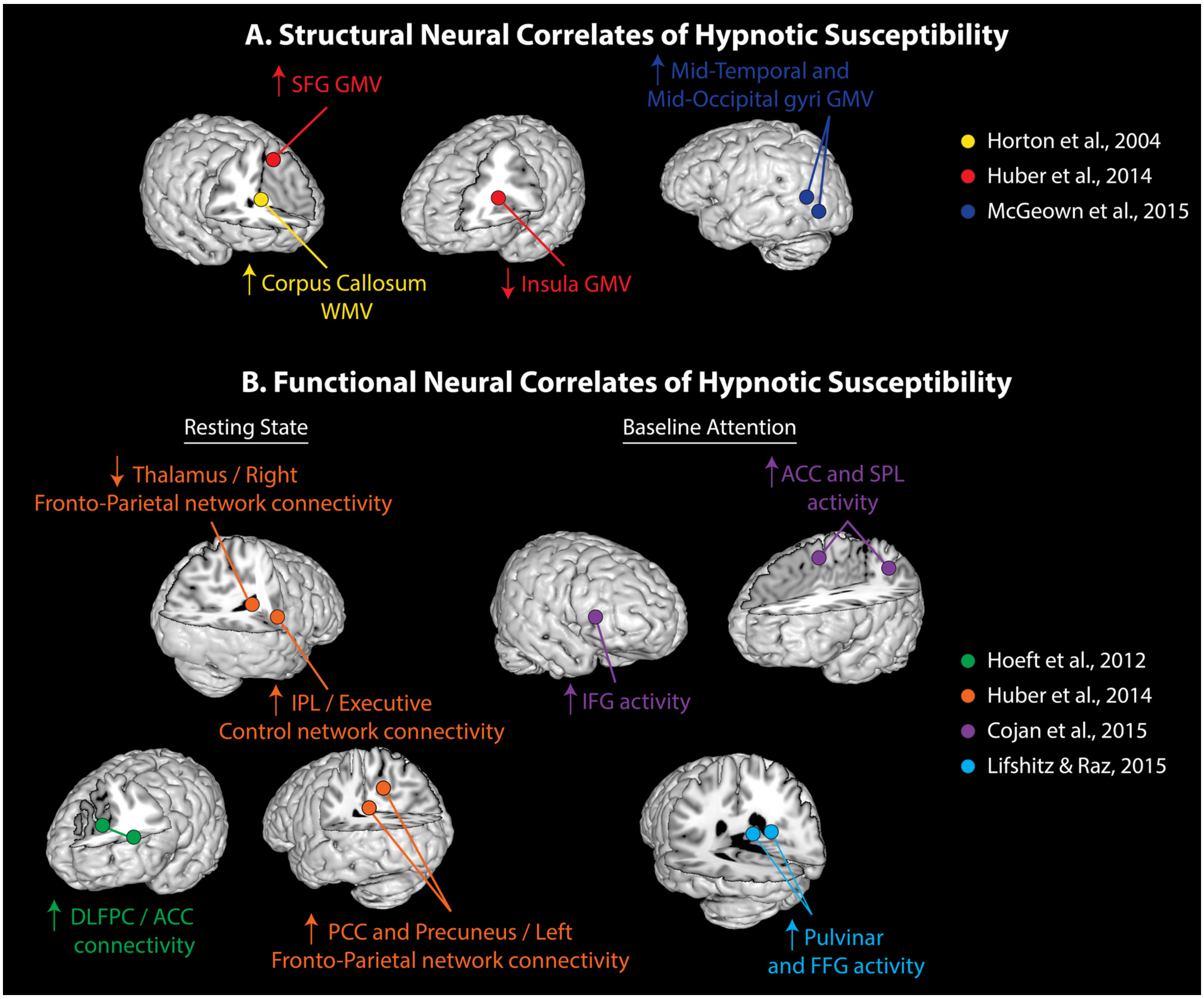

Fig. 3. A. Structural correlates of hypnotic susceptibility. Change in gray matter volume (GMV) and white matter volume (WMV) as a function of hypnotic susceptibility. B. Functional correlates of hypnotic susceptibility. Increased activity and functional connectivity patterns in experiments contrasting high and low susceptibility individuals in resting state (i.e., no task or stimuli) and baseline attention (i.e., using an attention task). The colors indicate the different studies (see online version of the article). ACC = Anterior Cingulate Cortex. DLPFC = Dorsolateral Prefrontal Cortex. FFG = Fusiform Gyrus. IFG = Inferior Frontal Gyrus. IPL = Inferior Parietal Lobule. SFG = Superior Frontal Gyrus. SPL = Superior Parietal Lobule. PCC = Posterior Cingulate Cortex.

more traction by examining differences in attention strategies and processing styles.

The idea that hypnotic susceptibility follows from differences in cognitive processing is hardly new (Bergerone et al., 1981; Brown and Oakley, 1998; Bryant and McConkey, 1990; McConkey and Barnier, 2004; Oakley, 1999; Oakley and Frasquilho, 1998; Sheehan and McConkey, 1982). Rather than focus on enhanced attention performance, this framework posits that HHSIs process suggestions by deploying effective cognitive strategies to implement corresponding hypnotic responses (McConkey et al., 1989). This formulation gains support from findings demonstrating profound heterogeneity of response styles even among HHSIs (Terhune, 2015; Terhune and Cardeña, 2015b; Terhune et al., 2011b, 2011c). For example, pre-existing cognitive traits seem to predispose a subset of HHSIs to experience hypnosis in a particularly dissociated and imaginative manner (Terhune, 2015; Terhune and Cardeña, 2015a; Terhune et al., 2011b, 2011c). Thus, whereas the overarching picture emerging from structural and functional neuroimaging studies supports the link between hypnotic susceptibility and differences in top-down brain processes, these neural divergences likely index complex differences in processing styles rather than a simple superiority of attentional control.

4. Hypnotic induction

Hypnotic sessions typically begin with an induction procedure designed to lead participants to a state of mental absorption and heightened response to suggestion (Elkins et al., 2015; Hammond, 1988). During this induction ritual, the hypnotic operator usually guides individuals to let go of everyday concerns and orient attention towards current and upcoming directives. In addition, the induction often involves concentrating on an object of focus such as the breath or a point in the visual field. Induction procedures putatively enhance the quality and reliability of hypnotic responses, while concurrently reducing awareness of extraneous events (Maldonado and Spiegel, 2008). And yet, because both the induction and the suggestion phases of the hypnotic process rest on instructions and directives from the hypnotic operator, differentiating them from a conceptual perspective is a complex matter (Kihlstrom, 2008; Nash, 2005). Thus, rather than situate inductions and suggestions on wholly different conceptual planes, we prefer to consider them as related yet distinct procedures relative to their respective purposes. Whereas directives and instructions during the suggestion phase usually aim to modify specific behaviors and mental processes (Halligan and Oakley, 2014; Michael et al., 2012), during the induction phase they typically strive to enhance the quality of ensuing hypnotic responses (Derbyshire et al., 2009; McGeown et al., 2012).

Some theorists argue against the notion that induction procedures meaningfully impact subsequent hypnotic responses (Kirsch and Lynn, 1997; Spanos, 1986). In support of this perspective, a handful of findings reveal that hypnotic and non-hypnotic suggestions yield comparable responses in HHSIs, thereby calling into question the role of induction and emphasizing the role of suggestion (Braffman and Kirsch, 1999; Raz et al., 2006). And yet, whereas induction seems unnecessary at times, it also appears to potentiate hypnotic phenomena in specific contexts (Connors et al., 2013; Cox and Barnier, 2010; McConkey et al., 2001). Such empirical discrepancies highlight the need for caution when generalizing theoretical accounts from a limited number of experiments.

Whereas hypnosis yields observable behaviors, most effects transpire at the subjective level. Inductions elicit a wide range of phenomenological changes, including feelings of mental absorption and relaxation as well as alterations in time perception, sense of self, volitional control, emotion, and mental imagery (Cardeña, 2005; Pekala and Kumar, 2007; Terhune and Cardeña, 2010, 2016). Many factors shape the emergence of such experiences as well as their neural correlates. These factors include individual hypnotic susceptibility, the precise wording of the procedure, and the specific social context of the experience (Barrett, 1996; Cardeña et al., 2013; Gandhi and Oakley, 2005; Hinterberger et al., 2011; Kihlstrom and Edmonston, 1971; Kumar and Pekala, 1988, 1989; Lynn et al., 1987). Hypnotic inductions are far from standard. Furthermore, any given induction represents a multifaceted ritual encompassing multiple socio-cognitive factors – including contextual, instructional and expectation-related parameters – each of which likely exerts its own specific influence on hypnotic response (Terhune and Cardeña, 2016). Combined with inter-individual differences and the broad array of possible suggestions, the variable process of induction likely impacts hypnosis in a diversity of ways. Given the limited empirical evidence deconstructing the mechanisms of inductions as well as the mixed bag of findings concerning the impact of these rituals on subsequent response to suggestion, it seems premature to disregard the role of induction altogether.

Neuroimaging studies of induction reveal sweeping changes of activity and connectivity among intrinsic brain networks (see Table 2 and Fig. 4), overlapping in some respects with the functional correlates of hypnotic susceptibility (e.g., see Section 3 above; Hoeft et al., 2012). In particular, multiple reports indicate that hypnotic induction modulates neural systems implicated in higher-order cognition, especially the CEN, SN, and DN (Bressler and Menon, 2010; Dosenbach et al., 2008, 2007; Fair et al., 2007; Fox et al., 2005; Menon, 2015; Menon and Uddin, 2010; Nee et al., 2013; Seeley et al., 2007; Shirer et al., 2012; Sridharan et al., 2008; Vincent et al., 2008). By tying hypnotic induction to higher-order cognitive functions, these neuroimaging findings accordingly support the top-down view of hypnosis. As we explain below, hypnotic modulations of these intrinsic networks likely pertain to the control and monitoring of attention, as well as to the regulation of sensory and interoceptive information.

Anchored at the DLPFC and posterior parietal sites, the CEN guides cognitive control by integrating information from external and internal sources as well as planning and selecting appropriate responses (Spreng et al., 2010; Vincent et al., 2008). Evidence shows that this neural system exerts a commanding influence over other intrinsic networks (Chen et al., 2013). Consistent with its functional role, modulations of neural activity within this network following hypnotic induction may reflect altered control over endogenous representations. In particular, the induction procedure may facilitate maintaining focus on the directives and instructions of the hypnotic operator, as well as on a chosen object of focus (see Fig. 4). Supporting this interpretation, two independent investigations showed that self-reported level of hypnotic "trance" or "absorption" correlated with activation in the dorsolateral and frontopolar regions of the CEN, respectively (Deeley et al., 2012; Rainville et al., 2002). Beyond its involvement in control over ongoing mental representations, the CEN is also associated with anticipation and response preparation (Alahyane et al., 2014; Niendam et al., 2012). Thus, increased CEN activity supports socio-cognitive theories that explain hypnosis through the lens of response expectancies (Kirsch, 1985, 1991, 1997; Wickless and Kirsch, 1989). In contrast to the above models, however, one study found that reports of relaxation in hypnosis correlated to *reduced* CEN activity among HHSIs (Rainville et al., 2002). This discordant result should serve to caution us against oversimplified explanations and to remind us of the phenomenological and neural complexity of hypnotic induction (Jensen et al., 2015; Landry and Raz, 2015, 2016; Lynn et al., 2015).

While activity of the CEN likely pertains to cognitive control during mental absorption and response anticipation, modulations of the SN following hypnotic induction may denote modifications in the processing of external and internal signals. The SN includes the anterior insula and anterior cingulate cortices as well as subcortical regions including the amygdala. This network plays a key role in detecting and integrating relevant signals arising from both the external environment and the internal cognitive landscape (Cai et al., 2014; Seeley et al., 2007). This system monitors various sources of information in a manner that orients higher-order cognitive resources (Dosenbach et al., 2007, 2006; Menon, 2015; Menon and Uddin, 2010; Nelson et al., 2010), and facilitates the advent of well-adapted responses (Medford and Critchley, 2010). For example, the SN supports error detection and prompts relevant task adjustment from executive systems (Ham et al., 2013). In this fashion, the coordination of the SN with others networks enables the emergence of complex behaviors (Bonnelle et al., 2012; Sridharan et al., 2008). Such coordinated interactions between networks seem commonplace during hypnosis (see Fig. 4).

Consistent with previous research linking the SN to the detection and perception of sensory, affective, and interoceptive signals (Menon, 2015; Menon and Uddin, 2010; Uddin, 2014, 2017), SN changes in hypnosis may additionally correspond to altered *awareness* of internal and external events (Demertzi et al., 2016; Jamieson, 2016). Given that hypnotic absorption typically involves focusing attention on a specific subset of mental experiences to the exclusion of others (Maldonado and Spiegel, 2008; Markovic and Thompson, 2016; Ott, 2016; Rainville and Price, 2003; Tellegen and Atkinson, 1974), modulations of SN activity potentially index the monitoring of attentional focus to prioritize relevant signals and keep others outside the scope of awareness. Consistent with this interpretation, one study demonstrated that self-reported level of hypnotic absorption correlated with activity in the anterior insula and cingulate cortices – two core nodes of the SN (Rainville et al., 2002). Moreover, another study reported increased connectivity between the salience and executive networks following hypnotic induction (Jiang et al., 2016). Mounting evidence shows that the salience network mediates interactions between the central executive and default networks (Deshpande et al., 2011; Di and Biswal, 2014, 2015; Jilka et al., 2014; Liao et al., 2010; Sridharan et al., 2008; Yan and He, 2011). Thus, greater CEN and SN cross-network connectivity for HHSIs may facilitate the orientation and maintenance of attentional resources on relevant mental objects throughout the induction process (Deeley et al., 2012; McGeown et al., 2009). However, once again, inconsistent findings undercut one-dimensional explanations and propose a more complex picture.

In addition to alterations between the executive and salience networks, mounting evidence associates hypnotic induction with deactivation of the DN (see Fig. 4) – a robust cortical network com-

Table 2
Neuroimaging studies that investigated hypnotic induction.

Study	Imaging technique	Sample Size/Population	Experiment	Results
Deeley et al. (2012)	*fMRI*	N = 8 HHSIs only	Resting state following hypnotic induction	Positive correlation between self-reported hypnotic depth and CEN. Negative correlation between self-reported hypnotic depth and DN.
Demertzi et al. (2011)	*fMRI*	N = 12 High levels on absorption and dissociation scales	Resting state following hypnotic induction	Increased anterior DN connectivity
Jiang et al. (2016)	*fMRI*	N = 57 LHSIs and HHSIs	Resting state following hypnotic induction	Modulations of the CEN, SN and DN
Lipari et al. (2012)	*fMRI*	N = 1 Hypnotic virtuoso	Resting state following hypnotic induction	Modulations of DN
Maquet et al. (1999)	*PET*	N = 15 HHSIs only	Resting state following hypnotic induction	Modulations of SN and DN
McGeown et al. (2015)	*fMRI*	N = 29 Highly, medium and low hypnotic susceptible individuals	Resting state following hypnotic induction	Reduced connectivity in anterior part of the DN
McGeown et al. (2009)	*fMRI*	N = 18 LHSIs and HHSIs	Resting state following hypnotic induction	Decreased activity in anterior part of the SN and DN
Rainville et al. (1999a,b)	*PET*	N = 8 HHSIs only	Painful and neutral stimulations following a hypnotic induction	Modulations of CEN, SN and DN
Rainville et al. (2002)	*PET*	N = 10 HHSIs only	Resting state following hypnotic induction	Modulations of CEN, SN and DN

prising the mPFC, posterior cingulate cortex (PCC), angular gyrus, and medial temporal lobe. Various explanations may account for the dampening of DN activity in hypnosis. First, prominent models associate DN activation to internal attention and mind-wandering – a form of spontaneous mentation wherein individuals disengage attention from sensory input and engage in task-unrelated thoughts often centering on personal events (Christoff et al., 2009; Fox et al., 2015; Mason et al., 2007; Raichle, 2015; Raichle and Snyder, 2007; Smallwood and Schooler, 2015). Whereas the DN tends to activate in correspondence with episodes of waking rest or internally directed thought, this network typically deactivates when individuals engage in externally oriented tasks (Anticevic et al., 2012; Fox et al., 2005; Greicius et al., 2003). Correspondingly, as we hinted earlier, decreased DN activity during hypnosis may index reductions in mind-wandering following from the engagement of top-down regulatory processes (Lynn et al., 2015).

Cognitive neuroscientists increasingly subdivide the DN into functional subcomponents (Andrews-Hanna et al., 2010, 2014), linking the frontal midline structures particularly with self-referential processing (Andrews-Hanna, 2012). Thus, reduced activity in the anterior part of the DN – specifically the mPFC – may additionally pertain to distortions in the sense of self, which participants commonly report during hypnosis (Cardeña, 2005; Pekala and Kumar, 2007). Other studies have linked modulations of mPFC activity to increased feelings of relaxation following induction (Isotani et al., 2001; Rainville et al., 2002). Such explanations may be complementary: it could be the case that feelings of relaxation proceed from, or indeed cause, the alterations in selfhood characteristic of hypnotic inductions. In sum, induction procedures seem to predominantly alter activity and connectivity among three intrinsic networks in the human brain: the CEN, SN, and DN. These induction-related patterns dovetail with findings concerning hypnotic susceptibility (see Section 3 above), further underlining the importance of these core networks in hypnotic phenomena.

5. Hypnotic suggestions

Suggestions are communicable representations intended to alter emotions, perceptions, cognitions, or ideomotor processes (Halligan and Oakley, 2014). Hypnotic operators frequently convey suggestions via metaphors and mental imagery (Strauss, 1993; Yapko, 2015), as these tactics tend to enhance the potency of hypnotic responses by prompting participants to enact structured mental strategies. Recent evidence highlights the power of imagery to alter perceptual and cognitive processes (Fardo et al., 2015; Pearson et al., 2015). This approach therefore offers a flexible means to aptly guide the response into a specific direction (Jensen and Patterson, 2014). However, hypnosis scantily reduces to imagination (Derbyshire et al., 2004). Suggestions come in several forms, including hypnotic (i.e., administered and carried out following a hypnotic induction), non-hypnotic (i.e., administered and carried out in normal waking consciousness), and post-hypnotic (i.e., coming into effect after termination of the hypnotic session in accordance with an instruction provided during hypnosis). Researchers disagree about the mechanistic differences that characterize these types of suggestion and especially about the relative importance of the induction (Braffman and Kirsch, 1999; Kirsch, 1997; Kirsch and Braffman, 2001; Kirsch and Lynn, 1997, 1999; Lynn et al., 2008). Nonetheless, most agree that an identical suggestion would usually produce greater effects when administered hypnotically or post-hypnotically, compared to when administered in normal waking consciousness (Kirsch et al., 2011; Parris et al., 2013; Terhune and Cardeña, 2016). Regardless of the specific role of induction, the collective evidence demonstrates that suggestions can dramatically sway a wide variety of cognitive processes and propel an equally diverse set of neural responses (Michael et al., 2012).

One striking example of the power of suggestion concerns the capacity for HHSIs to suppress the archetypical Stroop interference effect (Raz et al., 2002). Cognitive scientists typically consider automatic processes, such as the reading response in the Stroop task, to be impervious to conscious cognitive control (e.g., Augustinova and Ferrand, 2014). Yet, converging findings from independent groups demonstrate that a suggestion for alexia can override the ballistic Stroop effect (Augustinova and Ferrand, 2012, 2014; Campbell et al., 2012; Déry et al., 2014; Parris et al., 2012; Parris et al., 2013; Raz and Campbell, 2011; Raz et al., 2003; Raz et al., 2007). Reports have further demonstrated that de-automatization influences neural processing of Stroop stimuli (Casiglia et al., 2010; Raz et al., 2005). In particular, whereas cognitive conflict in incongruent Stroop trials yields increased ACC activity (Pardo et al., 1990), a post-hypnotic suggestion for alexia suppresses this ACC activa-

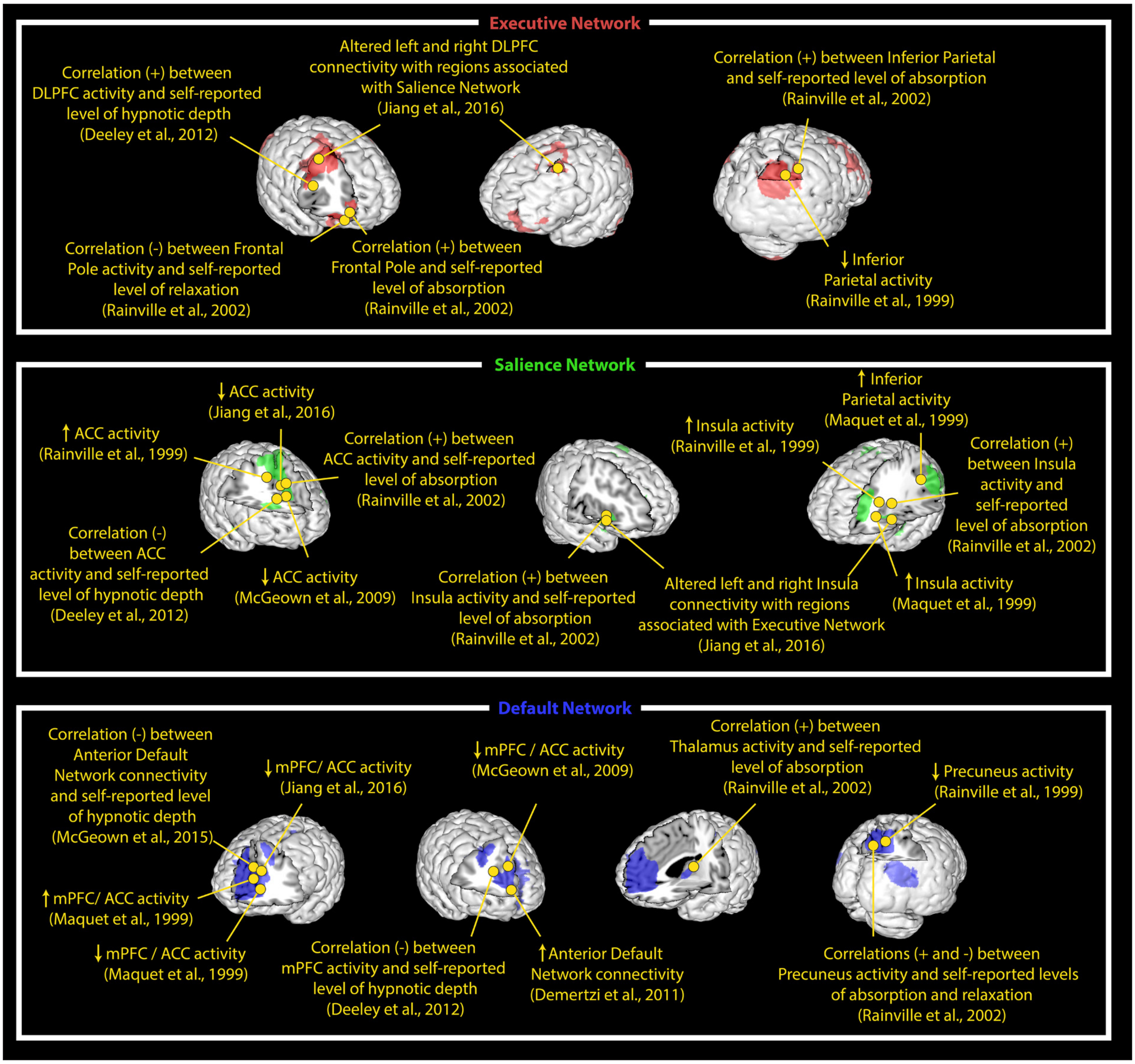

Fig. 4. Neural correlates of hypnotic induction. Regional activations and deactivations, as well as changes in functional connectivity within the central executive, salient, and default networks. ACC = Anterior Cingulate Cortex. DLPFC = Dorsolateral Prefrontal Cortex. mPFC = Medial Prefrontal Cortex. Central Executive Network, Salience Network, and Default networks come from Shirer et al. (2012).

tion (Casiglia et al., 2010; Raz et al., 2005). Beyond the modulation of Stroop interference, targeted suggestions can derail other automatic processes including cognitive conflict in the Flanker (Iani et al., 2006) and Simon tasks (Iani et al., 2009), as well as multisensory integration in synaesthesia (Terhune et al., 2010) and the McGurk paradigm (Déry et al., 2014; Lifshitz et al., 2013a).

While research has yet to clarify the relationship between hypnotic susceptibility and baseline attention abilities (see Section 3), HHSIs certainly seem capable of improving executive control when offered the appropriate suggestion. In other words, suggestions seem to provide HHSIs with the cognitive means to implement reliable top-down strategies. Exploring the mechanisms of hypnotic de-automatization of Stroop interference, a study found that the alexia suggestion hardly impaired semantic processing (Augustinova and Ferrand, 2012). These findings imply that, rather than relying on suppression of the reading response, these effects likely come about via improved response selection. And yet, electrophysiological recordings during suppression of Stroop interference revealed early dampening of lower-level visual processing in extrastriate regions (Raz et al., 2005). Furthermore, a neuroimaging study investigating hypnotic suppression of semantic priming also found limited behavioral effects but significant dampening of activation among several brain regions associated with semantic processing (Ulrich et al., 2015). Altogether, this body of findings intimates that suggestions for alexia likely alter low-level sensory and higher-order cognitive processes, while it remains doubtful that it fully suppresses reading and semantic processing.

Some findings reveal that suggestions can produce similar de-automatization effects even without an induction (Augustinova and Ferrand, 2012; Parris and Dienes, 2013; Raz et al., 2006). The ability to derail automatic processes therefore seems to follow primarily from the suggestions themselves, not from the influence of induction. This general finding lends support to socio-cognitive theories, which propose that hypnosis primarily reflects an extension of cognitive processes such as imagination, expectation and suggestion (Braffman and Kirsch, 1999; Kirsch, 1985, 1991, 1997; Kirsch and Braffman, 2001; Kirsch and Lynn, 1997; Kirsch et al., 1999; Lynn et al., 2008, 2015). Research on suggested hallucinations reinforces this perspective. Studies demonstrate that both hypnotic and non-hypnotic suggestions can alter visual color experiences in HHSIs and modulate concomitant activity in the fusiform area (Kosslyn et al., 2000; Mazzoni et al., 2009; McGeown et al., 2012) – a brain region associated with color perception and other visual recognition functions (Beauchamp et al., 1999; Chao and Martin, 1999). These experiments indicate that inductions only modestly amplify these effects (for similar findings, see Derbyshire et al., 2009, 2016). And yet, whereas the relationship between induction rituals and hypnotic responses remains poorly understood, preliminary findings intimate a potential link at the neural level: one study showed that the degree of DN deactivation brought about by induction correlated with the strength of fusiform response during subsequent hypnotic suggestions for color hallucination (Mazzoni et al., 2013).

Neuroimaging investigations have adopted various approaches to explore the neural mechanisms of hypnotic responses (Lynn et al., 2007). Placating doubts about the authenticity of hypnosis, this body of work highlights the ability for HHSIs to produce responses where the corresponding neural patterns align precisely with the content of the suggestions (see Table 3). Some of these investigations further confirm the authenticity of these responses using a matched simulation condition to control for demand characteristics (Cojan et al., 2009; Derbyshire et al., 2004; Ludwig et al., 2015; Ward et al., 2003). One series of findings demonstrates the accuracy of suggestions in targeting specific phenomenological components of pain (Hofbauer et al., 2001; Price and Rainville, 2013; Rainville et al., 1999a,b, 1997; Rainville and Price, 2004). This research program follows from the discovery that the experience of pain comprises discrete affective and sensory-discriminatory components (Fernandez and Turk, 1992), each associated with particular neural systems (Coghill et al., 1999; Rainville, 2002). Consistent with this double-dissociation, studies indicate that precise analgesia suggestions can selectively alter either one of these components of pain experience, as well as specifically target the corresponding neural systems (Hofbauer et al., 2001; Rainville et al., 1999a, 1997). Hypnotically modulating affective dimensions of pain mainly influences ACC activity, while targeting sensory aspects of nociception influences somatosensory activity. Other investigations report somewhat comparable patterns of responses for instructions aiming to disengage attention from nociceptive events (Faymonville et al., 2000; Faymonville et al., 2003). In addition to unravelling the mechanisms of hypnotic analgesia, such findings underline the precision of hypnosis as an instrument for exploring nuanced dimensions of human consciousness (Cardeña, 2014; Landry et al., 2014; Lifshitz et al., 2013b; Rainville and Price, 2003).

Hypnotic suggestions can alter metal processes and their neural correlates across a wide range of domains (see Table 3). Beyond the pain neuromatrix, findings demonstrate similar effects for visual perception (e.g., Kosslyn et al., 2000), cognitive conflict (e.g., Raz et al., 2005), and ideomotor actions (e.g., Blakemore et al., 2003), to name but a few examples. Yet, whereas hypnotic suggestions may target a wide variety of mental processes, two patterns of brain activity appear to reliably emerge across these different responses. Consistent with findings concerning hypnotic susceptibility and induction reviewed in Sections 3 and 4 above, a large number of reports investigating variations of hypnotic suggestion feature modulations of the executive and salience networks (see Table 3). This collection of evidence intimates that suggested hypnotic responses largely follow from alterations of higher-order control processes, as per the dominant top-down model. However, these seemingly consistent patterns of brain activity hardly expose the underlying mechanisms of hypnosis. Such correlational findings convey only limited information about how CEN and SN dynamics contribute to hypnotic response and could well represent epiphenomenal by-products of hypnosis (Wagstaff, 2000). For example, they might pertain only to the subjective appraisal of the hypnotic experience (Barnier et al., 2008) rather than contribute to the differences in top-down regulation that ostensibly characterize hypnotic responding. Moreover, at least some findings linking the CEN and SN to hypnotic phenomena may in fact reflect task-related, as opposed to hypnotic, effects. As we alluded to previously, modulations of the SN when processing sensory events under hypnosis most likely index an interaction of hypnosis and sensation, rather than a mechanism specific to hypnosis as such. While few studies have adopted fully balanced designs to disentangle these various possibilities (Mazzoni et al., 2013), a single experiment demonstrated the causal influence of a specific brain region in hypnotic response by using rTMS to directly perturb functioning of the DLPFC (see Fig. 2; Dienes and Hutton, 2013). Further investigations along these lines will be necessary to elucidate more precisely how the salience and executive systems contribute to hypnotic responding.

Some evidence provides valuable insights about the functional role of these brain systems in hypnosis beyond these epistemic limitations. Examining a hypnotic suggestion to experience pain, one report unveiled a strong relationship between CEN activity during the initial phase of hearing the suggestion and the intensity of the response at its heights (Raij et al., 2009). Specifically, this study found that activity in the right DLPFC during the initial suggestion phase correlated positively with both self-reported levels of pain intensity and corresponding secondary somatosensory cortex activity at the peak of the response. Activity pertaining to a core hub of the CEN thus forecast the quality of the hypnotic response. Interestingly, analogous DLPFC patterns emerge for the anticipation of pain in the placebo response (Wager et al., 2004). By linking the strength of the hypnotic response to prior CEN activity, this finding supports theoretical proposals relating hypnotic behavior to executive functions. Various explanations may account for these captivating results. For example, this neural pattern may reflect greater attentiveness to the instructions of the operator, wherein more efficient responses follow from greater mental focus (Rainville et al., 2002, 1999b). Or this finding might reveal mounting response anticipation, consistent with the socio-cognitivist view (Lynn et al., 2008) and evidence linking the CEN to response preparation (e.g., Pochon et al., 2001), Finally, increased DLPFC activity during this initial phase can also pertain to the deployment of a suggestion-induced mental strategy to achieve a successful response (Egner and Raz, 2007). This stimulating result therefore opens novel research trajectories to unravel these competing accounts and identify the specific role of the CEN in hypnotic response.

6. A general framework to understand the neural correlates of hypnosis

The heterogeneity of findings across neuroimaging assays of hypnotic phenomena has challenged ongoing efforts to develop a reliable theory of hypnosis. We have proposed a comprehensive synthesis that integrates findings into a cogent framework to overcome this difficulty and identify emerging patterns. Drawing from the burgeoning field of connectomics, our appraisal highlights modulations of the central executive, saliency, and default networks. While hypnotic phenomena do not reduce to interactions between these particular networks, their involvement across numerous studies and experimental conditions ascribe them a central role in hypnosis. Various investigations aiming to uncover the neural correlates of hypnosis support our view (Deeley et al., 2012; Demertzi et al., 2011; Hoeft et al., 2012; Jiang et al., 2016; McGeown et al., 2009). And yet, one might trivialize the notion that hypnotic phenomena relate to changes in large-scale networks involved in higher-order cognition. After all, given the broad range and inherent socio-cognitive complexity of hypnotic phenomena, it seems hardly unexpected that such behaviors would involve modulations in higher-order brain networks. Nevertheless, spec-

Table 3
Neuroimaging studies that investigated hypnotic suggestions.

Study	Imaging technique	Sample Size/Population	Experimental conditions	Results: Modulation of corresponding regions to the suggestion?	Results: Modulation of executive network?	Results: Modulation of salience network
Hypnotic suggestions to modulate pain						
Abrahamsen et al. (2010)	*fMRI*	N = 19 Individuals suffering from temporomandibular pain disorder	Noxious stimulations through (1) Control condition; (2) Hypnotic hypoalgesia; (3) Hypnotic hyperalgesia	**Modulations of pain neuromatrix (PNM)** (Control condition vs. hypnotic hypoalgesia)	**No**	**No**
Aleksandrowicz et al. (2007)	*fMRI*	N = 14	Noxious stimulations through (1) Control condition; (2) Suggestion for analgesia; (3) Hypnotic induction, (4) Hypnotic suggestion for analgesia	**Modulation of PNM** (Control condition vs. Hypnotic induction)	**N/A**	**N/A**
Derbyshire et al. (2004)	*fMRI*	N = 8 HHSIs only	(1) Rest; (2) Noxious Stimulations; (3) Hypnotic functional pain; (4) Imagined pain	**Modulation of PNM** (Hypnotic functional pain vs. rest; hypnotic functional pain vs. noxious stimulation; hypnotic functional pain vs. imagined pain)	**Yes** (Hypnotic functional pain vs. rest; hypnotic functional pain vs. noxious stimulation; hypnotic functional pain vs. imagined pain)	**Yes** (Hypnotic functional pain vs. rest; hypnotic functional pain vs. imagined pain)
Derbyshire et al. (2009)	*fMRI*	N = 13 HHSIs suffering from fibromyalgia	Non-hypnotic and hypnotic suggestions for low, medium and high changes in pain experience	**Modulation of PNM** (Correlation with self-reported pain experience during non-hypnotic and hypnotic suggestions for low, medium and high changes in pain experience)	**Yes** (Correlation with self-reported pain experience during non-hypnotic and hypnotic suggestions for low, medium and high changes in pain experience)	**Yes** (Correlation with self-reported pain experience during hypnotic non-hypnotic and hypnotic suggestions for low, medium and high changes in pain experience
Derbyshire et al. (2016)	*fMRI*	N = 28 HHSIs participants and fibromyalgia patients	Non-hypnotic and hypnotic suggestions for low, medium and high changes in pain experience	**Modulation of PNM** (Hypnotic suggestions for low, medium and high changes in pain experience)	**Yes** (Hypnotic suggestions for low, medium and high changes in pain experience)	**Yes** (Hypnotic suggestions for low, medium and high changes in pain experience)
Hofbauer et al. (2001)	*PET*	N = 10	Inert and noxious stimulation through (1) Control condition; (2) Hypnotic induction (3) Hypnotic suggestion for analgesia (4) Hypnotic suggestion for hyperalgesia	**Modulation of PNM** (Hypnotic suggestion for analgesia vs. hypnotic induction; hypnotic suggestion for hyperalgesia vs. hypnotic induction; hypnotic suggestion for analgesia vs. hypnotic suggestion for hyperalgesia)	**Yes** (Hypnotic suggestion for hyperalgesia vs. hypnotic induction)	**Yes** (Hypnotic suggestion for analgesia vs. hypnotic induction; hypnotic suggestion for hyperalgesia vs. hypnotic induction; hypnotic suggestion for analgesia vs. hypnotic suggestion for hyperalgesia)
Nusbaum et al. (2010)	*PET*	N = 14 Patients with chronic lower back pain showing scores on Stanford Hypnotic Susceptibility Scale: Form R > 3	(1) Rest; (2) Direct and indirect suggestions for analgesia; (3) Direct and indirect hypnotic suggestions for analgesia	**Modulation of PNM** (Rest vs. direct and indirect hypnotic suggestions for analgesia)	**No**	**Yes** (Rest vs. direct and indirect hypnotic suggestions for analgesia)

Table 3 (*Continued*)

Study	Imaging technique	Sample Size/Population	Experimental conditions	Results: Modulation of corresponding regions to the suggestion?	Results: Modulation of executive network?	Results: Modulation of salience network
Raij et al.(2005)	*fMRI*	N = 14 HHSIs only	(1) Noxious stimulation; (2) Hypnotic suggestion for functional pain	**Modulation of PNM** (Correlation of PNM with self-reported feelings of pain following hypnotic suggestion for functional pain)	**No**	**Yes** (Correlation with self-reported feelings of pain following hypnotic suggestion for functional pain)
Raij et al. (2009)	*fMRI*	N = 14 HHSIs only	(1) Hypnotic induction (2) Hypnotic suggestion for functional pain	**Modulation of PNM** (Hypnotic induction vs. hypnotic suggestion for functional pain; Correlation of PNM with S2 for self-reported feeling of pain)	**Yes** (Correlation of ECN with S2 during self-reported feeling of pain)	**Yes** (Hypnotic induction vs. hypnotic suggestion for functional pain; Correlation of PNM with S2 for self-reported feeling of pain)
Rainville et al. (1997)	*PET*	N = 8 HHSIs	Inert and noxious stimulation through (1) Control condition; (2) Hypnotic induction (3) Hypnotic suggestion for analgesia (4) Hypnotic suggestion for hyperalgesia	**Modulation of PNM** (Hypnotic suggestion for analgesia vs. hypnotic induction; hypnotic suggestion for hyperalgesia vs. hypnotic induction;)	**N/A**	**Yes** (Hypnotic suggestion for analgesia vs. hypnotic induction; hypnotic suggestion for hyperalgesia vs. hypnotic induction;)
Rainville et al. (1999a,b)	*PET*	N = 8 HHSIs	Inert and noxious stimulation through (1) Control condition; (2) Hypnotic induction (3) Hypnotic suggestion for analgesia (4) Hypnotic suggestion for hyperalgesia	**Modulation of PNM** (Hypnotic suggestion for analgesia and hyperalgesia vs. hypnotic induction)	**Yes** (Hypnotic suggestion for analgesia and hyperalgesia vs. hypnotic induction)	**Yes** (Hypnotic suggestion for analgesia and hyperalgesia vs. hypnotic induction)
Röder et al. (2007)	*fMRI*	N = 7 HHSIs	Noxious stimulation through (1) Control condition; (2) Hypnotic suggestion for analgesia; (3) Hypnotic suggestion for depersonalization	**Modulation of PNM** (Control condition vs. hypnotic suggestion for analgesia; control condition vs. hypnotic suggestion for depersonalization)	**No**	**Yes** (Control condition vs. hypnotic suggestion for analgesia; control condition vs. hypnotic suggestion for depersonalization)
Wik et al. (1999)	*PET*	N = 8 HHSIs	(1) Control condition (rest); (2) Hypnotic suggestion for analgesia;	**Modulation of PNM** (Control condition vs. hypnotic suggestion for analgesia)	**No**	**No**
Hypnotic suggestions to modulate perception						
Kosslyn et al. (2000)	*PET*	N = 8 HHSIs	Non-hypnotic and hypnotic suggestions to (1) To perceive gray stimulus as grey; (2) To perceive gray stimulus as colorful; (3) To perceive colorful stimulus as grey; (4) To perceive colorful stimulus as colorful.	**Modulation of visual areas** – lingual gyrus and fusiform gyrus – as a function of hypnotic induction and suggestions	**N/A**	**N/A**

McGeown et al. (2012)	*fMRI*	N = 18 LHSIs and HHSIs	Non-hypnotic and hypnotic suggestions to (1) To perceive gray stimulus as grey; (2) To perceive gray stimulus as colorful; (3) To perceive colorful stimulus as grey; (4) To perceive colorful stimulus as colorful; as function of hypnotic susceptibility	**Modulation of expected visual areas** (e.g., lingual gyrus and fusiform gyrus) as a function of suggestions, hypnotic induction and hypnotic susceptibility	**Yes** (Correlation between ECN and self-reported changes in perception following hypnotic suggestion)	**Yes** (Main effect of hypnosis across suggestions; correlation between SN and self-reported changes in perception following hypnotic suggestions)
Szechtman et al. (1998)	*PET*	N = 14 HHSIs	Hypnotic hallucinator vs. nonhallucinator (1) Rest; (2) Hearing auditory stimulus; (3) Imaging hearing the auditory stimulus (4) Hallucinating hearing the auditory stimulus	**Modulation of auditory areas** (albeit for nonhallucinators group)	**N/A**	**N/A**
Hypnotic suggestions to modulate cognition						
Ludwig et al. (2015)	*fMRI*	N = 32 HHSIs	(1) Targeted vs. Non-target food stimulus; (2) Cued vs. uncued posthypnotic suggestion and autosuggestion	**Modulation of ventromedial prefrontal cortex, a brain region often linked with evaluation process during decision making** (Targeted vs. non-targeted food by cue vs. uncued suggestion interaction)	**Yes** (Targeted vs. non-targeted food by Cue vs. uncued suggestion interaction)	**Yes** (Targeted vs. non-targeted food by Cue vs. uncued suggestion interaction)
Mendelsohn et al. (2008)	*fMRI*	N = 23 HHSIs	(1) Individuals sensitive to posthypnotic amnesia (PHA) vs. Individuals not sensitive to PHA; (2) PHA suggestion vs. Cancellation of PHA suggestion	**Reduced activity in regions linked with retrieval process during posthypnotic amnesia** (Individuals sensitive to PHA vs. individuals not sensitive to PHA during following PHA suggestion; PHA suggestion vs. cancellation of PHA suggestion for individuals sensitive to PHA)	**Yes** (PHA suggestion vs. cancellation of PHA suggestion for individuals sensitive to PHA)	**No**
Raz et al. (2005)	*fMRI*	N = 16 LHSIs and HHSIs	Congruent, neutral, incongruent Stroop conditions across: (1) No suggestion vs. Posthypnotic suggestion for alexia (2) Hypnotic susceptibility	**Reduced activity in ACC, a brain region associated with cognitive conflict** (No suggestion vs. posthypnotic suggestion for alexia across hypnotic susceptibility and Stroop conditions)	**Yes** (No suggestion vs. posthypnotic suggestion for alexia across hypnotic susceptibility and Stroop conditions)	**Yes** (No suggestion vs. posthypnotic suggestion for alexia across hypnotic susceptibility and Stroop conditions)

Table 3 (*Continued*)

Study	Imaging technique	Sample Size/Population	Experimental conditions	Results: Modulation of corresponding regions to the suggestion?	Results: Modulation of executive network?	Results: Modulation of salience network
Ulrich et al. (2015)	*fMRI*	N = 24 LHSIs and HHSIs	Congruent and incongruent priming conditions across: (1) No suggestion vs. hypnotic suggestion for alexia (2) Hypnotic susceptibility	**Reduced activity in regions associated with semantic processing, including temporal and supplementary motor areas, as well as pre- and post-central gyri** (Congruent versus incongruent priming conditions across no suggestion and hypnotic suggestion for alexia)	**No**	**Yes** (Congruent versus incongruent priming conditions across no suggestion and hypnotic suggestion for alexia)
Hypnotic suggestions to modulate feelings of agency						
Blakemore et al. (2003)	*PET*	N = 6 HHSIs only	(1) Rest; (2) Real passive movement; (3) Suggested passive movement; (4) Active movement	**Modulations of brain regions associated with feelings of agency** (Suggested passive movement versus Active movement)	**Yes** (Suggested passive movement versus Active movement)	**Yes** (Suggested passive movement versus Rest)
Deeley et al. (2013)	*fMRI*	N = 15 HHSIs only	Hand movement during (1) Control non-hypnotic condition; (2) Hypnotic suggestion for normal awareness of involuntary movement; (3) Hypnotic suggestion for normal awareness of voluntary movement; (4) Hypnotic suggestion for reduced awareness of involuntary movement	**Hypnotic modulations of control and awareness over movements were associated with changes in ideomotor and agency-related brain systems** (Hypnotic suggestions for normal awareness of involuntary movement vs. hypnotic suggestions for normal awareness of voluntary movement; hypnotic suggestions for normal awareness of involuntary movement vs. hypnotic suggestions for reduced awareness of involuntary movement)	**Yes** (Hypnotic suggestions for normal awareness of involuntary movement vs. hypnotic suggestions for normal awareness of voluntary movement)	**Yes** (Hypnotic suggestions for normal awareness of involuntary movement vs. hypnotic suggestions for normal awareness of voluntary movement; hypnotic suggestions for normal awareness of involuntary movement vs. hypnotic suggestions for reduced awareness of involuntary movement)
Deeley et al. (2014)	*fMRI*	N = 15 HHSIs only	Hand movement during (1) Control non-hypnotic condition; (2) Control hypnotic condition; (3) Hypnotic suggestion for impersonal alien control; (4) Hypnotic suggestion for personal external alien control (5) Hypnotic suggestion for personal internal alien control	**Altered phenomenologies of agency linked with modulations of ideomotor, monitoring and agency-related brain systems** (Changes from impersonal to personal interior and exterior feelings of alien control)	**Yes** (Change from impersonal to personal interior and exterior feelings of alien control)	**Yes** (Change from impersonal to personal interior and exterior feelings of alien control)

Walsh et al. (2015)	*fMRI*	N = 18 HHSIs only	Writing during instructions for (1) Voluntary control over thoughts and action; (2) Alien control over thoughts and voluntary control over action; (3) Voluntary control over thoughts and alien control over action; (4) Controlled/simulation condition for alien control over thoughts and action;	**Altered phenomenologies for agency over thoughts and actions link with modulations of ideomotor and agency-related brain systems** (Modulations as a function of voluntary control over thoughts and actions)	**Yes** (Modulations as a function of voluntary control over thoughts and actions)	**Yes** (Modulations as a function of voluntary control over thoughts)
Hypnotic suggestions to induce ideomotor paralysis						
Burgmer et al. (2013)	*fMRI*	N = 19 HHSIs only	Observation and imitation of left and right hands movements during (1) Controlled non-hypnotic condition; (2) Hypnotic left-hand paralysis	**Decreased activity in motor areas during hypnotic paralysis** (Controlled condition vs. hypnotic paralysis as a function of experimental conditions and side)	**Yes** (Controlled condition vs. hypnotic paralysis as a function of experimental conditions and side)	**Yes** (Controlled condition vs. hypnotic paralysis as a function of experimental conditions and side)
Cojan et al. (2009)	*fMRI*	N = 18 HHSIs only	Go-nogo task during (1) Controlled normal condition; (2) Feigned paralysis condition; (3) Hypnotic left-hand paralysis	**Altered connectivity patterns between frontal and parietal regions with motor areas** (Controlled normal condition vs. hypnotic left-hand paralysis)	**Yes** (Controlled normal condition vs. hypnotic left-hand paralysis)	**No**
Deeley et al. (2013)	*fMRI*	N = 8 HHSIs only	(1) Rest; (2) Hypnotic induction; (3) Hypnotic suggestion for left-hand paralysis	**Decreased activity in motor areas during hypnotic paralysis** (Hypnotic induction vs. hypnotic suggestion for left-hand paralysis)	**Yes** (Hypnotic suggestion for left-hand paralysis vs. rest)	**Yes** (Hypnotic induction vs. hypnotic suggestion for left-hand paralysis; rest vs. hypnotic suggestion for left-hand paralysis)
Halligan et al. (2000)	*PET*	N = 1	Preparation for movement and attempted movement of left and right left leg during left-leg hypnotic paralysis hypnotic	**Absence of motor activity during attempted movement**	**No**	**No**
Ludwig et al. (2015)	*fMRI*	N = 12 Susceptible to ideomotor suggestions	For right- and left-hand (1) Controlled condition; (2) Controlled stimulated weakness of right-hand; (3) Controlled simulated paralysis of right-hand; (4) Hypnotic paralysis of right-hand	**Absence of motor activity during attempted movement**	**No**	**Yes** Right hypnotic paralysis vs. left non-paralyzed hand
Pyka et al. (2011)	*fMRI*	N = 19 HHSIs only	(1) Controlled non-hypnotic condition; (2) Hypnotic paralysis of left-hand	**No change in connectivity patterns including primary motor cortex as a function of hypnosis experimental conditions**	**Yes** (Changes in connectivity as a function hypnotic experimental conditions)	**Yes** (Changes in connectivity as a function hypnotic experimental conditions)
Ward et al. (2003)	*PET*	N = 12 HHSIs only	(1) Feigned left-leg paralysis; (2) Hypnotic left-leg paralysis	**No**	**Yes** (Feigned left-leg paralysis vs. hypnotic left-leg paralysis as a function of rest)	**Yes** (Feigned left-leg paralysis vs. hypnotic left-leg paralysis as a function of rest)

ifying the respective functions of the CEN, SN and DN within the context of hypnosis would serve to clarify prevailing theoretical accounts, including the various top-down theories we surveyed. The present framework therefore opens novel avenues for examining how higher-order processes generate the vast array of hypnotic responses.

Our synthesis proposes broad hypotheses regarding the contribution of the CEN, SN and DN to hypnosis (see Fig. 5). In particular, the CEN likely enables the maintenance of attentional focus towards relevant mental representations during cognitive absorption, and may partake in the deployment of reliable mental strategies during the hypnotic response. This interpretation is consistent with a large body of evidence relating this network to mental processes that underlie cognitive flexibility, such as the generation, maintenance, manipulation and updating of mental representations (D'Esposito and Postle, 2015; Rottschy et al., 2012). In this fashion, we propose that CEN-related functions potentially contribute to the generation and maintenance of mental images - a valuable strategy in hypnosis. In turn, this neural pattern likely impacts activity of DN (Chen et al., 2013). Changes in CEN activity during hypnosis may also correspond to altered subjective appraisals of agency during the hypnotic response, as per dissociated and COLD control theories of hypnosis (Dienes and Hutton, 2013; Jamieson and Woody, 2007). Evidence on the neural correlates of agency links this network to retrospective monitoring of fluency between intentions and actions, as well as the resulting sense of control (Chambon et al., 2013; Haggard and Chambon, 2012). With respect to the SN, because this network integrates signals from internal and external sources to govern neural responses to behaviourally relevant and salient events (Uddin, 2017), modulations of this network during hypnosis may correspond to wide-ranging changes in awareness (Demertzi et al., 2016). In addition, this network may coordinate altered CEN and DN dynamics frequently observed during hypnosis (Deeley et al., 2012; Demertzi et al., 2011; McGeown et al., 2009). In this regard, we highlighted the hypothesis that reduced activity in the frontal part of the DN parallels decreases in self-related or internally directed thoughts (Lynn et al., 2015; McGeown et al., 2009). Some components of the DN could also partake in the generation of mental images (Daselaar et al., 2010; Zvyagintsev et al., 2013). In summary, our comprehensive review offers a framework for exploring the neural correlates of hypnotic phenomena. In the next section, we evaluate this general framework by conducting a quantitative meta-analysis of neuroimaging studies concerning hypnosis.

7. Searching for commonalities across findings: a meta-analytic approach

To complement our systematic review, here we report the results of an ALE meta-analysis of the neural correlates of hypnosis. The advantage of this methodological framework lies in the ability to estimate a quantitative response to theoretical questions (e.g., Are hypnotic responses best typified by top-down processes in the CEN and SN or rather by reduced spontaneous cognition in the DN?). In addition, the ALE approach weights results from each study according to respective sample size, thereby affording a better estimate of convergence over multiple studies (Eickhoff et al., 2012; Eickhoff et al., 2009; Fox et al., 2014). Our meta-analytic investigation aimed to ascertain whether common brain patterns emerge across studies of induction and suggestion. Consistent with the idea that the induction and suggestion phases both rely on implementing directives from the hypnotic operator to promote changes in experience and behavior, we collapsed across these two phases of the hypnotic procedure. To characterize the underlying neural correlates of hypnosis, we examined both activation and deactivation signal patterns. We first examined studies that contrasted hypnosis against a control condition outside of hypnosis and then examined the opposite contrast: control condition minus hypnosis. Based on the findings of our systematic review (see Sections 2–5 above), we hypothesized that hypnosis would correspond to activation in regions of the CEN and SN and deactivation in regions of the DN.

7.1. Methods

7.1.1. Identifying neuroimaging studies of hypnosis

We searched for functional neuroimaging studies of hypnosis using various combinations of the following key words in *Google Scholar (scholar.google.com)*; *PubMed* (www.ncbi.nlm.nih.gov/pubmed); and *PsycINFO* (www.apa.org/pubs/databases/psycinfo/): “hypnosis”; “neuroimaging”; “fMRI”; and “PET”. The covered period ranged from 1997 to September 2016. We further refined our search by focusing on experimental studies that reported results from neuroimaging experiments. We also consulted the reference lists of recent reviews (Casale et al., 2012; Halligan and Oakley, 2013; Kihlstrom, 2013; Oakley and Halligan, 2009, 2013) to ensure we included all relevant studies. Our search identified 56 studies (see supplementary material).

7.1.2. Inclusion and exclusion criteria

Our meta-analysis focused only on functional imaging studies of hypnosis (i.e., fMRI and PET); we excluded other imaging assays, such as morphometric investigations (e.g., Horton et al., 2004). We used the following criteria to carefully select pertinent data for our analysis:

(1) Publications had to come from a peer-reviewed scientific journal;
(2) Reports had to include Talairach and Tournoux (1988) or Montreal Neurological Institute (MNI) stereotaxic coordinates for group-wise results;
(3) To assure compatibility with ALE and minimize bias, neuroimaging results had to report peak coordinate foci from whole-brain analysis (Fox et al., 2014);
(4) Studies had to have a reasonable sample size; we excluded case-studies or single-subject data.
(5) To assure quality control, studies had to provide sufficient detail regarding the hypnotic induction procedure;
(6) To isolate the neural correlates of hypnosis, we included only imaging studies that contrasted task-related or resting-state brain activity during hypnosis with comparable brain activity in a matched control condition outside of hypnosis, as well as studies that correlated hypnotic depth with brain activity;
(7) We excluded all investigations that measured the effects of post-hypnotic suggestions, thus limiting our analyses to findings under hypnosis.

Of the initial 56 published papers, a total of 16 studies satisfied the aforementioned criteria: 15 for the first analysis (i.e., hypnosis minus control) and 10 for the second (i.e., control minus hypnosis). The different number of studies in each of the two analyses reflects the fact that certain studies report only activation patterns (i.e., hypnosis > control) or vice versa. We included multiple results from the same published paper if these results came from different experimental conditions or distinct sample groups. We also incorporated two studies with atypical populations (Nusbaum et al., 2010; Wik et al., 1999). The table provided in supplementary material lists all the studies we considered and whether we included or excluded them.

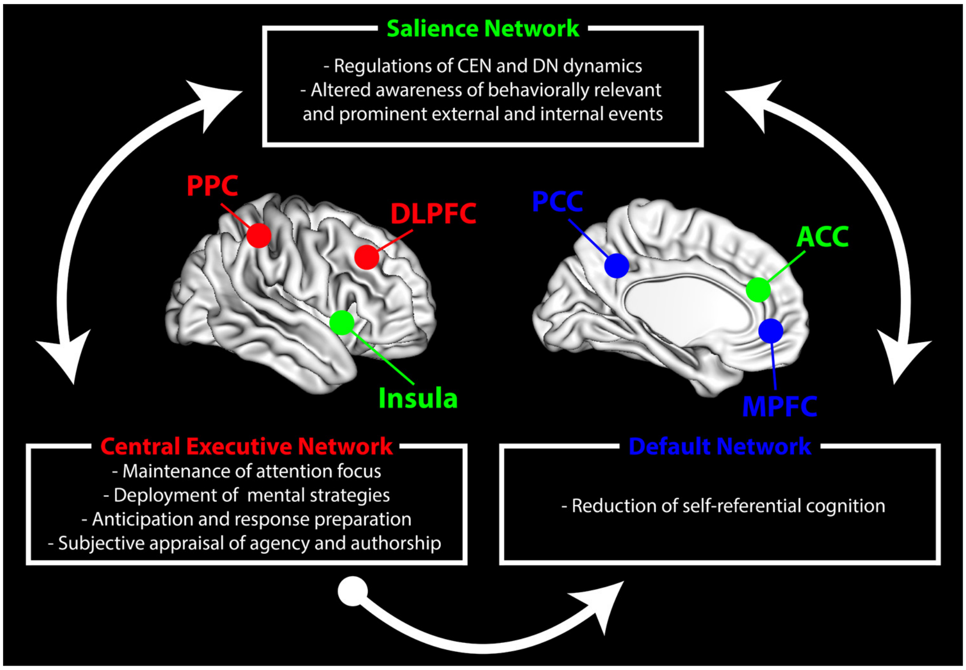

Fig. 5. A general framework for integrating the neural correlates of hypnosis. Within this overarching model, central hubs of the CEN play a central role in maintaining attentional focus on relevant information, deploying mental strategies to produce a reliable hypnotic response, anticipate and prepare the hypnotic response, and appraise the subjective feelings of agency. Moreover, the CEN likely exerts a causal influence over the DN (Chen et al., 2013). The SN regulates CEN and DN dynamics as a function of behaviorally and prominent events. Modulations of this network alter awareness of external and internal signals. Finally, hypnosis relates to reduced DN activity (see Section 4). This neural pattern likely reflect decreased self-referential thoughts during hypnosis. ACC = Anterior Cingulate Cortex. DLPFC = Dorsolateral Prefrontal Cortex. MPFC = Medial Prefrontal Cortex. PCC = Posterior Cingulate Cortex. PPC = Posterior Parietal Cortex.

7.1.3. *Activation likelihood estimates*

ALE is a random-effect quantitative meta-analytic approach developed to isolate common neural patterns across coordinate-based neuroimaging results (Eickhoff et al., 2012; Eickhoff et al., 2009; Turkeltaub et al., 2012). The ALE algorithm, implemented by the *GingerALE 2.3.6* software (San Antonio, TX: UT Health Science Center Research Imaging Institute), considers reported foci as spatial Gaussian probability distributions to yield unitless voxel-wise ALE scores. Specifically, to account for uncertainties, the software applies spatial smoothing to the coordinates as a function of the corresponding sample size. These smoothed values specify the ALE. The software then evaluates these scores against an ALE null distribution that it generates based on random permutations in the same number of foci. The resultant voxel-wise ALE threshold determines significant neural patterns.

Prior to our analyses, we converted the foci from MNI coordinate space into Talairach coordinate space for three studies (Burgmer et al., 2013; Nusbaum et al., 2010; Ulrich et al., 2015) using the *Convert Foci* option in *GingerALE.*

Our first analysis, hypnosis versus control, included 143 foci extracted from 18 experiments (15 studies; N = 252 participants), while our second analysis, control versus hypnosis, comprised 109 foci from 14 experiments (11 studies; N = 182 participants). Because false discovery rate, a prevalent threshold strategy, seems suboptimal for ALE analyses (Chumbley and Friston, 2009), we used a cluster-wise inference threshold method implemented in *GingerALE*, which provides a statistically acceptable trade-off between unfitting and highly-conservative approaches (Eickhoff et al., 2012). Using randomized data simulated from the characteristics of the reported coordinates, this procedure employs a cluster-forming threshold to pinpoint adjacent volumes that surpass the selected value. The cluster-inference procedure determines the minimum cluster size relative to the cluster-forming threshold from a null-distribution of cluster sizes, whereby only a pre-determined proportion of corrected clusters exceeds the level of inference as a function of their volume. We set the cluster-forming threshold to an uncorrected $p < 0.001$, a conservative voxel-wise value, and the cluster-inference threshold to 1%, a conservative threshold (Fox, 2007, February 23rd). Due to our strong a priori hypotheses regarding the involvement of clusters in the CEN, SN and DN, and despite our small sample size, we performed additional analyses using more lenient cluster-forming (<0.005) and cluster inference threshold (5%). These additional analyses fail to add meaningfull results.

We used the Multi-Image Analysis image-viewing software (*MANGO*; San Antonio, TX: UT Health Science Center Research Imaging Institute) to visualize all results.

7.2. *Results*

The first analysis – i.e., hypnosis minus control – unraveled a single activation cluster located in lingual gyrus (see Fig. 6). Five studies contributed to this cluster (Burgmer et al., 2013; Cojan et al., 2009; Maquet et al., 1999; McGeown et al., 2012; Rainville et al., 2002). No cluster survived the clustering inference in the second analysis focusing on deactivations – i.e., control minus hypnosis. Adopting more lenient statistical clustering criteria yielded the same results. Our results therefore highlight activation clusters in the visual area as the sole reliable neural pattern relative to the current body of neuroimaging findings.

7.3. *Discussion of results from ALE*

We aimed to uncover reliable neural correlates of hypnosis using a meta-analytic approach. Instead of revealing changes in the CEN, SN or DN and supporting our hypotheses, our ALE results associate hypnosis with activation in the medial lingual gyrus (see Fig. 6), an occipital region mainly involved in higher-order visual processing (Machielsen et al., 2000; Mechelli et al., 2000).

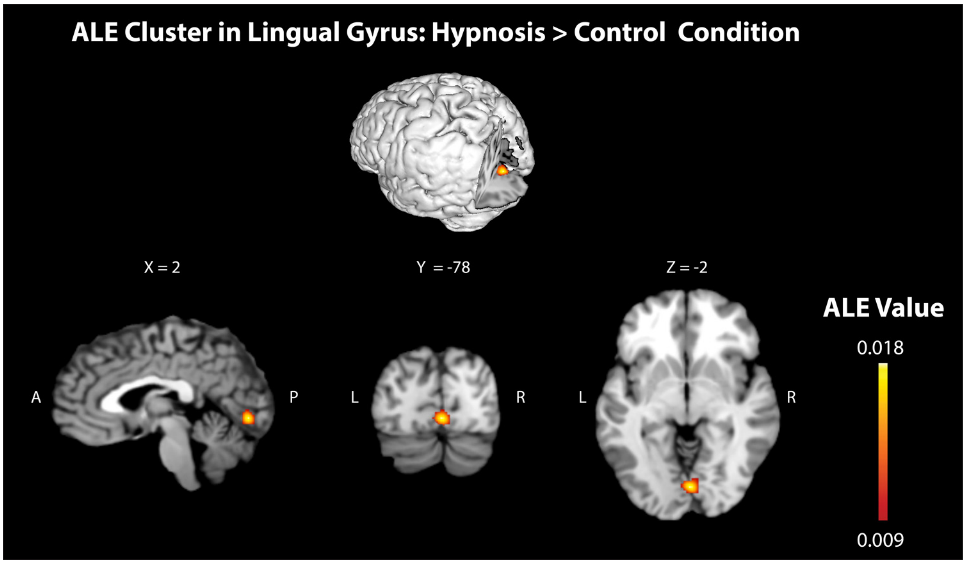

Fig. 6. Meta-analytic activation patterns related to hypnosis (Hypnosis > Control Condition) across the entire brain. Color bar indicates ALE values. Stereotaxic coordinates according to Talairach and Tournaux Atlas.

At least two explanations may account for this result. On the one hand, activation in these visual areas may reflect an intrinsic component of hypnosis, wherein mental imagery plays a central role in driving hypnotic phenomena (Bowers, 1992; Glisky et al., 1995; Hilgard, 1970; Lynn and Rhue, 1986; Nadon et al., 1987; Spanos, 1991). Supporting this construal, a body of evidence links the lingual gyrus to mental imagery (Ganis et al., 2004; Rosenbaum et al., 2004; Stokes et al., 2009). Moreover, as we briefly alluded to earlier, imagery represents a reliable tool for altering perception (Fardo et al., 2015), cognition (Tartaglia et al., 2009), and motor action (Hétu et al., 2013). Our result therefore promotes the idea that mental imageries represent common strategies in the production of reliable hypnotic responses. On the other hand, the significant clusters in the lingual gyrus could pertain to suggestion-specific effects, confining these findings to the domain of visual perception. Two of the five contributing studies to the significant cluster aimed specifically to bring about changes in visualization (McGeown et al., 2012; Maquet et al., 1999); and yet, the other three studies sought to induce non-visual effects – either hypnotic paralysis of the hand (Cojan et al., 2009; Burgmer et al., 2013) or a general hypnotic state (Rainville et al., 2002). Hence, this latter interpretation appears unlikely. Beyond these divergent accounts, and contrary to our predictions, the current meta-analytic results highlight sensory-based mental processes as a reliable marker of hypnosis and underscore the involvement of neural activity beyond the top-down view.

Several limitations may account for the absence of significant ALE findings relative to our leading hypotheses. The main limitation of the present approach pertains to the modest sample size (i.e., number of included papers), which compromises the ability of ALE to accurately identify de/activation patterns. The absence of a standardized experimental approach in neuroimaging studies of hypnosis (Mazzoni et al., 2013; Oakley and Halligan, 2010) further compounds this caveat. Moreover, we had to exclude most imaging studies because they featured a strong reliance on hypothesis-driven analytical strategies, which are largely incompatible with the underlying assumptions of quantitative meta-analytic approaches. At the same time, our sample size is comparable to other recently-published ALE meta-analyses and should be appropriate to detect relevant effects (e.g., Bisenius et al., 2015; Fox et al., 2015). The inherent heterogeneity of hypnotic phenomena – i.e., as a function of inter-individual differences and discrepancies across hypnotic suggestions – may further undermine generalizability (Barber, 1999; Landry and Raz, 2015, 2016; Laurence et al., 2008; Spiegel and Barabasz, 1988; Terhune et al., 2010, 2011c). Collapsing results over a wide variety of neural effects considerably flattens differences in the data. This limitation speaks to a weakness of many a meta-analysis: such approaches miss fine-grained nuances that may well be pertinent.

8. Conclusion

Despite the growing number of neuroimaging studies probing hypnosis, there remains little consensus concerning the neural mechanisms and a great deal of inconsistency among findings (Landry and Raz, 2015; Raz, 2011a). The multifaceted nature of hypnosis, combined with the dearth of coherent methodological standards in the field, likely account for this heterogeneity of results. We conducted a comprehensive review and quantitative meta-analysis of neuroimaging findings to assess the reliability of brain patterns associated with hypnosis. We grounded our appraisal in leading theoretical perspectives featuring top-down mental processes such as attention, executive control, and cognitive monitoring, as well as their putative neural correlates. Our review highlighted the CEN, SN and DN as key networks implicated in hypnotic susceptibility, hypnotic induction, and response to hypnotic suggestions. Activity and connectivity both within and between these higher-order networks seem to support mental absorption and facilitate the deployment of reliable top-down strategies for producing hypnotic responses. In addition, these network dynamics may contribute to reduced awareness of extraneous events and decreased episodes of mind-wandering. Our overarching synthesis highlights novel ways to link higher-order neurocognitive processes with hypnotic phenomena. We carried out the ALE meta-analysis to quantify brain patterns associated with hypnosis. However, instead of confirming the role of higher-order networks, our ALE analysis revealed that hypnotic responses correlate most robustly with activation of the lingual gyrus, likely indexing mental imagery. Whereas several limitations may account for the absence of predicted CEN, SN or DN clusters in our meta-analysis, our results nonetheless invite researchers to explore hypotheses beyond the top-down model of hypnosis. Collectively, our systematic review and meta-analysis pave the road to a more scientific understanding of the dramatic subjective, behavioral, and neurobiological phenomena that fall under the rubric of hypnosis.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.neubiorev.2017.02.020.

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