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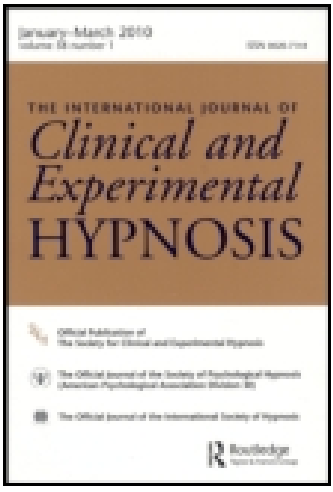

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Modulating the Default Mode Network Using Hypnosis

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MODULATING THE DEFAULT MODE NETWORK USING HYPNOSIS[1]

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Abstract: Debate regarding the neural basis of the hypnotic state continues, but a recent hypothesis suggests that it may produce alterations in the default mode network (DMN). DMN describes a network of brain regions more active during low-demand compared to high--demand task conditions and has been linked to processes such as task-independent thinking, episodic memory, semantic processing, and self-awareness. However, the experiential and cognitive correlates of DMN remain difficult to investigate directly. Using hypnosis as a means of altering the resting ("default") state in conjunction with subjective measures and brain imaging, the authors found that the state of attentional absorption following a hypnotic induction was associated with reduced activity in DMN and increased activity in prefrontal attentional systems, under invariant conditions of passive visual stimulation. The findings that hypnosis and spontaneous conceptual thought at rest were subjectively and neurally distinctive are also relevant to understanding hypnosis itself.

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Hypnotic suggestion is increasingly used as an experimental tool in cognitive neuroscience particularly in conjunction with functional imaging techniques (Oakley, 2008; Oakley & Halligan, 2009a, 2009b). However, little attention has been paid to the neurocognitive basis of the hypnotic "state" and its potential for investigating forms of consciousness and in particular the normal resting state of brain activity (Zhang & Raichle, 2010). In contrast, there is a long history of theoretical debate as to whether hypnosis is a uniquely altered state of consciousness or whether the hypnotic induction procedure per se produces its own distinctive brain activity, and also the extent to which behavioral effects seen in hypnosis can be attributed to alterations in normal psychological functions such as expectancy and attentional changes (Kirsch & Lynn, 1995). One hypothesis is that evidence for such changes might be found in the default mode network (DMN) of brain activity (Oakley, 2008; Oakley & Halligan, 2009a, 2009b). This raises the possibility that the state of hypnosis (i.e., the neural consequences of the hypnotic induction procedure) given its relation to attentional processes (Gusnard & Raichle, 2001) may prove to be a novel means of manipulating and exploring the DMN.

Evidence for a "default" mode of brain function originally stemmed from convergent findings from several neuroimaging studies all of which suggested the existence of a distinctive network of brain regions more active at rest or in low-demand conditions than during goal-directed cognitive tasks (Gusnard & Raichle, 2001; Mazoyer et al., 2001). While early studies proposed a single "default mode" of brain function (Gusnard & Raichle, 2001), subsequent research has established that a variety of networks are involved in such rest conditions, such as the dorsal attention network, sensorimotor network, and "default mode network" (DMN; Zhang & Raichle, 2010). The DMN (previously described as the more generic "default mode of brain function") comprises cortical midline structures including medial prefrontal cortex, superior frontal cortex, anterior cingulate cortex, posterior cingulate cortex, precuneus, and retrosplenial cortex, along with parahippocampal gyri and lateral parietal cortices (Binder et al., 1999; Mazoyer et al., 2001; Northoff & Bermpohl, 2004; Raichle & Snyder, 2007). Task-induced deactivation in parts of this network have been reported where the control condition consisted of lying quietly in an alert state with eyes shut or open, or when passively viewing a stimulus such as a fixation cross or a checkerboard display (Greicius, Krasnow, Reiss, & Menon, 2003; Greicius & Menon, 2004; Gusnard, Akbudak, Shulman, & Raichle, 2001; Mazoyer et al., 2001; Northoff & Bermpohl, 2004; Raichle & Snyder, 2007). Critically the magnitude of task-dependent decreases in activity of DMN structures has been shown to depend on relative attentional task demands (McKiernan, D'Angelo, Kaufman, & Binder, 2006; McKiernan, Kaufman, Kucera-Thompson,

& Binder, 2003). Moreover, momentary lapses in attention have been shown to be associated with both reduced activity in ventrolateral prefrontal regions and less task-induced deactivation in the DMN (Weissman, Roberts, Visscher, & Woldorff, 2006).

However, uncertainty remains regarding the cognitive and subjective correlates of DMN. This arises because attempts to measure the experiential state and/or cognitive performance of subjects at rest runs the risk of altering the target phenomena under investigation by engaging goal-directed cognitive activity, when the aim is elucidating the subjective and neural correlates of task-independent cognitive activity (cf. Grecius & Menon, 2004). Given this methodological problem, previous attempts to establish the cognitive correlates of brain activity in the DMN have tended to rely on extrapolations from experiments using various goal-directed tasks (Binder et al., 1999; Greicius et al., 2003; McKiernan et al., 2003; Northoff & Bermpohl, 2004). However, the brain structures thought to comprise the DMN have been shown to be active under different cognitive task conditions, leading to various characterizations of cognitive and subjective correlates such as episodic memory, problem solving and planning, conceptual processing, and reflexive or "autonoetic" awareness (Binder et al., 1999; Greicius et al., 2003; Greicius & Menon, 2004; Gusnard et al., 2001; Mazoyer et al., 2001).

A more direct approach for investigating the DMN has been to measure the neural correlates of "stimulus-independent" or "task-unrelated" thoughts (SITs/ TUTs) in subjects who concurrently perform cognitive tasks (Mason et al., 2007; McGuire, Paulesu, Frackowiak, & Frith, 1996; McKiernan et al., 2006). This method has demonstrated correlations between SITs and activation in DMN structures, including medial prefrontal regions (McGuire et al., 1996), anterior cingulate gyrus, and parieto-occipital cortex (McKiernan et al., 2006). Nevertheless, the requirement that subjects restrict themselves to merely reporting the frequency of SITs during task performance provides limited information about the phenomenological content of SITs and their association with brain activity.

Hypnosis offers a novel method for directly investigating the cognitive and experiential correlates of DMN whilst circumventing these methodological limitations (Oakley, 2008; Oakley & Halligan, 2009a, 2009b). Firstly, the standard hypnotic induction procedure employed in "neutral hypnosis" is designed to promote attentional focusing and disattention to extraneous stimuli (Cardeña, 2005; Oakley, Deeley, & Halligan, 2007). As such, it engages cognitive changes (increased sustained attention) with corresponding experiential changes (a sense of increased attentional focus and decreased stimulus-independent thoughts) (Cardeña, 2005; Rainville & Price, 2004) predicted on the basis of prior studies to produce a decrease in DMN activity and

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increased activity in prefrontal systems supporting sustained attention (Oakley, 2008; Oakley & Halligan, 2009a, 2009b). These changes could be described as "task-related" to the extent that the induction procedure can be envisaged as a "task" eliciting alterations in cognition and experience until the point at which they are reversed by the experimenter (or otherwise remit). However, it should be emphasized that the cognitive and experiential effects of the induction procedure are qualitatively distinct from the "task-related" procedures typically employed in fMRI experimentation—that is, they are not elicited by performance of a goal-directed task (e.g., an n-back task) (Raichle & Snyder 2007). Further, subjects are able to describe aspects of their experience in both the normal alert state and following a hypnotic induction procedure using self-report measures, in addition to more detailed phenomenological interviews following reversal of the hypnotic state (Oakley et al., 2007). The ability of subjects to describe aspects of experience both in the normal alert state and hypnosis potentially allows associated changes in DMN and other aspects of brain activity to be related more directly to cognitive and experiential changes than previous paradigms.

It should be noted that one previous study employed fMRI to investigate the effects of induction of hypnosis on DMN (McGeown, Mazzoni, Venneri, & Kirsch, 2009). Eleven highly hypnotizable subjects required to attend to a fixation point in and out of hypnosis showed reduced activity in anterior DMN regions (anterior cingulate, medial and superior frontal gyri bilaterally), in addition to the left inferior and middle frontal gyri. The reverse contrast of hypnosis versus the normal alert state at rest revealed no significant differences (McGeown et al., 2009). The study provided preliminary support for the hypothesis that induction of hypnosis is associated with reduction in activity in components of the DMN. Nevertheless, the study design was based on between-condition contrasts without detailed self-report and phenomenological measures and consequently did not allow a more direct investigation of the experiential and cognitive correlates of DMN by employing correlations between self-rated depth of hypnosis and brain activity, supplemented with qualitative descriptions of experience before and after induction of hypnosis.

In the present study, we report an fMRI experiment that employed hypnosis as a means of systematically varying neurocognitive function (sustained attention and stimulus-independent thought) under identical low-demand stimulus conditions, in conjunction with self-report and phenomenological measures as the means to define the experiential correlates of changes in DMN and other brain systems. We employed a standard hypnotic induction procedure in 8 highly hypnotizable subjects, all of whom had been hypnotized on at least two previous occasions (Oakley et al., 2007). Brain activity was measured with fMRI

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before hypnosis (prehypnosis), following hypnotic induction (hypnosis), and following reversal of hypnosis (posthypnosis) under identical conditions of passive visual stimulation with reversing checkerboards. The use of passive visual stimulation as a low-demand experimental condition has been shown to be associated with activity in the DMN and thus was appropriate for investigating subjective and neurocognitive dimensions of the resting state (Greicius & Menon, 2004). Subjects were told that the study was concerned with motor function in hypnosis and a variety of motor tasks were carried out but are not reported on here. The checkerboard displays were presented completely independently of the motor tasks. Subjects were simply asked to look at the screen while it was present and no suggestions were given at any time that related to the checkerboard display. This served to minimize the possible influence of task-related expectations and demand characteristics on brain activity during the checkerboard stimulation.

Currently, there is no neural measure of *hypnotic depth* (the degree to which an individual has entered into the experience of hypnosis). There are, however, well-established self-report procedures such as the hypnotic depth scale described by LeCron (1953), later developed as the Long Stanford Scale (Tart, 1970), and more recently, McConkey, Wende, and Barnier (1999) have used a more sensitive method in which the participant moves the pointer on a dial to indicate changes in the intensity of their experience of hypnosis. Given space limitations in the scanner and to avoid unnecessary motor movement, we employed a more traditional self-report approach. Subjects rated their depth of hypnosis immediately prior to, and after, each presentation of the checkerboard display (see Oakley et al., 2007). We used correlation analyses to explore the relationship between this experiential state and brain activity. Most studies of hypnosis and cognitive control relate to the state produced by hypnosis plus suggestion. Where hypnosis has been explored in the absence of task-specific suggestion (neutral hypnosis), as in our study, alterations in attentional control in particular seem to be involved; though evidence on the direction of these changes is inconsistent (Egner & Raz, 2007; Raz, 2005). Given that hypnosis appears to be associated with alterations in sustained attentional focus (Price & Barrell, 1990; Raz, 2005), we predicted (Oakley, 2008; Oakley & Halligan, 2009a) that (a) increasing the depth of hypnosis would be associated with increased activity in prefrontal attentional networks (Bunge, Ochsner, Desmond, Glover, & Gabrieli, 2001; Fletcher & Henson, 2001; Gehring & Knight, 2002), and (b) decreased activity in cortical midline and other DMN structures previously proposed to be active during spontaneous (stimulus-independent) thought (Binder et al., 1999; Greicius et al., 2003).

We also used qualitative findings from postscanning phenomenological interviews to explore a related set of hypotheses. At an experiential

level, we predicted that compared to the normal alert resting state, hypnosis would be associated with increasingly focused attention and absorption (indexed by an increase in self-reported absorption and a reduction in distraction by outside stimuli) accompanied by decreased spontaneous thought (indexed by a reduction in self-reported analytic thinking and the feeling that the mind is "cluttered up" with thoughts and associations) (Cardeña, 2005; Rainville & Price, 2004).

Method

Subjects

We studied 8 right-handed healthy volunteers (male = 4, female = 4) with a mean age of 22.6 years (Range 19–36; *SD* = 5.6). Subjects were selected from a larger sample tested on the Harvard Group Scale of Hypnotic Susceptibility, Form A (HGSHS:A; Shor & Orne, 1962) as being of medium to high hypnotizability (8+ out of 12) and had experienced at least two subsequent standardized hypnotic induction procedures before the present study. Their mean HGSHS:A score was 10.25 (Range 8–12; *SD* = 1.49). Ethical approval was obtained from the Ethical Committee of the South London and Maudsley Trust and Institute of Psychiatry, United Kingdom. After description of the study to the subjects, written informed consent was obtained.

Passive Viewing Condition

The three experimental conditions were all carried out in the scanner and involved a visual stimulus display presented at the beginning of the session (prehypnosis/ condition 1); in the middle of the session after hypnotic induction (during-hypnosis/ condition 2); and at the end of the session after reversal of hypnosis (posthypnosis/ condition 3). A 16-second period of stimulation, consisting of a reversing checkerboard pattern presented at one of three reversal frequencies (2, 4, or 8 Hz), was alternated with a 16-second period of central crosshair fixation. This cycle was repeated nine times in the course of the condition. The order of reversal frequencies was randomized within each set of three consecutive stimulation/fixation cycles. The total duration of each condition was 4 minutes 48 seconds, resulting in acquisition of 144 total brain volumes.

Hypnosis procedure. Participants remained in the scanner for the duration of the hypnosis induction procedure spread over a 10-minute period. The induction was based on Gruzelier's Three-Stage model (1998) and is described in detail elsewhere (Oakley et al., 2007). Briefly, this involved (a) visual fixation on a projected central crosshair and listening to the experimenter's voice, (b) suggestions of fatigue at

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continued fixation, eye closure and tiredness, with deep relaxation and counting from 1 to 20, and (c) instructions for relaxed and passive imagery (Special Place or "Safe Place"; Heap & Aravind, 2002). Suggestions of Special Place imagery were reversed before the during-hypnosis passive viewing condition (Condition 2) was administered. Prior to presentation of each of the three passive viewing conditions, subjects were simply told "Keep your eyes open. Please look at the screen—you will not be asked to make any movements." No other instructions were given and no suggestions were made at any time regarding the checkerboard display. Hence, subjects were in a state of neutral hypnosis during the second passive viewing condition. That is, they were in the mental state produced by the hypnosis procedure in the absence of any suggestions that related to their experience of viewing the reversing checkerboard display (Oakley et al., 2007). Hypnosis was subsequently terminated by reversing Steps a and b.

As noted above, the study reported here was carried out alongside an unrelated study of motor function. The hypnosis part of the study (including motor function tests) lasted for approximately 1 hour and 15 minutes and hypnosis was finished approximately 15 minutes before the participant left the scanner. A detailed description, complete with scripts, of the experimental sequence for the motor function study and the hypnosis induction and reversal procedures common to both studies is provided in Oakley et al. (2007). For the present study, the prehypnosis passive viewing condition (Condition 1) took place before the motor function study commenced. There then followed a motor testing condition that involved the subject moving a joystick repeatedly from side to side with their dominant hand when instructed to do so. This was followed by the hypnosis induction procedure and then the during-hypnosis passive viewing condition (Condition 2). The motor function test was then repeated twice—once with a suggested paralysis of the dominant hand and once with the paralysis suggestion removed and normal limb function restored. Hypnosis was then terminated and the passive viewing condition was repeated for a third time (posthypnosis passive viewing condition—Condition 3).

Self-Ratings of Depth of Hypnosis and Postscanning Assessments

Subjects were asked to rate the subjective depth of their hypnotic experience immediately before and after each of the passive viewing conditions on a scale of 1–10 (Tart, 1970), where 0 was defined as *not hypnotized at all* and 10 was *as deeply hypnotized as you have ever been*. To secure a more detailed account of the experience of hypnosis, we conducted a semi-structured interview immediately after subjects had left the MR scanner in which they were asked to describe their experience of hypnosis compared to their normal alert state. The duration of the complete session in the scanner was approximately

2 hours. Six of the 8 subjects also completed visual analogue scales consisting of two measures of attentional focus (absorption and distraction by outside stimuli), two measures of spontaneous thought (tendency to analytic thinking and the feeling of the mind being cluttered by thoughts and associations), and a measure of relaxation. Subjects completed these scales in relation (a) to when they had felt most hypnotized and (b) to when they were not hypnotized. Each of the scales consisted of a 100 mm horizontal line marked at one end "Not at all (relaxed/distracted/ analytical/absorbed/cluttered up)" and at the other end "Very (relaxed/distracted/ analytical/absorbed/cluttered up) indeed." Subjects were asked to make a mark on the line to represent the extent to which they experienced each of these feelings. Scores were derived by direct measurement in mm from the left of each scale where *Not at all* . . . corresponded to 0 and *Very. . . . indeed* to 100.

Image Acquisition

Gradient-echo echoplanar imaging (EPI) data were acquired with a 1.5 Tesla (T) MR system based at the Maudsley Hospital, United Kingdom. A GE LX-NV/CV system equipped with ultrafast SR 150 magnetic field gradients was employed, allowing a maximum gradient amplitude of 40 mT/m (General Electric, Milwaukee, Wisconsin, USA). Functional MRI examinations were conducted using the following scanner parameters: pulse sequence = single shot, echo planar, gradient echo imaging; repetition time = 2000 msec; echo time = 40 msec; RF flip angle = 70 degrees; slice orientation = near-axial; number of slices = 16; slice thickness = 7 mm; gap between slices = 0.7 mm; acquisition matrix resolution = 64 × 64 (for a 24 cm field of view); acquisition mode = interleaved; K-space sampling = FULL, ramp sampling ON; frequency direction = right-left; number of dummy acquisitions = 4; total number of images per slice = 144.

Brain Image Analysis

Data were analyzed with XBAM software developed at the Institute of Psychiatry, London, using a nonparametric statistical approach (for a full description and references, see www.brainmap.co.uk). The nonparametric approach is of importance here to achieve rigorous statistical inference given the difficulty of establishing normality in fMRI experiments (Thirion et al., 2007). A 3D volume consisting of the average intensity at each voxel over the whole experiment was calculated and used as a template. The 3D-image volume at each time point was then realigned to this template by computing the combination of rotations (around the x-, y-, and z-axes) and translations (in x, y, and z) that maximized the correlation between the image intensities of the volume in question and the template. Following realignment, data were then smoothed using a Gaussian filter to improve the signal to noise

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characteristics of the images. Experimental responses were analyzed by convolving the contrast of visual stimuli versus fixation cross with two-gamma variate functions (peak responses at 4 and 8 seconds). The best fit between the weighted sum of these convolutions and the time series at each voxel was computed using a constrained Blood Oxygen Level Dependent (BOLD) effect model (Friman, Borga, Lundberg, & Knutsson, 2003). Following computation of the model fit, a goodness-of-fit statistic was computed. This consisted of the ratio of the sum of squares of deviations from the mean image intensity (over the whole time series) due to the model to the sum of squares of deviations due to the residuals (Sum of Squares [SSQ] ratio or value). The data were permuted by a wavelet-based method (Bullmore et al., 2001) in order to test for significance nonparametrically. The detection of activated voxels is extended from voxel to cluster level using a method described elsewhere (Bullmore et al., 1999).

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Correlation Analyses

We undertook a correlation analysis employing the whole range of self-rating measures acquired before and after each checkerboard stimulation/fMRI acquisition block. For each of the three conditions, the pre- and postblock measures were averaged to create a single self-rating measure of depth of hypnosis per condition (see "Results"). In addition, the mean self-rated depth of hypnosis for the normal alert state (Condition 1 [prehypnosis] and Condition 3 [posthypnosis]) was calculated because self-rated depth of hypnosis did not significantly differ between the normal alert conditions (see "Results"). Employing averaged self-rated depth of hypnosis and brain activation maps for the normal alert conditions, therefore, made maximal use of available data sampling a condition of interest (the normal alert state), whilst minimizing the risk of overestimating degrees of freedom. In summary, self-rated depth of hypnosis and the respective SSQ values for the visual-fixation cross contrasts for the hypnosis and the averaged normal alert state conditions were combined into a single correlation analysis. Pooling data in this way ensured a large spread of values for hypnotic depth to allow correlations with brain activity. This allowed inferences to be made about BOLD activity and self-rated depth of hypnosis across both the normal alert state and following induction of hypnosis, rather than restricting inferences to one or other condition.

Correlations of hypnotic depth with brain activity involved calculating the Pearson product moment correlation coefficient between the self-rated hypnotic depth for each subject and the fMRI responses at each voxel for each subject, yielding one correlation coefficient (r) per intracerebral voxel. To determine the significance of these correlation coefficients, the appropriate null distribution of r was computed robustly using data permutation. The order of the behavioral

data (self-rated hypnotic depth) was randomly permuted without replacement (i.e., each data value occurs once but the order is changed) breaking the association between self-rated hypnotic depth and its corresponding fMRI responses. The correlation coefficient was then recomputed many times at each voxel and the resulting values of r combined over all voxels to produce a whole brain null distribution of r. The critical value of r for significance at any particular p value can then be obtained from this distribution after simply sorting it by value of r and selecting the appropriate point from the sorted distribution; for example, the critical value of r for a one-tailed test at $p < .05$ would be the value of r in the null distribution chosen such that 95% of all the null values of r lay below that point.

Testing can then be extended to cluster level as described previously (Bullmore et al., 1999). The cluster probability under the null hypothesis was chosen to set the level of expected Type I error clusters at an acceptable level (e.g., <1 per whole brain). In the present experiment, a voxel wise $p = .01$ and cluster wise $p = .005$ was chosen to give less than one false activated cluster per analysis.

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Results

Analyses of Self-Ratings of Hypnotic Depth

Analysis of variance (ANOVA) and post hoc t tests of self-ratings of hypnotic depth before and after each checkerboard display revealed temporal stability of the self-rated conscious state (depth of hypnosis) within the respective phases of the experiment. Specifically, subjective hypnotic depth before and after each checkerboard display (time) across the three hypnosis conditions (condition) was examined in 2×3 repeated measures ANOVA. This revealed a significant quadratic trend in hypnosis depth for condition, $F(2, 12) = 196.25$, $p < .001$, with no significant effect of time or interaction between these two factors.

Further, subjective hypnotic depth was significantly greater in the hypnosis condition compared to both the prehypnosis condition and the posthypnosis condition. Mean subjective hypnotic depth scores, based on the average values of the before and after depth measurements for each subject, for the first (prehypnosis), the second (hypnosis), and the third (posthypnosis) checkerboard displays were 0.81 (SD +/− 1.41), 7.25 (SD +/− 2.28), and 0.71 (SD +/− 0.91), respectively. Comparing these scores with related means t tests (two-tailed) showed that subjective hypnotic depth in the hypnosis condition differed significantly from both the prehypnosis condition and the posthypnosis condition, $t(7) = -8.18$, $p < .001$ and $t(7) = 17.32$, $p < .001$, respectively. There was, however, no significant difference in hypnotic depth between the prehypnosis and posthypnosis conditions. Hence, following hypnotic induction, the subjects' self-reports were

consistent with the establishment of a state of hypnosis, which was subsequently effectively reversed. Consequently, the phenomenological evidence supports an effect of hypnotic procedure on the experience of depth of hypnosis, but not an order effect.

Postscanning Assessments

Analysis of the postscanning visual analogue rating scales (0–100 mm) using a related means *t* test (one-tailed) comparing hypnosis versus no hypnosis scores ($df = 5$ in all comparisons) showed that subjects rated themselves as significantly more relaxed ($t = 5.320$, $p = .002$) and more absorbed ($t = 2.711$, $p = .021$) during hypnosis than when not hypnotized (see Figure 1). Conversely, they rated themselves in hypnosis as being significantly less distracted by outside stimuli ($t = -3.254$, $p = .011$), having a reduced tendency to analytical thinking ($t = -3.891$, $p = .006$), and experiencing less of a feeling of their mind being cluttered up ($t = -2.183$, $p = .041$) compared to the nonhypnotized condition. This is consistent with a view that the type of hypnotic induction procedure used here is accompanied by relaxation and a state of

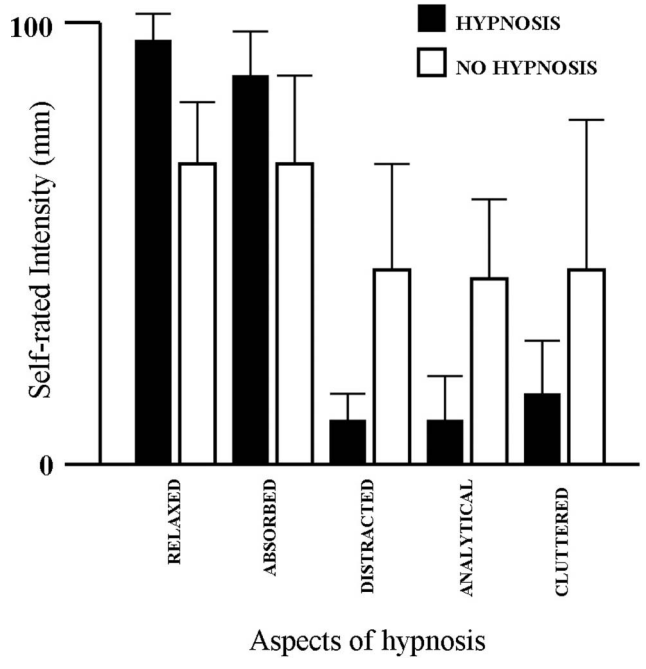

Figure 1. **Means (and standard deviations) of postscanning visual analogue scale scores relating to subjective state when subjects were hypnotized and not hypnotized (see text for further details).**

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sustained attentional absorption characterized by a low level of spontaneous conceptual thought relative to the nonhypnotized condition.

In response to semi-structured interviews about the experience of hypnosis, subjects made comments such as "I am completely absorbed, not distracted and my mind is clear"; "I am at my most concentrated on whatever I am supposed to be concentrating on. I have the least interest or knowledge of what is happening around me." These findings are consistent with prior reports of the subjective correlates of hypnosis established by comparable induction methods (Cardeña, 2005; Rainville & Price, 2004).

Correlations of Brain Activity With Self-Rated Depth of Hypnosis

Brain regions, which demonstrated decreased activation during the passive visual stimulation with increasing depth of hypnosis, are shown in Figure 2 and Table 1. These regions included established DMN regions, including cortical midline structures of the left medial frontal gyrus, right anterior cingulate gyrus, and bilateral posterior cingulate gyrus; and bilateral parahippocampal gyri (see Figure 2 and Table 1).

Brain regions that showed increased activation during the same passive visual stimulation with increasing depth of hypnosis are shown in Figure 3 and Table 2. These included the right middle frontal gyrus (BA 45), the inferior frontal gyrus bilaterally (right BA 46, left BA 47), and the precentral gyrus bilaterally (right BA 44/ 6, left BA 6).

Discussion

In this study, we employed hypnosis as a way of reducing activity in the DMN in a nongoal-directed task and in conjunction with

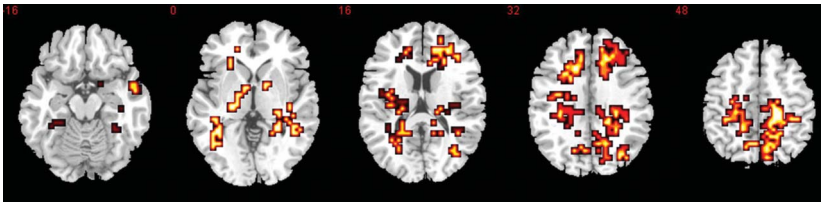

Figure 2. **Brain regions that decrease activation to passive visual stimulation with increasing depth of hypnosis. Voxel wise $p = .01$, Cluster wise $p = .005$ (threshold to <1 false positive cluster per brain). The right side of each slice represents the left side of the brain. See Table 1 for full description of functional anatomy and Talairach coordinates (color figure available online).**

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Table 1
Brain Regions That Decrease Activation to Passive Visual Stimulation With Increasing Depth of Hypnosis

Size	Tal(x)	Tal(y)	Tal(z)	Probability	BA	Cerebral Region
111	−22	41	15	0.000002	9	Medial Frontal Gyrus
11	18	−15	53	0.000330	6	Medial Frontal Gyrus
20	14	37	4	0.000002	32	Anterior Mid Cingulate Gyrus
49	11	30	26	0.000002	32	Anterior Mid Cingulate Gyrus
9	14	−44	15	0.000051	29	Posterior Cingulate Gyrus
22	−32	−67	9	0.000005	30	Posterior Cingulate Gyrus
29	36	−41	−2	0.000002	19	Parahippocampal Gyrus
11	29	−56	9	0.000549	30	Parahippocampal Gyrus
16	−22	−37	−7	0.000002	35	Parahippocampal Gyrus
20	−40	−41	−7	0.000002	19	Parahippocampal Gyrus
16	−36	−19	−13	0.000002		Hippocampus
13	−47	7	−29	0.000005	21	Middle Temporal Gyrus
332	−11	−33	15	0.000002		Thalamus
193	25	−22	15	0.000002		Claustrum
5	−11	4	−7	0.000316		Lentiform Nucleus

Table 2
Brain Regions That Increase Activation to Passive Visual Stimulation With Increasing Depth of Hypnosis

Size	Tal(x)	Tal(y)	Tal(z)	Probability	BA	Cerebral Region
15	−51	19	−7	0.000002	47	Inferior Frontal Gyrus
11	43	41	9	0.000014	46	Inferior Frontal Gyrus
19	43	19	20	0.000062	46	Middle Frontal Gyrus
11	51	−4	48	0.000876	6	Precentral Gyrus
13	58	11	4	0.000035	44	Precentral Gyrus
49	−40	−11	42	0.000002	6	Precentral Gyrus
18	−4	−33	−7	0.000002		Cerebellum
6	−29	7	−2	0.000845	72	Claustrum

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subjective measures and brain imaging. We measured brain activity with fMRI and recorded self-ratings of hypnotic depth in 8 subjects before, during, and after hypnosis, whilst subjects passively attended to flashing checkerboard stimuli. We then conducted correlation analyses to detect relationships between hypnotic depth and brain activity during passive visual processing. Specifically, we tested the hypothesis that increasing depth of hypnosis would be associated with increased activity in prefrontal attentional networks (Bunge et al., 2001; Fletcher & Henson, 2001; Gehring & Knight, 2002) and decreased activity in cortical midline and other DMN structures previously proposed to

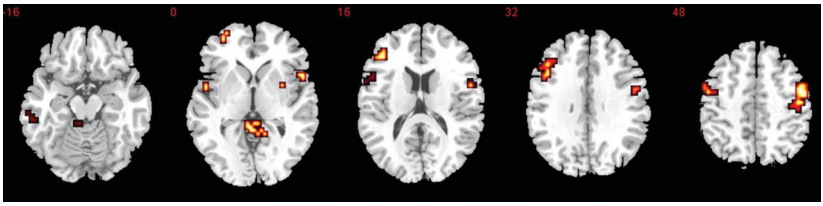

Figure 3. **Brain regions that increase activation to passive visual stimulation with increasing depth of hypnosis. Voxel wise $p = .01$, Cluster wise $p = .005$ (threshold to < 1 false positive cluster per brain). The right side of each slice represents the left side of the brain. See Table 2 for full description of functional anatomy and Talairach coordinates (color figure available online).**

be active during spontaneous (stimulus-independent) thought (Binder et al., 1999; Greicius et al., 2003). At an experiential level, we predicted that compared to the normal alert resting state, hypnosis would be associated with increased attention (indexed by an increase in self-reported absorption and a reduction in distraction by outside stimuli) and decreased spontaneous thought (indexed by a reduction in self-reported analytic thinking and the feeling that the mind is cluttered up with thoughts and associations).

The experiment was designed to avoid potential confounds whilst maximizing information about the relationship between subjective experience and brain activity under cognitively undemanding, task-free stimulus conditions. The experiment was explained to subjects as being a study about hypnosis and motor activity. The checkerboard displays were presented separately from the motor testing conditions that were included in the experimental procedure in such a way that the subjects were not aware that the MR data acquired during these displays was concerned with anything other than ongoing monitoring of scanner function. Moreover, they were specifically informed that motor responding would not be required during the checkerboard displays. Additionally, measurement of experiential state was limited to a self-rating judgment of hypnotic depth immediately before and after each block of checkerboard stimulation so that subjects were not required to engage in any self-monitoring during MR acquisition. Collectively these measures aimed to reduce concurrent task-demands and experimentally imposed cognitive activity, particularly relating to social cognition and reflexive awareness.

Analyses of hypnotic depth with brain activity during passive visual stimulation revealed both positive and negative correlations (Tables 1 and 2). Figure 3 shows that increasing depth of hypnosis is associated with increased activity in lateral prefrontal regions involved in the maintenance of attention (Bunge et al., 2001; Fletcher & Henson, 2001;

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Gehring & Knight, 2002; Weissman et al., 2006), including the right middle frontal gyrus (BA 45), the inferior frontal gyrus bilaterally (right BA 46, left BA 47), and the precentral gyrus bilaterally (right BA 44/ 6, left BA 6).

In contrast, increasing depth of hypnosis was associated with reduced activity in DMN structures (Binder et al., 1999; Greicius et al., 2003; Greicius & Menon, 2004; Gusnard & Raichle, 2001) under identical conditions of passive visual stimulation, including cortical midline structures of the left medial frontal gyrus, right anterior cingulate gyrus, bilateral posterior cingulate gyri, and bilateral parahippocampal gyri (Figure 2, Table 1).

At an experiential level, postscanning self-report measures confirmed that, compared to the normal alert resting state, hypnosis was associated with increased attentional focus (indexed by increased levels of absorption and a reduction in self-reported distraction by outside stimuli) and decreased spontaneous thought (indexed by a reduction in self-reported analytic thinking and the feeling that the mind is cluttered up with thoughts and associations) (Figure 1). Verbal descriptions of the experience of hypnosis were consistent with these self-rating measures (see "Results").

Hence, activity in DMN was clearly attenuated with increasing depth of hypnosis. Given evidence of the subjective correlates of hypnosis from this and prior studies employing comparable induction methods (Cardeña, 2005; Rainville & Price, 2004), the present findings suggest that neural activity in DMN is inversely associated with attentional absorption and directly associated with spontaneous or stimulus-independent conceptual thought. Hence, our method of correlating a scalar index of experiential state with brain activity in conjunction with self-report measures provides direct evidence of an association between spontaneous conceptual thought and DMN activity compared to previous studies employing indirect inference from cognitive activation paradigms (Binder et al., 1999; McKiernan et al., 2003).

A negative correlation between hypnotic depth and activity in the anterior cingulate cortex (BA 32) was also observed (that is, as subjects became more deeply hypnotized, anterior cingulate activity decreased). Anterior cingulate cortex has previously been described as part of DMN (Binder et al., 1999; Mason et al., 2007; Mazoyer et al., 2001; McKiernan et al., 2003) and has additionally been found to be active during self-related cognitive processing (Northoff & Bermpohl, 2004). Hence, its relative reduction in activity in association with increasing depth of hypnosis is consistent with our overall finding of reduction in DMN and spontaneous conceptual thought in association with hypnosis.

Nevertheless, anterior cingulate cortex activation has also been observed under a variety of attentional task conditions (Bunge et al.,

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2001; Bush, Luu, & Posner, 2000; Weissman et al., 2006). This raises the more general question as to why anterior cingulate cortex should show task-related deactivation under some task conditions (along with other DMN components) (Lawrence, Ross, Hoffmann, Garavan, & Stein, 2003), as opposed to increased activation under other attentionally demanding task conditions that are otherwise associated with DMN deactivation (e.g., Weissman et al., 2006). We suggest that relative activation of anterior cingulate is modulated by the nature of the high-demand/goal-directed tasks, as with other components of DMN more generally (Binder et al., 1999). Specifically, a prior study demonstrated that anterior cingulate activation correlates with the ability to keep relevant information in mind (working memory load), but not with the ability to keep irrelevant information out of mind (interference resolution or behavioral inhibition) (Bunge et al., 2001). By contrast, activation of ventrolateral prefrontal cortex (PFC; middle and inferior frontal gyri) correlates with keeping irrelevant information out of mind (interference resolution), but not working memory load (Bunge et al., 2001). In the present study, the neutral hypnosis condition required the subjects to disengage from distracting stimuli (interference resolution), in the absence of a high-working-memory load. Hence, we suggest that the increased experience of attentional absorption in association with relative engagement of interference resolution at a cognitive level and ventrolateral PFC at a neural level, along with relative deactivation of anterior cingulate in association with low-working-memory load, accounts for our findings of differential activation in components of prefrontal attentional networks.

Negative correlations between hypnotic depth and activity were also found in the thalamus bilaterally. This may reflect the role of the thalamus in mediating arousal and alertness (Rainville, Hofbauer, Bushnell, Duncan, & Price, 2002). In other words, as the "normal" alert state attenuates, and mental calmness associated with hypnosis increases, thalamic activity progressively lessens (Rainville et al., 2002).

These findings also complement those of McGeown et al. (2009), who reported reduced activity in DMN regions in 11 highly hypnotizable subjects required to attend to a fixation point in and out of hypnosis (McGeown et al., 2009). In both studies, hypnosis relative to the normal alert state was associated with reduced activity in bilateral anterior cingulate gyrus (BA 32) and left BA 9. However, the current study found that hypnosis was additionally associated with reduced DMN activity extending into the posterior cingulate and parahippocampal gyri. In the McGeown et al. (2009) study, reduced thalamic activation was found in low suggestible subjects following hypnotic induction rather than high suggestible subjects; this may reflect the involvement of thalamus in relaxation rather than the absorptive component of hypnosis (McGeown et al., 2009; Rainville et al., 2002). Similarly, our finding

of hypnosis-related increases in the precentral gyrus bilaterally may be related to relaxation (Rainville et al., 2002). These possibilities will need to be investigated in future studies by taking self-ratings of depth of hypnosis, absorption, and relaxation in subjects before and after scan acquisitions, to determine which component of hypnosis (absorption and relaxation) most closely correlate with DMN, thalamic, and precentral gyrus activity, respectively.

Finally, we found that hypnosis was associated with increased activity in ventrolateral brain regions involved in the maintenance of attention, while McGeown et al. (2009) reported that activity in these regions decreased with hypnosis, along with more medial DMN prefrontal regions (McGeown et al., 2009). Our findings are consistent with the subjective reports of subjects that showed that relative to the normal alert state, hypnosis is associated with increased absorption and disattention to outside stimuli as well as with reduction in analytic thinking and feeling that the mind is cluttered up with thoughts and associations. The findings are also consistent with prior evidence of the association between hypnosis and sustained attention (Cardeña, 2005; Rainville & Price, 2004) and with a reciprocal relationship between activity in attentional and DMN regions (Fox et al., 2005). Future studies employing larger samples and self-ratings of hypnosis, absorption, and relaxation as well as different resting state conditions will help resolve discrepancies that have been found between studies.

The current study has a number of limitations. First, the present study embedded investigation of the effects of the induction of neutral hypnosis on activity in DMN and other brain regions in a larger study that employed instrumental suggestions to produce symptoms of motor paresis. We believe our experimental design prevented covert order effects or task expectancies accompanying induction of hypnosis that could have affected our results (see "Methods"). However, future studies may wish to investigate the effects of neutral hypnosis on brain function separately from other experimental applications of hypnosis, to exclude completely the possibility that covert order or task expectancy effects may affect results. Second, while studies such as the one we report here and that of McGeown et al. (2009) show the promise of establishing brain changes that correspond to the experience of hypnosis per se, it is important to keep in mind that in the absence of an established objective measure, we had little option but to adopt the traditional approach of relying on self-reports of hypnotic depth. These were taken at appropriate points during scanning immediately before and after passive viewing of the visual display in the absence of any suggested phenomena (neutral hypnosis). To reduce experimenter bias our participants were not prompted in any way as to what aspect of their experience they should base their depth of hypnosis rating on but all had prior experience of hypnosis that they could use as a

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reference point. Also, as we were interested in neutral hypnosis, the postscanning questionnaires referred only to "when you were at the greatest depth of hypnosis," not to the periods when hypnosis and suggestion were present together. Though "hypnosis" and "hypnosis with suggestion" have often been confounded in the past, there is evidence that self-reported depth of hypnosis is based upon a distinctly different experience from a nonhypnotic state and that ratings of that experience within and across subjects are consistent and are independent of responding to suggestion. Kirsch et al. (2008) found using a 4-point scale (1. normal state; 2. relaxed; 3. hypnotized; 4. deeply hypnotized) that even though the same group of highly hypnotizable individuals responded to suggestions in and out of hypnosis, they reported being in a hypnotic state only following a hypnotic induction procedure. Oakley et al. (2007), again using high hypnotizables, found consistent changes in depth reports across the various stages of a standardized hypnotic induction procedure before suggestions had been introduced and after they had been removed. Also, as noted above, our participants in postscanning questionnaires rated their hypnotic experience consistently across subjects in relation to a set of descriptive terms commonly encountered in hypnosis reports irrespective of suggestions (relaxed, distracted, analytical, absorbed, and mentally cluttered up). The hypnosis literature has frequently addressed the question of how to measure both hypnotizability and the product of the hypnotic induction—the hypothesized state of hypnosis. It is clear these both are multidimensional and subject to individual differences (see, e.g., McConkey, 2008; Woody & Barnier, 2008). There remains, therefore, a question over whether a single measure of depth can completely capture the essence of the underlying change in experience, which we acknowledge. Future studies of neutral hypnosis should take measures of components such as relaxation and absorption along with depth at the appropriate points within the experimental session rather than relying on retrospective ratings as we did here. However, in the context of the present study, it could be argued that asking for a single response has the advantage of keeping task demands in the period before and after the passive viewing condition to a minimum.

Thirdly, we included self-ratings of depth of hypnosis from two nonhypnotized conditions (pre- and posthypnosis) as well as following the induction of hypnosis. This was done in order to maximize our sampling of self-ratings of hypnotic depth (i.e., from low to high) and to increase our number of observations to increase experimental power. However, in the future, we plan to use a modified induction procedure in a larger sample, allowing depth of hypnosis to be varied following induction to ensure a wider sampling of the phenomenon and its neural correlates—so allowing correlation analysis from the within-hypnosis

condition alone. This would help control for nonspecific effects of the induction procedure on DMN and other brain systems.

In summary, we suggest that the present investigation of DMN links experiential dimensions (levels of absorption and spontaneous thought) with cognitive processes (relative engagement of attentional interference resolution in the context of low-working-memory load) and activity in underlying neural substrates (reciprocal activity in DMN and ventrolateral PFC attentional networks). Specifically, our findings show that increasing depth of hypnosis away from the normal alert state is associated with reduced activity in DMN under invariant conditions of passive visual stimulation. Furthermore, the focused attentional state of hypnosis and spontaneous conceptual thought of DMN at rest are not only subjectively distinctive but demonstrate inverse activity in their respective neural substrates. Also, although brain structures comprising DMN have been shown to be active under a variety of different cognitive task conditions (Binder et al., 1999; Greicius et al., 2003; Greicius & Menon, 2004; Gusnard et al., 2001; Mazoyer et al., 2001), it would appear that one mechanism for deactivation of DMN includes relative engagement of inferior and middle frontal gyri, associated with sustained attention and disattention to distracting stimuli at an experiential level and enhanced interference resolution at a cognitive level (Bunge et al., 2001; Lawrence et al., 2003). In addition to contributing to a better understanding of DMN, the results inform the long-running debate as to the nature of the hypnotic state itself.

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Veränderung der Ruheaktivität durch die Anwendung von Hypnose

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Abstrakt: Die Diskussion bezüglich der neuralen Grundlagen des hypnotischen Zustandes gehen weiter. Doch eine kürzlich aufgestellte Hypothese legt nahe, daß er Veränderungen der Ruheaktivität (default mode network, DMN) hervorruft. Ruheaktivität bezieht sich auf das Netzwerk derjenigen Hirnregionen, die während geringer Anforderungen mehr aktiv sind, im Vergleich zu der in Situationen mit hohen Anforderungen. Sie wurde mit Prozessen wie aufgabenunabhängigem Denken, episodischem Gedächtnis, semantischer Verarbeitung und Selbstbewußtsein in Verbindung gebracht. Allerdings bleibt es schwierig, empirische und kognitive Korrelate für den DMN direkt zu untersuchen. In Bezug auf die Anwendung von Hypnose als Möglichkeit, den ruhenden („Standard") Zustand zu verändern im Zusammenhang mit subjektiven Meßmethoden und Darstellung des Gehirns durch bildgebende Verfahren fanden die Autoren, daß der Zustand der Absorption der Aufmerksamkeit, der einer hypnotischen Induktion folgt, unter gleichbleibender passiver visueller Stimulation mit reduzierter Aktivität im DMN und vermehrter Aktivität im präfrontalen Bereich der Aufmerksamkeit einherging. Dieses Ergebnis, daß Hypnose und spontanes begriffliches Denken in Ruhe subjektiv wie neural unterschiedlich waren, ist relevant, um Hypnose als solches zu verstehen.

Stephanie Reigel, MD

Modulation du réseau du mode par défaut à l'aide de l'hypnose

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Résumé: Le débat se poursuit toujours sur le sujet de la base neurale de l'état hypnotique, mais une récente hypothèse semble indiquer que l'hypnose pourrait produire des changements dans le réseau du mode par défaut (RMD). Le RMD est un réseau de zones du cerveau plus actives durant l'exécution de tâches peu exigeantes que durant celle de tâches très exigeantes, et il a été lié à des processus tels que la pensée indépendante des tâches, la mémoire épisodique, le traitement sémantique et la conscience de soi. La corrélation entre l'expérientiel et le cognitif relativement au RMD demeure toutefois difficile à étudier directement. En utilisant l'hypnose comme moyen de modifier l'état de repos (l'état de défaut), en concomitance avec des mesures subjectives et l'imagerie du cerveau, les auteurs ont découvert que l'état d'absorption attentionnelle qui suit une induction hypnotique était associé à une réduction de l'activité du RMD et à une augmentation de l'activité des systèmes attentionnels préfrontaux, dans diverses conditions invariantes de stimulation visuelle passive. La découverte de la distinction subjective et neurale entre l'hypnose et la pensée conceptuelle spontanée au repos est également pertinente dans la compréhension du phénomène de l'hypnose lui-même.

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Modulando el circuito de activación por defecto usando hipnosis

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Resumen: El debate sobre la base neuronal del estado hipnótico continua, pero una hipótesis reciente sugiere que pudiera producir alteraciones en el circuito de activación por defecto (CAD). El CAD describe una red de regiones cerebrales más activas en situaciones de poca demanda comparadas con condiciones de actividades altamente demandantes y ha sido ligada a procesos como el pensamiento independiente a la actividad, memoria episódica, procesamiento semántico, y auto-conciencia. Sin embargo, los correlatos experienciales y cognitivos del CAD siguen siendo difíciles de investigar directamente. Usando la hipnosis como medio para alterar el estado de reposo ("por defecto") en conjunción con mediciones subjetivas e imagenología cerebral, los autores encontraron que el estado de absorción atencional después de una inducción hipnótica estuvo asociado con una actividad reducida del CAD y un incremento en la actividad de los sistemas atencionales prefrontales, bajo condiciones invariantes de estimulación visual pasiva. Los hallazgos de que la hipnosis y el pensamiento conceptual espontáneo en reposo fueron subjetiva y neurológicamente distintos también son relevantes para el entendimiento de la hipnosis.

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