

Functional Brain Basis of Hypnotizability

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Audio Interview

Context: Focused hypnotic concentration is a model for brain control over sensation and behavior. Pain and anxiety can be effectively alleviated by hypnotic suggestion, which modulates activity in brain regions associated with focused attention, but the specific neural network underlying this phenomenon is not known.

Objective: To investigate the brain basis of hypnotizability.

Design: Cross-sectional, in vivo neuroimaging study performed from November 2005 through July 2006.

Setting: Academic medical center at Stanford University School of Medicine.

Patients: Twelve adults with high and 12 adults with low hypnotizability.

Main Outcome Measures: Functional magnetic resonance imaging to measure functional connectivity networks at rest, including default-mode, salience, and executive-control networks; structural T1 magnetic resonance imaging to measure regional gray and white matter volumes; and diffusion tensor imaging to measure white matter microstructural integrity.

Results: High compared with low hypnotizable individuals had greater functional connectivity between the left dorsolateral prefrontal cortex, an executive-control region of the brain, and the salience network composed of the dorsal anterior cingulate cortex, anterior insula, amygdala, and ventral striatum, involved in detecting, integrating, and filtering relevant somatic, autonomic, and emotional information using independent component analysis. Seed-based analysis confirmed elevated functional coupling between the dorsal anterior cingulate cortex and the dorsolateral prefrontal cortex in high compared with low hypnotizable individuals. These functional differences were not due to any variation in brain structure in these regions, including regional gray and white matter volumes and white matter microstructure.

Conclusions: Our results provide novel evidence that altered functional connectivity in the dorsolateral prefrontal cortex and dorsal anterior cingulate cortex may underlie hypnotizability. Future studies focusing on how these functional networks change and interact during hypnosis are warranted.

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HYPNOSIS IS THE OLDEST Western conception of psychotherapy and a powerful means of altering pain, anxiety, and various somatic functions, even under highly stressful circumstances, such as during interventional radiology procedures and breast cancer surgery.¹⁻⁵ Hypnotic alteration of perception, most thoroughly studied in the somatosensory and visual systems, involves a top-down resetting of perceptual response itself rather than just an alteration in postperception processing, with reduction in early (p100) and late (p300) components of somatosensory event-related potential⁶ and reduced activity of dorsal anterior cingulate (dACC) and somatosensory cortices during hypnotic analgesia.⁷⁻⁹ Hypnotic alteration of color vision results in congruent changes in blood flow in the lingual and fusiform

gyri.¹⁰ Hypnotic suggestion can reduce or eliminate the well-known Stroop color-word interference phenomenon, with concomitant reduction in activation of the dACC.¹¹⁻¹³ The time delay in naming a color word presented in a different color is mediated by the interaction between the dorsolateral prefrontal cortex (DLPFC) and dACC.¹⁴ This is an example of how hypnosis can provide a model system for brain control over perception and behavior. Such hypnotic reduction of similar interference tasks has been found in some studies¹⁵ to occur only when the hypnotic state is induced rather than as a trait difference.

The capacity to exert this top-down processing control varies considerably among people. Although most children are highly hypnotizable, substantial variation in responsiveness to hypnosis develops in adult life. Hypnotizability then becomes a stable trait, with a test-retest correlation of 0.7 dur-

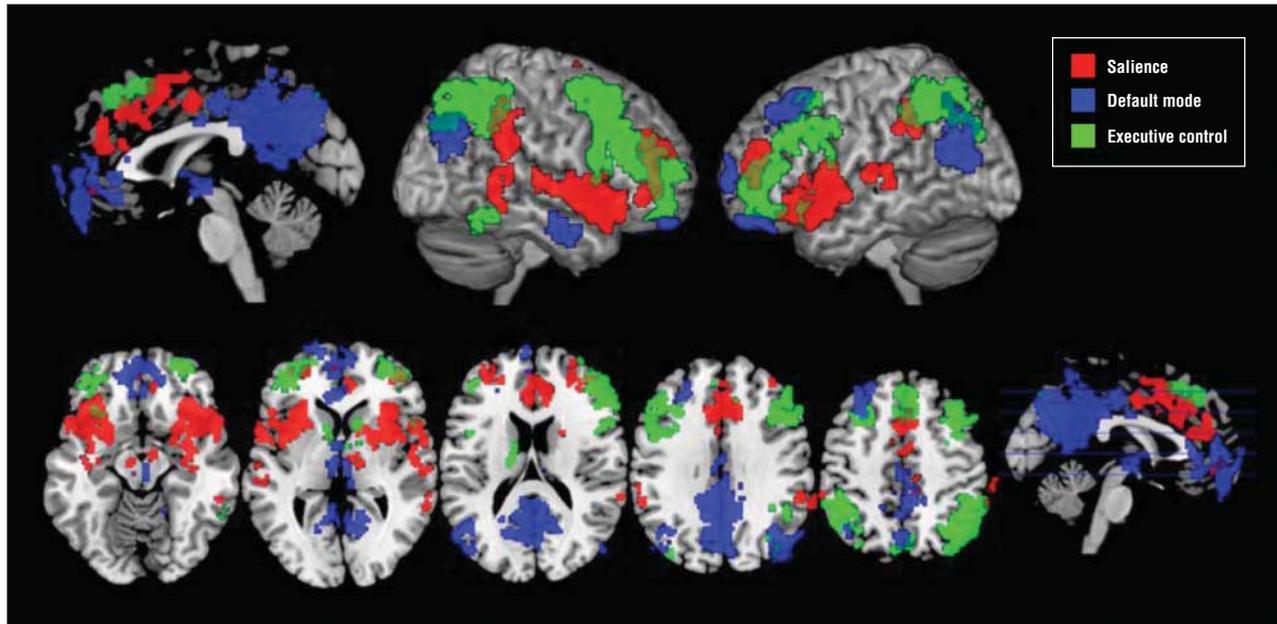


Figure 1. Templates used to select decomposed spatial maps for each network per study participant.

ing a 25-year interval.¹⁶ Despite this reliability, few meaningful correlates of this trait, either psychological or neurobiological, have been identified despite many efforts to do so.^{11,12,17,18} This remains a major challenge for the field. Clear understanding of brain functional correlates of hypnotizability would improve effective application of hypnosis in clinical settings and provide insights into the brain basis of sensory modulation and hypnotizability.

Attention has long been described as a phenomenon of narrowing and focusing of senses by philosophers, including Aristotle, Lucretius, and Descartes, which is similar to how hypnotic induction is described.¹⁹ The dACC and lateral prefrontal cortex (PFC) may contribute importantly to hypnotizability and sensory control. These regions are thought to be involved in the executive network of attention, including selective attention and conflict resolution.²⁰ The dACC and lateral PFC are also targets of the mesocortical dopamine system,¹¹ and hypnotizability has been correlated with levels of homovanillic acid, a dopamine metabolite, in the cerebrospinal fluid.²¹ High hypnotizable individuals, but not low hypnotizable individuals, have altered activation in the dACC^{7-9,12,22-27} and PFC^{7,11,23,24} when modulating pain perception, reducing Stroop interference, and during rest when they are in vs out of hypnotic states.²⁸ This finding suggests that these 2 brain regions are involved in top-down modulation of perception during hypnosis. The implication of these findings is that there should be detectable differences in functional connectivity between these regions when comparing high and low hypnotizable individuals and that such a difference in functional brain organization may be essential in determining who is and is not hypnotizable and therefore who is capable of top-down sensory modulation.

To examine the functional brain basis of hypnotizability, we compared matched groups of 12 healthy high hypnotizable and 12 low hypnotizable individuals on measures of (1) functional magnetic resonance imaging (MRI)

of brain blood oxygenation level–dependent response during the resting state,²⁹⁻³³ (2) high-resolution T1 structural MRI to examine voxel-based morphometry of gray and white matter, and (3) diffusion tensor imaging (DTI) fiber tractography to examine white matter microstructure. For the resting functional MRI scan, independent component analysis (ICA) was performed and an automated, 2-step process³⁴ was used to select the component in each person that most closely matched the default-mode, saliency, and executive-control resting state networks^{35,36} (**Figure 1**). The *default-mode network* involves the posterior cingulate cortex and precuneus, medial prefrontal and pregenual cingulate cortices, temporoparietal regions, and medial temporal lobes and is implicated in episodic memory retrieval, self-reflection, mental imagery, and stream-of-consciousness processing.^{32,37-39} The *saliency network* includes the dACC, fronto-insular cortices, and limbic structures and is involved in detecting, integrating, and filtering relevant somatic (interoceptive), autonomic, and emotional information.^{35,39} The *executive-control network* involves the DLPFC and lateral parietal cortices and is required for the selection and maintenance in working memory of relevant information necessary for action preparation.^{35,39} We hypothesized that there would be functional differences in and between brain networks that involve regions associated with attention and executive-control (dACC and DLPFC) between the high hypnotizable and low hypnotizable groups.

METHODS

STUDY PARTICIPANTS

Twenty-four individuals (12 high hypnotizable and 12 low hypnotizable individuals) participated as paid volunteers recruited through lectures about hypnosis and advertisements that asked, “Are you interested in finding out how hypnotizable you

Table 1. Demographic Characteristics of the Study Participants

Characteristic	High	Low
Age, mean (SD), y	22.8 (4.7)	26.1 (5.1)
HIP score, mean (SD)	8.48 (0.84)	0.79 (1.01)
Sex, F/M, No.	6/6	6/6
Handedness, left/right, No.	1/11	1/11

Abbreviation: HIP, Hypnotic Induction Profile.

are?" (Table 1). The participants in the study (performed from November 2005 through July 2006) were included in the high hypnotizable group if they scored 7 to 10 and in the low hypnotizable group if they scored 0 to 3 on the Hypnotic Induction Profile (HIP; range, 0-10).⁴⁰ The HIP is a structured hypnotic induction that assesses subjective and behavioral response to hypnotic suggestion of the following: (1) dissociation; (2) levitation of the hand following its being lowered; (3) a sense of involuntariness during elevation of the hand; (4) response to the signal cutting off the instruction of lightness and movement; and (5) a sensory alteration of floating, lightness, or buoyancy. Handedness was determined using the Edinburgh Handedness Questionnaire-Revised.²² Individuals had no neurologic or psychiatric disorders, were not taking any medication, and had no contraindications to MRI. By design, a significant difference was found in the HIP scores between the 2 groups ($t_{22}=20.24, P<.001$). No significant differences were found in age, handedness, or sex between the groups (sex and handedness: $\chi^2=0, P>.99$; age: $t_{22}=1.61, P=.12$) (Table 1). The median duration between these assessments and the MRI session was 2 months 1 day (range, 0 months to 8 months 20 days). The study was approved by the Stanford University Panel on Human Subjects in Medical Research, and informed consent was obtained. Supplementary methods are available in the eAppendix (<http://archpsyc.jamanetwork.com/journal.aspx>).

FUNCTIONAL MRI

Image Acquisition

All functional MRIs and structural MRIs of each participant's brain were acquired at the Lucas Center (Stanford University) using a 1.5-T GE Signa scanner and a standard GE whole-head coil (Lx platform; GE Medical Systems). Participants underwent a 6-minute resting-state scan in which they were given no specific instructions except to keep their eyes closed and hold still: T2*-weighted, gradient-echo spiral pulse sequence⁴¹; 30 axial sections (anterior commissure–posterior commissure aligned); 4-mm thick; 1-mm skip; repetition time (TR), 2500 milliseconds; echo time (TE), 40 milliseconds; flip angle, 85°; 1 interleave; field of view (FOV), 22 cm; and matrix size, 64 × 64.

Data Processing

Data were preprocessed using Statistical Parametric Mapping (SPM2; <http://www.fil.ion.ucl.ac.uk/spm>) using standard methods. Specifically, images were section-time corrected, realigned, and normalized to the functional (echo planar image) Montreal Neurological Institute template (12-parameter affine transformation, nonlinear normalization using 7 × 8 × 7 basis functions, resampled to 2-mm voxel).⁴² Images were then smoothed with an isotropic gaussian kernel of 4-mm full width at half maximum. Then, ICA was performed on these images

using FSL melodic software (<http://fsl.fmrib.ox.ac.uk/fsl/melodic/>).

Component Selection

An automated 2-step process as described in the article by Greicius et al³⁵ was then used to select the component in each participant that most closely matched the salience, default-mode, and executive-control networks using Matlab (Mathworks) (Figure 1). First, if a high-frequency signal (<0.1 Hz) constituted 50% or more of the total power in the Fourier spectrum, a frequency filter was applied to remove any components. Second, templates of these networks, which were derived from a separate group of 14 healthy controls, were used to select the best fit of the remaining low-frequency components in each participant. This was done by using a nonlinear template-matching procedure that involves taking the mean *z* score of voxels falling within the template minus the average *z* score of voxels falling outside the template and selecting the component in which this difference (the goodness of fit) was the greatest.

Goodness-of-Fit Scores

To test how well this approach works in selecting uniquely representative components and to be certain that the approach did not differ across groups, we compared the mean goodness-of-fit scores for the best-fit component and the second best-fit component within and across groups using paired and 2-sample *t* tests, respectively. All group analyses were performed on the participants' best-fit component images. Across the 24 participants, the mean (SD) goodness-of-fit score was 0.99 (0.36) for the salience network best-fit component, which was significantly larger than the second best-fit component (0.65 [0.21]; $t_{23} = 5.55; P < .001$). The 2 groups did not differ in their mean (SD) goodness-of-fit score for the best-fit component (high hypnotizability group, 1.06 [0.40]; low hypnotizability group, 0.97 [0.35]; $t_{22} = 0.62; P = .54$) or the second best-fit component (high hypnotizability group: 0.70 [0.19]; low hypnotizability group: 0.62 [0.25]; $t_{22} = 0.82; P = .42$). These data suggest that our automated selection procedure was effective in selecting a unique component in each participant that corresponds to the salience network and further that the selection procedure worked equally well across the 2 groups. The default-mode and executive-control networks produced similar effects (default-mode network: high hypnotizability group: mean [SD], 1.96 [0.69]; low hypnotizability group: mean [SD], 1.83 [0.56]; $t_{22} = 0.50; P = .62$, between the first and second best-fit components: $t_{23} = 6.9; P < .001$; executive-control network: high hypnotizability group: mean [SD], 1.58 [0.65]; low hypnotizability group: mean [SD], 1.65 [0.69]; $t_{22} = 0.24; P = .81$, between the first and second best-fit components: $t_{23} = 6.7; P < .001$).

Statistical Analysis

First, using SPM2, decomposed spatial maps from the selected components were submitted to 1-sample and 2-sample *t* tests to compare the salience, default-mode, and executive-control networks between the 2 groups. Significant clusters were determined using the joint expected probability distribution⁴³ with height ($P = .01$) and cluster extent ($P = .01$ familywise error corrected) thresholds. To obtain a measure of effect size of the salience network, we created a whole-brain Cohen *d* map comparing the high and low hypnotizability groups.⁴⁴ Statistical maps were superimposed on T1 templates using MRIcro and cluster locations interpreted using known neuroanatomical landmarks. Statistical images were overlaid onto the MRIcro (<http://www.sph.sc.edu/comd/rorden/mricro.html>) template image

for viewing. To aid in localization, peak coordinates of brain regions with significant effects were converted from Montreal Neurological Institute to Talairach space using the mni2tal function (<http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach>). Brain regions were identified from these x, y, and z coordinates using Talairach Daemon (Research Imaging Center, University of Texas Health Science Center in San Antonio) and confirmed with the Talairach atlas.⁴⁵

Second, confirmatory seed-based functional connectivity analyses were performed by calculating Pearson product moment correlation coefficients using extracted time series of the DLPFC and dACC regions defined from the ICA between-group analyses of the salience network. This was calculated for each participant separately and by removing spurious sources of variance similar to Whitfield-Gabrieli et al⁴⁶ by using white matter and cerebrospinal fluid time series. Fisher r-to-z transformation was performed to compare difference between the high and low hypnotizable groups.

Finally, decomposed time series from selected components for the default-mode, salience, and executive-control networks were correlated with one another to examine the relationships between different networks in Matlab. These data were calculated for each participant separately. Fisher r-to-z transformation was performed and compared between the high and low hypnotizability groups.

VOXEL-BASED MORPHOMETRY

Image Acquisition

A 3-dimensional, high-resolution, T1-weighted anatomical gradient and a receptive field, spoiled gradient recalled pulse sequence with the following parameters were used: TR, 9 milliseconds; TE, 1.8 milliseconds; flip angle, 15°; number of excitations, 1; matrix size, 220 × 220; FOV, 22 cm; and 124 contiguous sections of 1.2-mm width.

Data Processing

Data processing and statistical analysis were performed using SPM2. Optimized and modulated voxel-based morphometry techniques were performed as described in the article by Good et al.⁴⁷

Statistical Analysis

Between-group differences of regional gray and white matter were compared using independent sample *t* tests. Significant clusters of activation were determined using the joint expected probability distribution⁴³ with height ($P = .01$) and extent ($P = .01$) thresholds, which were familywise error corrected at the whole-brain level and for nonisotropic smoothness. A lenient threshold of $P = .001$ (uncorrected) was also used to confirm that no significant effects were found at the corrected threshold.

DIFFUSION TENSOR IMAGING

DTI Acquisition

The DTI sequence was based on a single-shot, spin-echo, echo-planar imaging sequence with diffusion-sensitizing gradients applied on either side of the 180° refocusing pulse.⁴⁸ Imaging parameters for the diffusion-weighted sequence were as follows: FOV, 26 cm; matrix size, 128 × 128; TE, 58.1 milliseconds; TR, 4500 milliseconds; 60 axial-oblique sections; and

section thickness, 2 mm. Diffusion weighting was $b = 815$ s/mm². In addition, 2 reference measurements ($b0$ scans) were performed and averaged for each section after removing the diffusion-sensitizing gradients. Diffusion was measured along 12 noncollinear directions. This pattern was repeated 6 times for each section, with the sign of all diffusion gradients inverted for odd repetitions.

DTI Processing

First, diffusion-weighted images were corrected for eddy-current distortions and head motion using linear image registration (Automated Image Registration algorithm).⁴⁹ Thereafter, DtStudio⁵⁰ (<https://www.mristudio.org>) was used.

Diffusion Tensor Fiber Tracking

All analyses were performed using DtStudio⁵¹ by a researcher masked to the individual's group assignment. Fiber tracking was performed using the Fiber Assignment by Continuous Tracking method,⁵² and regions of interest (ie, the left DLPFC and dACC) were derived based on regions that were in the resting state functional connectivity analysis ($P = .01$ corrected).

Descriptive statistics, including fractional anisotropy, apparent diffusion coefficient, fiber volume (in voxels), and density (number of fibers per voxel) for each selected group of fibers, were collected and included in the overall between-group statistical analysis. Planned between-group comparisons (high vs low hypnotizable groups) were conducted using 2-sample *t* tests with a statistical threshold of $P < .05$ (2-tailed).

RESULTS

With the use of ICA, direct comparison of salience network ICA maps between the high hypnotizable group compared with the low hypnotizable group revealed increased functional connectivity between one brain region that is central to the salience network, the dACC ($P = .004$ corrected), and the left DLPFC ($P = .01$ corrected; **Figure 2A** and **Table 2**). A whole-brain Cohen *d* map comparing the high and low hypnotizable groups for the salience network revealed large effect sizes in the left DLPFC and the dACC (bilateral with peak centered on left hemisphere) regions ($d > 0.8$; Figure 2A). In no brain region did the high hypnotizable group display reduced connectivity in the salience network compared with the low hypnotizable group.

These results were supplemented by the high hypnotizable group showing left DLPFC, normally found as part of the executive-control network, incorporated into the salience network during rest, which included the dACC, whereas this did not occur in the low hypnotizable group ($P = .01$ corrected; Figure 2B). The 2 groups did not differ reliably in functional connectivity within the default-mode or executive-control network.

Confirmatory seed-based analyses were performed by examining temporal associations between time series of the left DLPFC and dACC regions. Significantly greater functional connectivity was found between the left DLPFC and dACC regions in the high hypnotizable group compared with the low hypnotizable group (high hypnotizable group: mean $z = 0.60$; low hypnotizable group: mean $z = 0.23$; $P < .001$; Figure 2C).

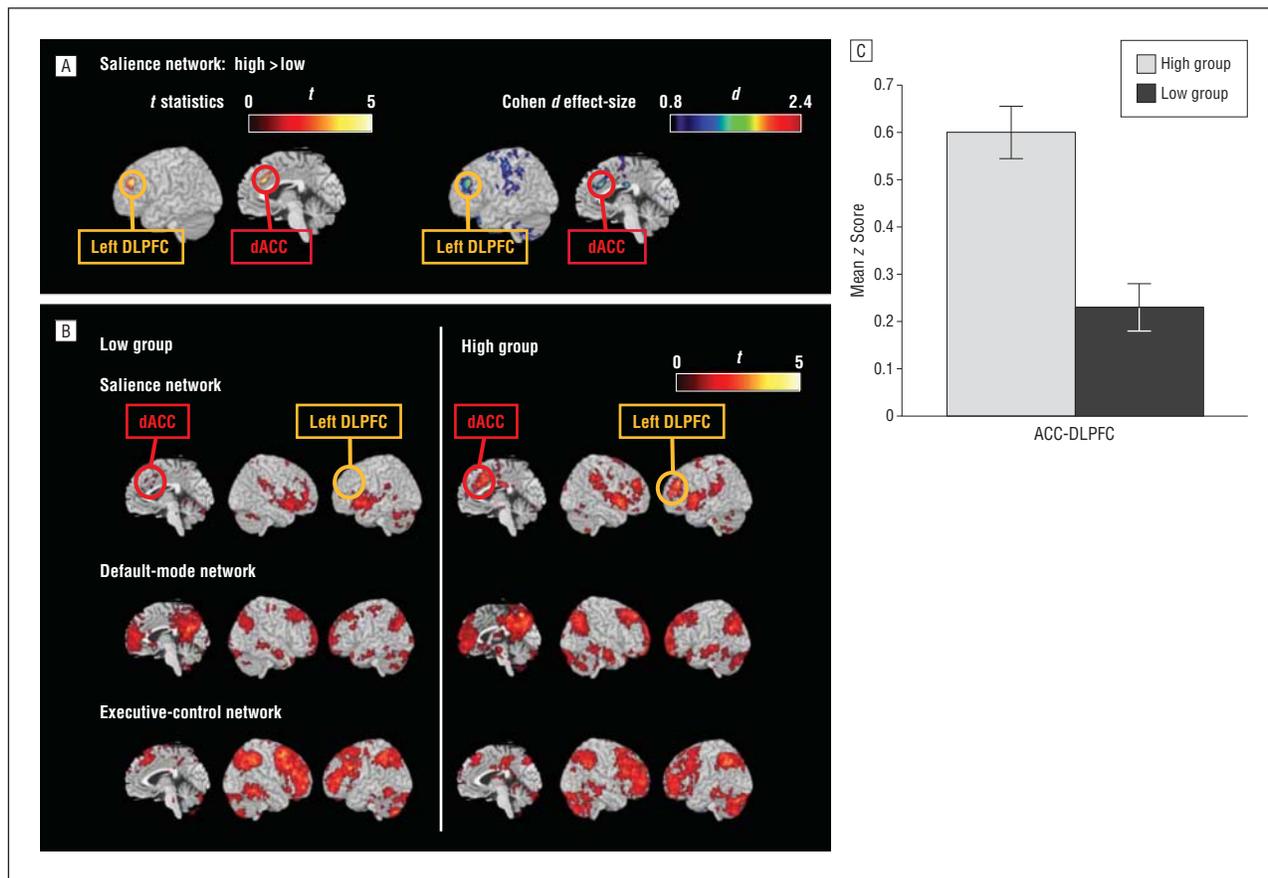


Figure 2. Functional connectivity in the high and low hypnotizable groups within each network. A, Difference in independent component analysis maps of the salience network between the high and low hypnotizable groups. Brain regions show significantly greater connectivity in the high compared with the low hypnotizable groups using *t* tests (left) and large effect size (right). B, Significant clusters derived from 1-sample *t* tests of independent component analysis maps for the salience, default-mode, and executive-control networks for individuals with high and low hypnotizability. Coactivation of left dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex (dACC) is seen in high but not in low hypnotizable individuals in the salience network. C, Mean *z* scores for seed-based correlations show significantly higher functional connectivity between left DLPFC and dACC among high compared with low hypnotizable individuals.

Table 2. Clusters Obtained From 2-Sample *t* Tests Showing Significantly Greater Functional Connectivity in the High Compared With the Low Hypnotizable Group

Brain Region	Brodmann Area	Talairach Coordinates			z Score	P Value	Cluster Size, Voxels
		x	y	z			
Left middle frontal gyrus	46,9,10	-40	40	22	4.036	.01	191
Anterior cingulate, cingulate, and medial frontal gyri	32,9	-2	29	26	3.891	.004	247

Furthermore, the ICA time series extracted for each participant from the executive-control and salience networks revealed a consistent profile of higher correlation in the high hypnotizable group compared with the low hypnotizable group (high hypnotizable group: mean $z = 0.75$, low hypnotizable group: mean $z = 0.10$, between-group comparison: $P = .07$). No significant difference was found in functional connectivity between the default-mode and both the salience ($P = .21$) and the executive-control networks ($P = .17$).

The high and low hypnotizable groups did not differ on any measures of brain structure, including total volumes (gray: $t_{22} = 0.17$, $P = .87$; white: $t_{22} = 0.47$, $P = .64$) or regional voxel-by-voxel volumes using voxel-based

morphometry techniques ($P = .01$ corrected). Differences were found in the parietal, temporal, and cerebellar regions only when the threshold was reduced to $P = .001$ uncorrected but even then not in the dACC or DLPFC, where differences were seen in functional connectivity between the high and low hypnotizable groups. The DTI analyses of fractional anisotropy (typically representing greater white matter integrity), apparent diffusion coefficient (typically representing white matter organization), fiber volume (in voxels), and density (number of fibers per voxel) within the fiber tracts, identified by placing seeds in the DLPFC, dACC, or both from the functional connectivity analysis, revealed no significant differences between the groups ($P = .10$ for all). This find-

ing suggests that the observed differences in *functional* connectivity were not due to gross regional volumetric or *structural* connectivity differences.

COMMENT

We found that functional brain differences during the resting state were related to hypnotizability. High vs low hypnotizable individuals had significantly greater involvement of the DLPFC region, a key node of the executive-control network, in the salience network. Convergent on these findings from ICA, seed-based analysis confirmed elevated coupling between the dACC and the DLPFC in high compared with low hypnotizable individuals. These findings provide novel evidence for cross-network coupling in high hypnotizable individuals. Additional analyses revealed that functional differences were not associated with structural (regional gray and white matter voxel-based morphometry and white matter DTI) differences.

Activation of dACC and DLPFC has been observed during hypnotic task performance. Hypnotically imagined pain is accompanied by activation in the thalamus, dACC, DLPFC, insula, and parietal cortex.²⁴ Hypnotically imagined hand-grip activation also results in increased activity in the dACC and insula among high hypnotizable individuals.⁵³ Hypnotic inhibition of Stroop interference is associated with reduced dACC activation,¹² as is hypnotic analgesia directed at the affective component of pain.⁵⁴ Hypnotic analgesia is associated with reduced activity of the dACC⁵⁵ and hypnotically related increases in functional connectivity between the primary somatosensory area and anterior insular and prefrontal cortices. Furthermore, high, but not low, hypnotizable individuals had differences during rest in hypnotic vs non-hypnotic states, and these differences are reduced activation in dACC, PFC, and left DLPFC.²⁸

Although the participants in this study were not asked to engage in hypnotic tasks, the greater resting state coordination of the brain areas associated with conflict detection or focusing of attention (dACC) and motor planning, integration of sensory information, regulation of intellectual function, and working memory (DLPFC) observed among high hypnotizable individuals involved 2 components of the anterior attentional system.^{13,56} Coactivation of the salience and executive-control networks, of which the DLPFC is a key node, is consistent with evidence that the natural tendency to become intensely absorbed in everyday experience outside hypnosis is correlated with hypnotizability,^{17,57,58} leading to the description of hypnosis as “effortless experiencing.”⁵⁹ The next step in this research would involve functional MRI assessment during hypnotic states. On the basis of the current findings, the prediction would be that the combination of focused attention and conflict reduction that makes hypnosis an effective form of top-down control over sensation and motor function would involve networks, such as executive-control and salience, during hypnosis among high hypnotizable individuals but not after hypnotic induction among low hypnotizable individuals. Furthermore, working memory influence on conflict detection allows for hypnotic modulation of perception using instructed imagery, for example, in the visual¹⁰ and somatosensory^{7,9,60} systems.

Genetic and neurotransmitter findings are also consistent with the possibility that the DLPFC and dACC play an important role in hypnotizability. These regions are rich in dopamine-mediated synapses. Hypnotizability is correlated with levels of homovanillic acid, a dopamine metabolite, in the cerebrospinal fluid.⁶⁰ Catechol-*O*-methyl transferase, a gene that affects dopamine function, influences prefrontal executive cognition,⁶¹ and an association between a catechol-*O*-methyl transferase polymorphism and hypnotizability has been found.^{11,18,62,63} The val/met heterozygous form is associated with higher hypnotizability, except in one study⁶³ in which individuals with the val/val polymorphism were even more hypnotizable than those with the val/met variant, and may allow for greater frontal lobe dopamine-mediated flexibility in figure and ground attention, representing enhanced attentional control and therefore greater task engagement.

These findings provide new evidence that hypnosis and the related ability to modulate sensory experience, including pain and anxiety, involve focused attention and concentration and that those capable of it have more coordination between areas that integrate attention, emotion, action, and intention. Paradoxically, hypnosis is often seen as submission or a loss of control, despite the fact that high hypnotizable individuals show surprisingly enhanced control over sensory, motor, and somatic function. Yet they do this with a sense of involuntariness, somehow dissociated from their own abilities, as though they were observing rather than deliberately enacting them. It would seem that the enhanced cognitive control is associated with reduced conflict detection—absorption in the task coupled with dissociation of other competing tasks, as well as reduced awareness of self in accomplishing them, which has been referred to as “self-altering attention.”¹⁷ The data from this study would support a description of hypnosis as “conflict-free attention and intention.”

Increased functional connectivity between the dACC and DLPFC indicates more coordinated activity between these brain regions in high hypnotizable people. The hypnotic experience may involve enhanced focus of attention through linking working memory more closely with attention, thereby reducing the load on conflict detection. This effect could account for controlled dissociative experience in hypnosis, in which perceptions ordinarily available to consciousness are put outside conscious awareness (eg, analgesia^{4,9,54} or alteration of color perception¹⁰), despite the apparent incongruity of this sensory alteration. Furthermore, the intensity of engagement during hypnosis reduces self-consciousness about the experience, which further reinforces the intensity of the experience itself at the expense of awareness of the context in which the experience occurs.⁶⁴ Thus, reduced conflict detection may in turn facilitate the focusing and intensity of attentional modulation of perception. The results are of particular interest in that they highlight the role of 2 brain regions that have been associated with executive-control (DLPFC) and salience (dACC) in individuals with high hypnotizability.^{35,36} Studies are variable in whether the DLPFC appears to be part of the salience network,³⁹ and this variability may re-

flect such individual differences among participants in any given study.

These findings have several important limitations that should be addressed in future studies. First, although some have criticized the HIP as a tool for screening individuals with high and low hypnotizability, interrater reliability ranges from 0.68 to 0.76,⁶⁵⁻⁶⁷ and scores on the HIP are moderately and significantly correlated with scores on the Stanford Hypnotic Susceptibility Scale at the same level that any 1 item on the Stanford Hypnotic Susceptibility Scale is correlated with the overall score.⁶⁸⁻⁷⁰ Furthermore, the HIP scores are significantly higher among those with posttraumatic stress disorder⁷¹⁻⁷³ and pseudoepilepsy,⁷⁴ are significantly lower among those with schizophrenia,^{67,75,76} are positively associated with the trait of absorption,⁵⁷ and predict the outcome of hypnotic treatment for smoking control⁷⁷ and flying phobia.⁷⁸ Second, we examined the differences during the resting state without behavioral measures, so we have no evidence regarding the effect of hypnotic induction or specific tasks. However, the fact that we observed robust differences during the resting state despite the absence of tasks designed to elicit activation in specific brain regions suggests fundamental functional brain differences even in the absence of a task between the 2 groups. Third, despite the absence of any hypnotic instruction during the scanning (participants were simply asked to close their eyes and lie still) because hypnotizability assessment was conducted before scanning (although it was on average 2 months earlier), some individuals may have inferred that a hypnotic-like state was being studied during the imaging. Fourth, the sample was of modest size. Fifth, although we focused on ICA-based networks with complementary seed-based analysis of functional coupling between the dACC and DLPFC, other approaches, such as graph theoretical analysis, may provide additional insights into brain systems underlying hypnotizability. Finally, although we used the terms *executive-control network* and *salience network* in defining the networks based on prior work,^{35,36} depending on the analysis method and study, the key regions in our study, such as the dACC, may also be considered part of an attentional network. Furthermore, the effect of increased left DLPFC-dACC connectivity in highly hypnotizable individuals may extend beyond hypnotizability to other domains of attention and may be nonspecific. We did not explore this in our study. Other analytical approaches and inclusion of behavioral measures may help identify the networks that differ dependent on the trait of hypnotizability.

These results provide a neural basis for an important trait difference, which is an area of growing importance in neuropsychology.⁷⁹⁻⁸¹ Although enhanced psychological and somatic control has been observed with the use of mindfulness meditation, along with increases in left frontal activation,⁸² our findings differ in emphasizing coactivation of the DLPFC and dACC, which suggests that future research might examine such a potential difference between the 2 techniques. Mindfulness is considered a practice that must be developed with considerable time and effort. We observe differences in hypnotizability that are unrelated to training or experience in hypnosis, suggesting a difference in cognitive style

that is available to some more than others, independent of training.

These results are compatible with the idea that high hypnotizable individuals have an exceptional capacity for top-down sensory control via coordinated activity of the DLPFC and dACC, which is illustrated by reductions in the affective components of pain via reduced dACC activity during one type of analgesia and in Stroop interference and alteration of sensory cortex response to stimuli during hypnotic analgesia that reduces the sensory component of pain or modulates color processing. Hypnotizability involves a combination of cognitive control and engagement (self-altering attention) that may be mediated by enhanced frontal-anterior cingulate functional connectivity. The coactivation of these regions could provide the brain basis for helping patients to enhance pain and anxiety control and for clinically relevant symptom control, including the effects of social support, emotional control, and placebo effects.

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Online-Only Material: The eAppendix is available at <http://www.archpsych.jamanetwork.com/journal.aspx>. Also, listen to an author interview about this article, and others, at <http://bit.ly/L4AZtw>.

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