

Hypnosis Modulates Activity in Brain Structures Involved in the Regulation of Consciousness

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Abstract

■ The notion of consciousness is at the core of an ongoing debate on the existence and nature of hypnotic states. Previously, we have described changes in brain activity associated with hypnosis (Rainville, Hofbauer, Paus, Duncan, Bushnell, & Price, 1999). Here, we replicate and extend those findings using positron emission tomography (PET) in 10 normal volunteers. Immediately after each of 8 PET scans performed before (4 scans) and after (4 scans) the induction of hypnosis, subjects rated their perceived level of “mental relaxation” and “mental absorption,” two of the key dimensions describing the experience of being hypnotized. Regression analyses between regional cerebral blood flow (rCBF) and self-ratings confirm the hypothesized involvement of the anterior cingulate cortex (ACC), the thalamus, and the

ponto-mesencephalic brainstem in the production of hypnotic states. Hypnotic relaxation further involved an increase in occipital rCBF that is consistent with our previous interpretation that hypnotic states are characterized by a decrease in cortical arousal and a reduction in cross-modality suppression (disinhibition). In contrast, increases in mental absorption during hypnosis were associated with rCBF increases in a distributed network of cortical and subcortical structures previously described as the brain’s attentional system. These findings are discussed in support of a state theory of hypnosis in which the basic changes in phenomenal experience produced by hypnotic induction reflect, at least in part, the modulation of activity within brain areas critically involved in the regulation of consciousness. ■

INTRODUCTION

Modern popular views on the phenomenon of hypnosis are largely dominated by the idea that the “hypnotist” possesses an otherwise unspecified ability to induce “sleep-like states” within which individuals appear to behave like automatons. In contrast, contemporary scientific theories of hypnosis emphasize (a) the changes in phenomenal experience (e.g., Price, 1996), (b) the engagement or disengagement of specific neurocognitive processes and the effect on performance and psychophysiological activity (e.g., attention, executive control; Gruzelier, 1998; Crawford, 1994), (c) the contextual cues and psychosocial interaction between the participant and the hypnotist (e.g., Coe & Sarbin, 1977), or (d) the individual psychological characteristics predicting hypnotic susceptibility (e.g., Crawford & Gruzelier, 1992). These accounts differ in their main causative explanations of hypnotic phenomena and provide the background for an ongoing debate on whether or not hypnosis constitutes a distinct state of consciousness.

The combination of experiential measures (e.g., self-rating of subjective experience; Varela & Shear, 1999; Price & Barrell, 1980) and psychophysiological methods (e.g., functional brain imaging) has recently contributed some unique information on the neurophysiological correlates of (1) multiple pain dimensions (Hofbauer, Rainville, Duncan, & Bushnell, 2001; Rainville, Duncan, Price, Carrier, & Bushnell, 1997), (2) the feeling of “remembering” versus “knowing” in studies of memory (e.g., Henson, Rugg, Shallice, Joseph, & Dolan, 1999), and (3) the individuals’ self-confidence in their responses (e.g., Henson, Rugg, Shallice, & Dolan, 2000). These methods have also provided strong support for the notion that hypnotic suggestions can indeed modulate auditory perception (Szechtman, Woody, Bowers, & Nahmias, 1998), visual perception (Kosslyn, Thompson, Costantini-Ferrando, Alpert, & Spiegel, 2000), and pain (e.g. Willoch et al., 2000; De Pascalis, Magurano, & Bellusci, 1999; Crawford et al., 1998; Rainville et al., 1997). However, these studies have examined the effects of specific hypnotic suggestions on “contents of consciousness” and have not directly assessed the more general status of hypnosis as an altered “state of consciousness” (see a version of the proposed distinction between contents and “background” states of consciousness in Chalmers, 2000).

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Neurophenomenology of Hypnotic States

Hypnotic states may be described most adequately by the global changes produced in subjective experience and possibly in self-representation, as these may be essential and ubiquitous to all hypnosis-related phenomena. Studies of hypnosis using experiential analyses have identified a series of dimensions that characterize hypnotic states (Price, 1996). These dimensions include: (1) feelings of deep mental relaxation; (2) mental absorption; (3) a diminished tendency to judge, monitor, and censor; (4) a suspension of usual orientation toward time, location, and/or sense of self; and (5) the experience of one's own response as automatic or extravolitional. Notably, those effects are not restricted to specific sensory modalities or specific "contents" of consciousness, and pertain largely to the subjects' representation, monitoring, and regulation of their own body-self and mental state. These alterations in "self-representation," possibly underlying the changes in subjective experience, provide some support for the notion that hypnosis is a distinct "state" of consciousness, to the extent that self-representation is likely to play a key role in basic aspects of consciousness (e.g., Metzinger, 2000; Damasio, 1999). The identification and experimental manipulation of these basic dimensions of experience using hypnosis may further provide some leverage to investigate the neural correlates of background states of consciousness (see Chalmers, 2000).

At least two of the identified experiential dimensions, mental relaxation and mental absorption, can be readily associated with specific instructions used to induce hypnosis. Hypnotic relaxation results from direct instructions for relaxation, and suggestions for pleasant body feelings (e.g., warmth and heaviness), drowsiness, and mental ease. Mental absorption is likely induced by suggestions for continuous focus on the hypnotist's voice and on the conveyed instructions, and by suggestions for decreased orientation to, and interest in, other irrelevant external sources of stimulation and spontaneous thoughts. Consistently, mental absorption has been described as a state of "total attention that fully engages one's representational resources and results in imperviousness to distracting events" (Tellegen & Atkinson, 1974).

In the present study, 10 normal volunteers rated their level of relaxation and mental absorption immediately after each of 8 positron emission tomography (PET) scans performed before (4 scans) and during (4 scans) hypnosis. The subject's left hand was immersed in either warm or painfully hot water during each scan and the variance associated with this stimulation factor was removed in all regional cerebral blood flow (rCBF) analyses reported here (ANCOVA; pain-related activity is the subject of a separate report; Hofbauer et al., 2001). The reliability of the effects of hypnotic induction on brain activity is first assessed by comparing the present

results with those obtained in our previous study (Rainville, Hofbauer, et al., 1999). The present report further examines the cerebral correlates of hypnotically induced changes in the subjective experience of mental relaxation and mental absorption using regression analyses of rCBF on self-ratings. Directed searches are conducted on the anterior cingulate cortex (ACC) and the thalamus because of their suggested involvement in attention, cortical arousal, and self-regulation, and based on previous studies showing coactivation in these areas following the induction of hypnosis (Maquet et al., 1999; see Table 1 and Appendix in Rainville, Hofbauer, et al., 1999). The brainstem is further included as a specific search area based on the critical implication of brainstem nuclei in the regulation of conscious states, and on their important interactions with the thalamus and the ACC in the regulation of sleep-wakefulness and attention (e.g., Aston-Jones, Rajkowski, & Cohen, 1999; Kinomura, Larson, Gulyas, & Roland, 1996; Steriade & McCarley, 1990). Additional changes in cerebral activity are examined using global searches over the entire brain.

RESULTS

Hypnosis-Related Changes in Mental Relaxation and Mental Absorption

The induction of hypnosis produced significant increases in self-ratings of both mental relaxation and mental absorption (Figure 1). Likewise, both experiential measures showed modest but significant correlations with a standardized measure of individual hypnotic susceptibility (Stanford Hypnotic Susceptibility Scale—Form A [SHSS-A]; mental relaxation: Spearman's $R = .38$, $p < .01$; mental absorption: Spearman's $R = .27$, $p < .05$). These results and additional convergent evidence in the same subjects, or in different subjects using the same method, indicate that the procedure was effective in inducing hypnotic states

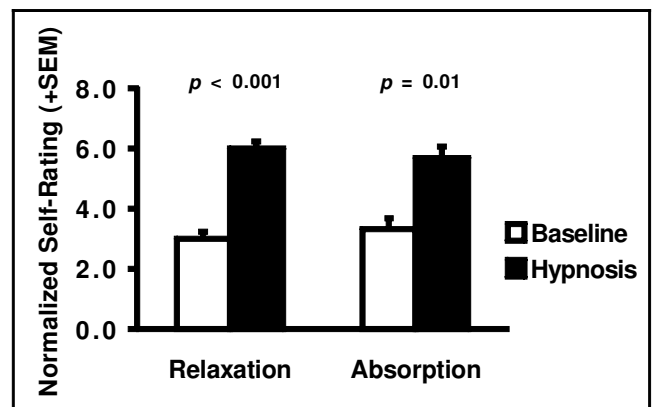


Figure 1. Hypnosis-related changes in mental relaxation and absorption. Self-rated relaxation and absorption (normalized within-subjects) increased significantly following the induction of hypnosis (see p values).

(Hofbauer et al., 2001; Rainville et al., 1997; Rainville, Carrier, Hofbauer, Bushnell, & Duncan, 1999; Rainville, Hofbauer, et al., 1999).

Heart rate, measured before and during scans, did not change significantly following the induction of hypnosis (see Hofbauer et al., 2001).

Reliability of Hypnosis-Related Changes in rCBF

The reliability of the effects of hypnosis on cerebral activity was examined by comparing the results of a subtraction analysis (Hypnosis minus Baseline conditions) with those of our previous study (see Table 2 in Rainville, Hofbauer, et al., 1999). Our current results replicated the previously reported rCBF increases in both occipital lobes, the right Sylvian region (peaks in the inferior frontal and superior temporal gyri), the left insula (more anterior and bilateral in the present study), and the right ACC. However, ACC activation was more extensive here with significant clusters of activated voxels covering multiple areas of the ACC and peaks found in both the right and left hemispheres, in the middle, rostral, and perigenual ACC. The frontal increases in rCBF extended further bilaterally in the central region, and in the medial frontal and prefrontal areas (superior frontal and orbito-frontal). Decreases in

rCBF observed in our previous study were replicated in the right inferior parietal lobule, the precuneus, and the left posterior temporal cortices (bilateral here). The effects previously reported and not replicated here are the increases in the right parietal operculum and the decreases in the medial frontal cortex and the posterior cingulate gyrus (here, medial parietal decreases were limited to the precuneus). Occipital increases in rCBF were again stronger in the warm stimulation condition, and prefrontal increases were stronger in the painful stimulation condition. These results largely confirm the reliability of the changes in rCBF associated with the induction of hypnosis.

Mental Relaxation- and Absorption-Related Effects

Directed Search over the Brainstem, the Thalamus and the ACC

The functional role of particular structures thought to be involved in the production of hypnosis was assessed by analyzing the degree of correlation between rCBF in these regions and subjects' estimates of the experiential indices of hypnosis (mental relaxation and absorption) (Table 1; Figure 2). Increases in mental relaxation were correlated with rCBF decreases in the mesencephalic tegmentum of the brainstem (Figure 2A) and with

Table 1. Peak *t* Values Observed in the Directed Search Areas in Regression Analyses on Self-Ratings and Thalamic rCBF

	<i>Relaxation</i>	<i>Relaxation-Specific</i>	<i>Absorption</i>	<i>Absorption-Specific</i>	<i>Thalamus Covariation</i>
Brainstem	-2.67* (-3, -33, -12)	-2.81* (-1, -38, -17)	<i>ns</i>	+2.78* (1, -26, -22)	+3.12* (13, -26, -15) +2.87* (3, -32, -24)
Thalamus	<i>ns</i>	-3.68** (-3, -16, 12)	+2.60* (-1, -18, 12)	+4.45*** (-3, -16, 12)	+3.50** (17, -11, 2)
ACC					
mid	+2.60* (1, 15, 35)	<i>ns</i>	<i>ns</i>	<i>ns</i>	+3.87** (8, 13, 44)
rostral	<i>ns</i>	-3.68** (5, 37, 45 ^a)	+3.45** (1, 29, 30)	+4.32** (3, 32, 39 ^a)	+3.82** (1, 43, 32 ^a)
perigenual	+3.02* (5, 34, 9)	<i>ns</i>	+2.96* (8, 32, 9)	<i>ns</i>	<i>ns</i>

Regression models were used to evaluate the slope of the relationship between relaxation or absorption ratings and rCBF. Relaxation-specific and absorption-specific effects were further tested after accounting for variance associated with absorption and relaxation, respectively (see Methods). Thalamic covariations were tested in a regression model evaluating the relationship between rCBF in the thalamus, at the site of absorption-specific activity, and rCBF in the brainstem, the rest of the thalamus, and the ACC. Stereotaxic coordinates are given for each peak according to the atlas of Talairach and Tournoux (1988) (*x, y, z* = lateral, anterior, superior).

ns = no significant peak found (-2.58 < *t* < 2.58; *p* > .01).

p* < .01; *p* < .001; ****p* < .0001 (uncorrected *p* values).

^aPeak is over the right medial superior frontal gyrus, within a cluster extending into the ACC at the site of significant absorption-related effect (*x, y, z* = 1, 29, 30).

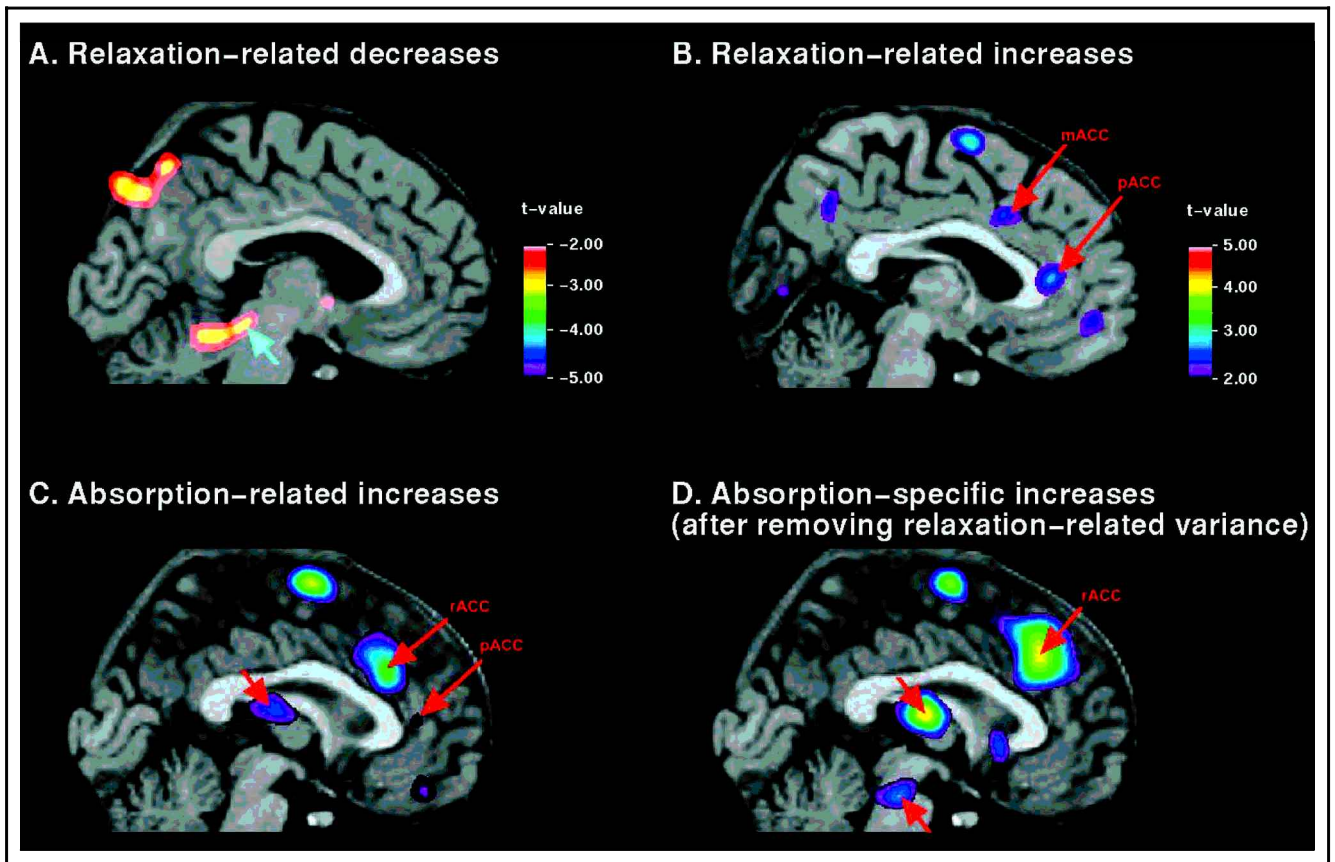


Figure 2. Statistical (t) maps, overlaid on a midsagittal view of a single-subject MRI anatomical image, showing the location of significant positive (red arrows) and negative (blue arrow) regression slopes between rCBF and self-ratings in the three regions of interest (brainstem, thalamus, and ACC; see Methods). (A) A negative regression peak is found with relaxation in the mesencephalic tegmentum and (B) positive regression peaks are found in the middle (mACC) and perigenual (pACC) portion of the ACC (note the reversal of the color scale). (C) Positive regression peaks are found with absorption in the thalamus, and in the rostral ACC (rACC) and pACC. (D) The regression of rCBF on absorption ratings, after accounting for relaxation-related effects, confirmed the positive regression peaks specific to absorption in the thalamus and rACC. This analysis further revealed an additional positive peak in the upper pons. Color scales in C and D are as in B. Stereotaxic coordinates of peaks are reported in Table 1.

increases in the middle and perigenual ACC (Figure 2B). Increases in absorption were correlated with rCBF increases in the thalamus, and in the rostral and perigenual ACC (Figure 2C).

The specificity of any changes in the rCBF associated with either mental relaxation (relaxation-specific) or absorption (absorption-specific) was further examined using ANCOVA (see Methods) to remove the variance shared with the other factor—absorption and relaxation, respectively (Table 1). Relaxation-specific negative correlations were found in the brainstem, in the thalamus, and in the superior frontal gyrus in a cluster of significant voxels extending over the rostral ACC. Absorption-specific effects confirmed the significant positive correlation between mental absorption and rCBF in the thalamus and in the rostral ACC and further revealed a significant positive peak in the upper pons of the brainstem (Figure 2D; Table 1). Although mental relaxation and absorption both increased during hypnosis, these results demonstrate that the negative correlation in the mesencephalic brainstem and the thalamus appears to be exclusively associated with

mental relaxation, while the positive correlations in the upper pons, the thalamus, and the mid-ACC appear to be exclusively associated with mental absorption.

Global Searches

Results of the global searches show additional differences between the patterns of activity related to mental relaxation and absorption. In the frontal lobe, increases in prefrontal rCBF were positively correlated primarily with mental absorption (Table 2), while increases in the precentral region were positively correlated with both relaxation (Figure 3A) and absorption (Table 2). Consistently, after removing the variance shared between mental relaxation and absorption, positive absorption-specific correlations (Table 2; Figure 3B) and negative relaxation-specific correlations (Table 2) were observed in prefrontal areas, while most precentral effects did not reach significance.

Posterior cortical areas displayed a mixed pattern of results. Negative correlations observed in both temporal lobes were more reliably related to mental relaxation

than absorption and the relaxation-related effects held after accounting for variance in absorption (Table 2—relaxation-specific). Additional sites of relaxation-specific effects included negative correlations in the right parietal operculum and lobule and positive correlations in the right precuneus, the left inferior parietal lobule, and the bilateral occipital cortices (Table 2—relaxation-specific).

The effects associated with absorption in the posterior cortices were strikingly different from the effects of relaxation. After accounting for relaxation-related variance, we observed both positive and negative absorption-specific correlations in both the right and left parietal lobules (see Table 2—absorption-specific). In the inferior parietal lobules, positive and negative correlations dominated in the right and left hemispheres, respectively (Figure 3B). Strong negative correlations were also observed over the right precuneus, the posterior cingulate cortex, and both occipital lobes (Figure 3B).

Additional statistical trends directly relevant to our hypotheses were also observed in the somatosensory cortices where rCBF was negatively correlated with mental relaxation (see Figure 3A; right S1 peak coordinates: 44, -35, 59, $t = -2.86$, p -uncorrected = .014, cluster $p = .06$; left S1: -44, -21, 16, $t = -2.51$, p -uncorrected = .026, cluster analysis, $p > .10$; right parietal operculum, S2: 48, -21, 24, $t = -3.51$, p -uncorrected = .003, cluster $p > .10$; right posterior insula: 44, -4, 15, $t = -2.96$, p -uncorrected = .011, cluster $p > .10$).

Covariations with Thalamic rCBF

In our previous study, thalamic activity was found to be correlated with hypnosis-related ACC activity (see Table 2 and Appendix in Rainville, Hofbauer, et al., 1999) and several studies suggest a pivotal role of the thalamus in arousal, attention, and consciousness, and in the interaction between the brainstem and the ACC (e.g., Paus et al., 1997; Paus, 2001; Portas, Howseman, Josephs, Turner, & Frith, 1998; Hofle et al., 1997). Here, we tested the association between absorption-related activity in the thalamus and activity in other sites of absorption-related changes using a covariation analysis centered on the absorption-specific peak in the thalamus reported in Table 1. Absorption-specific sites in the brainstem (upper pons) and the ACC showed significant covariations with thalamic rCBF (Table 1). Additional regions where rCBF showed a positive correlation with thalamic rCBF included bilateral frontal sites in the inferior, middle, and superior frontal gyri, extending medially into the right ACC, and the right insula (Table 3). Many of those peak locations matched frontal sites specifically related to mental absorption (italicized in Table 2). A strong positive peak was also observed in the right inferior parietal lobule, precisely at the location where rCBF correlated strongly and specifically with mental absorption (compare Table 2, absorption-

specific, and Table 3). Areas displaying negative correlation with thalamic rCBF were found bilaterally in the occipital lobes, consistent with the absorption-specific effects reported in Table 2.

DISCUSSION

The approach used in this study provided a description of cerebral activity associated with specific changes in phenomenal experience produced by a standard hypnotic induction. We discuss, in turn, the evidence for the production of hypnotic phenomena, the reliability of hypnosis-related effects, the effects associated with mental relaxation and absorption, and the implications of our results for a state theory of hypnosis.

Hypnosis and Phenomenal Experience

The induction of hypnosis produced the expected increases in both mental relaxation and absorption. These changes were positively correlated (see Methods), as predicted by the experiential model of hypnosis proposed by Price (1996), and the ability to maintain hypnotic relaxation and absorption depended upon the subjects' hypnotic susceptibility. The higher levels of absorption maintained in highly hypnotizable subjects are consistent with the positive association between absorption, attentional processes, and hypnotizability suggested in previous studies (Crawford 1994; Balthazard & Woody, 1992; Tellegen & Atkinson, 1974). These results, and additional convergent observations described in our previous report of pain-related effects (Hofbauer et al., 2001) and from several experiments using similar methodology (Rainville et al., 1997; Rainville, Carrier, et al., 1999), confirmed the reliable production of hypnotic phenomena.

Reliability of Hypnosis-Related Effects on rCBF

The experimental conditions examined here and in the first 8 scans in our previous study were identical—the same hypnotic induction procedure was applied by two different experimenters, and the two separate groups of subjects tested had comparable mean hypnotic susceptibility scores (Rainville, Hofbauer, et al., 1999). The results of the subtraction analysis largely replicated our previous findings as well as those reported by Maquet et al. (1999). In comparison to our previous experiment, differences in the methods were limited to the addition of relaxation and absorption ratings after the scans. The larger areas of frontal activation, including the precentral region, and the more restricted occipital activation observed here may reflect the emphasis put on hypnotic relaxation and absorption during the scans. As these dimensions of experience characterize standard hypnotic induction procedures, we submit that these differences further emphasize the functional significance of

Table 2. Results of the Global Searches of Cerebral Regions where rCBF Showed a Significant Regression with Relaxation and Absorption

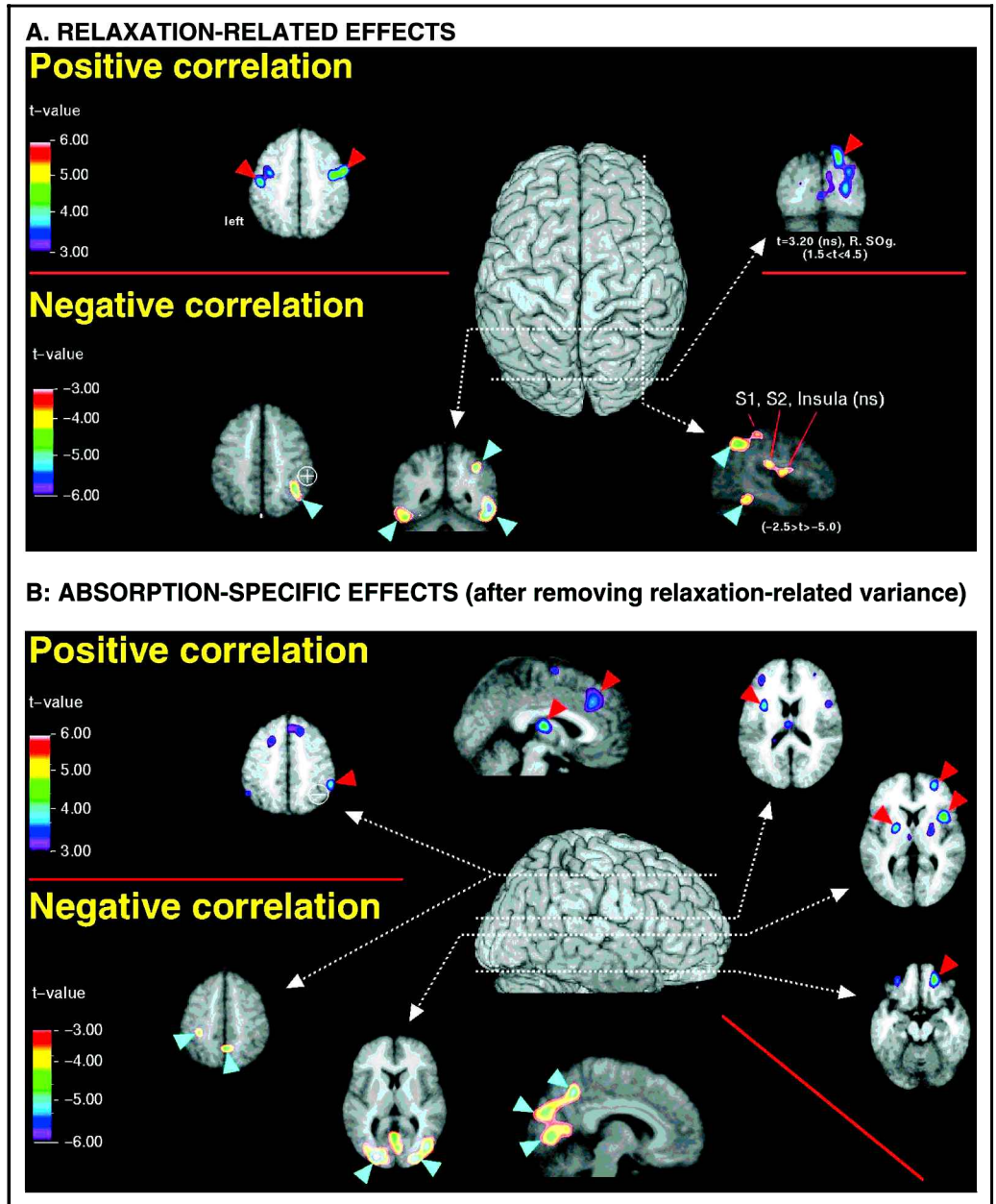
Region	Peak Location	Relaxation			Relaxation-Specific			Absorption			Absorption-Specific			
		x	y	z	t	x	y	z	t	x	y	z	t	
Frontal (F.)	R. F. Pole (BA 10)	-	34	56	2	-4.81	-	28	55	5	+4.21	-		
	R. lat. F. Orbital g. (BA 11)	-	19	46	-20	-4.29	-	19	44	-20	+4.75	-		
	R. middle F. g. (BA 46)	-	36	46	26	-3.81	-	34	46	26	+3.79	-		
	R. inf. F. g. (BA 47)	-	-	-	-	-	47	34	-18	+3.73	-	-		
	R. inf. F. g. (BA 45)	-	47	8	15	-3.86	55	20	11	+3.52	-	-		
	R. ant. insula/inf. F. g. (BA 14/44)	-	40	15	6	-3.77	43	10	2	+3.58	40	13	5	+4.81
	R. sup. F. g./cingulate g. (BA 8/32)	-	5	37	45	-3.68	-	3	32	39	+4.32	-		
	R. sup. F. g. (BA 6)	-	-	-	-	-	13	20	59	+3.69	15	22	57	+4.33
	R. medial sup. F. g. (BA 6)	-	-	-	-	-	3	-4	66	+4.23	3	-7	66	+3.92
	L. lat. F. Orbital g. (BA 11)	-	-	-	-	-	-30	41	-21	+3.68	-31	43	-18	+3.76
Central	L. middle F. g. (BA 8)	-	-	-	-	-	-46	15	35	+4.10	-44	10	29	+3.28
	L. middle F. g. (BA 46)	-	-	-	-	-	-36	37	18	+4.38	-38	39	24	+4.07
	L. ant. insula/inf. F. g. (BA 14/44)	-	-	-	-	-	-	-	-	-	-34	8	17	+4.25
	L. sup. F. g. (BA 6)	-	-	-	-	-	-	-	-	-	-26	6	56	+4.16
	L. sup. F. g. (BA 6)	-	-	-	-	-	-11	-4	66	+3.68	-	-	-	-
	R. precentral g. (BA 4)	54	-4	53	+5.16	-	52	-4	53	+5.05	-	-	-	-
	R. precentral g. (BA 4)	42	-7	50	+4.94	-	-	-	-	-	-	-	-	-
	R. pre/postcentral g. (BA 4/1/3)	-	-	-	-	-	36	-16	36	+3.78	-	-	-	-
	L. precentral/middle F. g. (BA 4/6)	-35	-6	53	+3.98	-	-	-	-	-	-	-	-	-
	L. precentral g. (BA 4)	-47	-16	47	+4.43	-	-48	-14	50	+4.36	-	-	-	-
Temporal (T.)	L. pre/postcentral g. (BA 4/1/3)	-	-	-30	-37	60	+4.03	-	-	-	-	-	-	
	R. middle T. g. (BA 21)	60	-33	-15	-5.71	59	-33	-13	-5.51	-	-	-	-	
	R. middle T. g. (BA 37)	56	-45	-9	-5.91	-	55	-47	-6	-4.41	-	-	-	
	L. parahippocampal g. (BA 35/36)	-36	-23	-18	-4.13	-	-	-	-	-	-	-	-	
	L. inf. T. g./fusiform g. (BA 37)	-52	-42	-20	-5.24	-59	-44	-12	-4.33	-48	-44	-20	-4.46	
	-	-	-	-	-	-	-	-	-	-	-	-	-	

Parietal (P.)	R. P. operculum (BA 40)	-	32	-30	27	-3.55	-	-	-	56	-44	50	-	-	-
	R. inf. P. lobule (BA 40)	-	56	-40	50	-3.77	-	-	-	56	-44	50	+4.24	+3.83	-4.09
	R. P. lobule (BA 40/7)	39	-49	45	-4.87	-	38	-47	45	-4.43	34	-56	42	+3.83	-4.09
	R. sup. P. lobule (BA 7)	-	-	-	-	-	21	-50	62	-4.45	21	-52	60	-4.09	-
	R. precuneus (BA 7)	-	5	-56	45	+5.33	-	-	-	-	5	-56	45	-5.10	-
	Precuneus/post. Cing. g. (BA 7/31)	-	-	-	-	-	-	-	-	-	0	-64	9	-5.05	-
	L. inf. P. lobule (BA 40)	-	-30	-37	60	+4.03	-	-	-	-	-35	-35	50	-4.48	-
	L. inf. P. lobule (BA 40)	-	-	-	-	-	-	-	-	-	-52	-56	47	+3.70	-
Occipital (O.)	Lingual g./post. Cing. g. (BA 18/31)	-	0	-66	9	+4.26	-	-	-	-	-	-	-	-	-
	R. inf. O. g. (BA 19)	-	43	-71	-6	+3.68	43	-75	5	-4.44	43	-75	-3	-5.17	-
	R. lingual g. (BA 18)	-	4	-76	3	+4.64	-	-	-	-	7	-78	2	-4.68	-
	R. cuneus (BA 18)	-	12	-83	27	+5.20	-	-	-	-	-	-	-	-	-
	R. sup. O. g. (BA 19)	-	17	-81	38	+5.59	-	-	-	-	15	-80	33	-6.02	-
	R. sup. O. g. (BA 19)	-	30	-87	26	+4.07	-	-	-	-	-	-	-	-	-
	R. O. pole (BA 18)	-	27	-92	9	+4.85	-	-	-	-	27	-92	8	-5.35	-
	L. fusiform g. (BA 18/19)	-	-40	-78	-3	+3.59	-	-	-	-	-40	-76	-3	-4.46	-
	L. sup. O. g./ precuneus (BA 19/7)	-	-13	-88	38	+4.07	-8	-76	36	-4.23	-13	-87	39	-5.18	-
	L. lingual g. (BA 18) /cerebellum	-	-	-	-	-	-17	-76	-18	-3.51	-	-	-	-	-
	L. lingual/fusiform g. (BA 18/19)	-	-15	-78	-3	+4.72	-27	-83	-11	-4.22	-16	-80	-2	-5.62	-
	L. sup. O. g. (BA 19)	-	-27	-83	27	+3.98	-	-	-	-	-27	-83	29	-4.19	-
	L. O. pole (BA 18)	-	-24	-90	8	+5.38	-26	-88	0	-4.18	-24	-90	5	-6.50	-
Subcortical	Thalamus (see Table 1)	-	-3	-16	12	-3.68	-	-	-	-	-3	-16	12	+4.45	-
	R. putamen	-	-	-	-	-	21	-7	5	+4.01	24	-4	6	+3.57	-
	L. globus pallidus	-	-	-	-	-	-19	-1	3	+3.68	-21	-1	2	+4.41	-
	L. cerebellum	-	-9	-88	-23	-4.29	-	-	-	-	-	-	-	-	-

Relaxation-specific and absorption-specific effects were examined after removing the variance associated with absorption and relaxation, respectively (ANCOVA; see Methods). The linear slope between rCBF and ratings is significant at peak locations listed (*t* threshold = ± 4.20 , in **bold**; see Methods). Peaks with $t > + 3.50$ or $t < - 3.50$ within a significant cluster (see Methods) are also indicated with their coordinates. Peaks close to, or within, regions where significant covariations with thalamic rCBF were found are *italicized* (see Table 3 and Methods). Peak locations are based on the stereotaxic atlas of Talairach and Tournoux (1988) (x = lateral, y = anterior, z = superior) and on morphological landmarks on the merged PET-MRI images (BA = probable Brodmann's area; L. = left, R. = right; g. = gyrus; ant. = anterior; post. = posterior; sup. = superior; inf. = inferior).

Figure 3. Brain regions showing positive (red arrowheads) and negative (blue arrowheads) regression peaks between rCBF and self-ratings of (A) relaxation and (B) absorption, after accounting for relaxation-related variance (absorption-specific). Statistical *t* maps are superimposed on the average anatomical MRI (left is on the left side). Slice locations are indicated on the 3-D anatomical image of a single subject's anatomical MRI. (A-positive) Positive relaxation-related effects are shown in the central region bilaterally (horizontal slice on the left). A positive peak is shown in the right superior occipital gyrus (SOg.) (coronal view on the right; note scale change). (A-negative) A negative relaxation-related effect in the right posterior parietal cortex is shown in horizontal (first from left), coronal (second), and lateral sagittal (third) views. The plus sign indicates the more anterior location of the peak positive regression in the analysis of absorption-related effects, as shown in B. Additional negative correlations are shown in the bilateral middle and inferior temporal gyri (second), and in the right somatosensory cortices (S1, S2, insula).

(B-positive) A positive absorption-specific peak is shown in the right inferior parietal lobule (first from left). The minus sign indicates the more posterior location of the negative regression peak in the analysis of relaxation-related effects, as shown in A. Other peaks are shown on the midsagittal view in the thalamus and the anterior cingulate cortex (second from left), and in the left lenticular nuclei and bilateral prefrontal cortices (last three cuts from left). (B-negative) Negative absorption-related effects are shown in the left inferior parietal lobule (first from left), in both occipital lobes (second and third from left), and in the precuneus (first and third). Stereotaxic coordinates of peaks are reported in Table 3 (see relaxation- and absorption-specific).



the underlying processes in the production of hypnotic states, as discussed below.

Role of the Brainstem, the Thalamus, and the ACC in Hypnosis

Results of the regression analyses suggest that neural activity in the brainstem, the thalamus, and the ACC contributes to the experience of being hypnotized. The relaxation-specific negative correlations in the mesen-

cephalic brainstem and the thalamus may reflect the well-established contribution of brainstem and thalamic nuclei to the regulation of wakefulness and cortical arousal. In functional brain imaging studies, rCBF decreases in the brainstem and the thalamus have been associated with decreased vigilance (Paus et al., 1997), sleep (Kajimura et al., 1999; Braun et al., 1997; Hofle et al., 1997; Maquet et al., 1997), and the loss of consciousness produced by the anesthetic propofol (Fiset et al., 1999). These effects and, to some extent,

the present relaxation-related decrease in brainstem rCBF, may reflect an attenuation of activity within brainstem cholinergic nuclei. Such reduction has been observed during slow EEG activity, before the onset of sleep, and during slow-wave sleep in animal studies (Steriade & McCarley, 1990). Consistent with this possibility, we previously reported an increase in slow (delta) EEG activity following hypnotic induction (Rainville, Hofbauer, et al., 1999). Although hypnotic and sleep states are clearly distinct, certain neurophysiolog-

ical mechanisms may be involved to a varying degree in the production of both states.

The positive association specifically observed between mental absorption and rCBF in the upper pons and the thalamus contrasts with the above relaxation-related effect, and is consistent with previous reports of attention-related brain activation (Kinomura et al., 1996). This activity may reflect the involvement of the noradrenergic system of the locus coeruleus in focused attention, and possibly in the interaction between cortical arousal

Table 3. Cerebral Sites of Covariation with Thalamic rCBF at the Absorption-Specific Peak Coordinates ($x = -2.7, y = -16.0, z = 12.0$)

Region	Peak Location	x	y	z	t
Frontal (F.)	<i>R. medial sup. F. g./ACC (BA 6/24)</i>	1	43	32	+3.82
	<i>R. anterior cingulate g./sup. F. g. (BA 32/6)</i>	8	13	44	+3.87
	R. inf. F. g. (BA 44)	51	12	8	+3.87
	R. ant. insula (BA 14)	38	12	5	+4.12
	R. sup. F. g. (BA 6)	16	20	59	+3.71
	R. medial sup. F. g. (BA 6)	3	-6	63	+4.98
	R. medial sup. F. g. (BA 6)	11	-23	53	+4.12
	L. middle F. g. (BA 46)	-38	46	23	+3.81
	L. middle F. g. (BA 46)	-31	39	39	+3.74
	L. inf. F. g. (BA 44)	-43	6	12	+4.30
	L. sup. F. g. (BA 6)	-19	20	53	+3.40
	L. medial sup. F. g. (BA 6)	-5	17	65	+3.53
	L. sup. F. g. (BA 6)	-20	12	65	+2.83
Parietal	R. inf. parietal lobule (BA 40)	56	-44	50	+5.19
Occipital (O.)	R. fusiform g. (BA 19)	26	-62	-30	-5.15
	R. lingual g. (BA 18)	7	-78	6	-6.23
	R. sup. O. g. (BA 19)	19	-85	30	-7.14
	R. O. pole (BA 18)	27	-90	9	-7.51
	L. cuneus (BA 18)	-11	-83	29	-6.33
	L. O. pole (BA 18)	-23	-88	6	-7.93
Subcortical	<i>R. thalamus</i>	17	-11	2	+3.50
	<i>R. brainstem</i>	13	-26	-15	+3.12
	<i>R. medial brainstem</i>	3	-32	-24	+2.87
	L. cerebellum	-4	-57	-21	+4.09
	L. globus pallidus	-20	-1	-2	+3.02
	L. caudate nucleus	-12	6	20	+2.91

Positive and negative regression slopes are significant at sites listed, based on cluster or peak analyses (peak t threshold $<> \pm 3.70$, in **bold**; all peaks reported with $t < 3.70$ are within a significant cluster, see Methods). Peaks in *italic* are also reported in Table 1. See legends to Tables 1 and 2 and Methods for further explanation.

and attentional processes (i.e., increased attention/absorption concurrent with decreased cortical arousal/increased relaxation) (Aston-Jones et al., 1999). The indirect nature of the rCBF measures and the relatively poor resolution of the PET method require some caution in evaluating the possible anatomo-functional implications of our results in the brainstem. However, the convergent findings observed in other brain imaging studies and the observations provided in animal studies support the notion that ascending cholinergic and noradrenergic pathways may contribute differentially to the multiple dimensions of experience that characterize hypnosis.

The overall pattern of results found in the ACC likely reflects the heterogeneity of functions associated with this area (Devinsky, Morrell, & Vogt, 1995). The location of the most posterior relaxation-related peak in the ACC (mACC) is consistent with our previous observation of ACC activation during hypnosis (Rainville, Hofbauer, et al., 1999). This relaxation-related peak is only slightly anterior to the motor area of the caudal ACC (Picard & Strick, 1996) and may be involved in the installment of a relaxed state (also see precentral area below). In contrast, a positive absorption-specific effect was observed in a more rostral region of the ACC (rACC) close to a negative relaxation-specific correlation (see Table 1). This area of the ACC has previously been involved in executive attention, in the detection of errors, and in the monitoring of conflict between competing cognitive processes (Bush, Luu, & Posner, 2000; Cohen, Botvinick, & Carter, 2000; Badgaiyan & Posner, 1998; Posner & Rothbart, 1998). A meta-analysis of PET studies investigating cognitive functions further suggested that the increase in activity within this sector of the ACC is related to the difficulty of the task performed (Paus, Koski, Caramanos, & Westbury, 1998). Our findings are consistent with these propositions, to the extent that the engagement of the cognitive and neurophysiological processes implied in each of those accounts may be accompanied by a subjective experience of increased mental absorption.

The coordinated pattern of rCBF changes in the brainstem, the thalamus, and the ACC may reflect the interrelationships between the multiple components of a network (e.g., Paus et al., 1997), herein shown to be associated with the feeling of being “mentally absorbed.” The precise location of the observed absorption-specific thalamic peak is consistent with an involvement of the intralaminar and medio-dorsal nuclei, which have reciprocal connections with the ACC (Vogt & Gabriel, 1993). The finding that the coordinated activity in the thalamus and the ACC is disrupted in persistent vegetative states is consistent with the notion that these structures work in tandem to regulate consciousness (Laureys et al., 2000; also see Jeanmonod, Magnin, & Morel, 1996). Furthermore, a functional interaction between arousal and attentional processes has been reported in the thalamus

where the putative attention-related activity associated with the performance of a simple visual discrimination task was found to increase in states of low arousal (Portas et al., 1998). This increase in thalamic activity was suggested (1) to reflect a compensatory mechanism that permitted the maintenance of stable levels of performance in states of low arousal, and (2) to prevent the generalized thalamo-cortical synchronization that would lead to sleep. Here, the opposite effects of relaxation and absorption on thalamic activity may reflect this compensatory mechanism that maintains high levels of focused attention in deeply relaxed subjects during hypnosis. This function may be critical not only in hypnosis, but also in other conditions of deep relaxation distinct from both sleep and normal wakefulness such as meditative states (Lou et al., 1999). Furthermore, the coactivation of the ACC and the ponto-mesencephalic brainstem may reflect the contribution of the ACC to the regulation of attention-related activity in the locus coeruleus (Cohen et al., 2000). The positive regression found with absorption in the ponto-mesencephalic brainstem and the more robust regression observed in the thalamus and the ACC, after accounting for relaxation-related changes (absorption-specific; Table 1), further substantiate the possibility that brainstem and thalamic nuclei interact with the ACC to regulate the interaction between attention and cortical arousal. Taken together, these results are consistent with a contribution of brainstem nuclei, the intralaminar and medio-dorsal nuclei of the thalamus, and the ACC, to the changes in phenomenal experience that characterize hypnotic states.

Additional Relaxation- and Absorption-Related Changes in rCBF

Relaxation-Related Activity

We observed strong relaxation-related increases in rCBF in the precentral gyrus bilaterally, and reciprocal decreases in somatosensory areas (S1, S2, and insula). Precentral and premotor activation has been reported during hypnosis in an independent study (Maquet et al., 1999), and precentral rCBF was correlated with the rCBF measured at the ACC site of hypnosis-related activity in our previous study (see Appendix in Rainville, Hofbauer, et al., 1999). Similar increases in activity in motor and premotor areas have been associated with voluntary muscular relaxation (Toma et al., 1999), but the present results may reflect more than physical relaxation.

All standard hypnotic procedures include instructions for relaxation. However, the specific contribution of muscular relaxation and decreased arousal to the production of hypnotic states is unclear as hypnotic phenomena have been produced during muscular exercise (Banyai & Hilgard, 1976) and with suggestions of active-alertness (Vingoe, 1968, 1973). Here, the absence of significant effect of hypnosis on heart rate indicates that changes in cerebral activity did not correlate with

changes in peripheral arousal and suggests that subjects were already physically relaxed in the baseline control condition. This implies that the hypnosis-induced changes in self-ratings of relaxation may not simply reflect changes in “peripheral” arousal but may attest more specifically of an increase in “mental” relaxation and a reduction in “cortical” arousal. This is consistent with Price’s experiential model of hypnosis (see Introduction) and with our previous study showing an increase in slow (delta) EEG activity during hypnosis.

Relaxation-related effects observed outside primary somatomotor areas may partly reflect subjective feelings of mental ease more closely. In the subtraction analysis, hypnosis-related decreases were found in the right lateral posterior parietal rCBF both here (x, y, z : 40, -52, 44) and in our previous study (x, y, z : 46, -50, 42; from Table 1 in Rainville, Hofbauer, et al., 1999). Here, these changes were strongly, but not specifically, associated with relaxation (x, y, z : 39, -49, 45; see Table 2, Figure 3A). Furthermore, after accounting for absorption-related variance, right prefrontal activity was negatively correlated with relaxation (Table 2). Those additional changes in the right posterior parietal cortex and the right prefrontal cortices may contribute to the subjective feelings of mental ease rather than, or in addition to, physical relaxation.

Fronto-Parietal Attention Networks

Absorption-related activity was widespread and bilateral in the prefrontal cortices, but peaks were generally stronger in the right hemisphere. Positive regression peaks were maximal in the ventrolateral frontal cortices, over the inferior frontal gyrus, and in the anterior insula. A positive absorption-related regression peak was also significant in the right inferior parietal lobule. These areas also displayed strong coactivation with absorption-related thalamic activity. Very similar patterns of activation have been associated with attentional processes in tasks involving visual (e.g., Coull, Frackowiak, & Frith, 1998), auditory (Paus et al., 1997), and somatosensory stimuli (Peyron et al., 1999). Notably, the location of the positive parietal peak observed here closely matches the activation sites reported in those studies, and the site of covariation with the right ventrolateral attention-related activity reported in Paus et al. (1997), suggesting the activation of a similar network. The coordinated absorption-related activity observed here in the brainstem, the thalamus, the ACC, the right inferior frontal gyrus, and the right inferior parietal lobule provides very strong evidence that mental absorption is an experiential correlate of the activation of the brain’s “executive attentional network,” and suggests that this system plays a critical role in the production of hypnotic states.

Negative absorption-related regression peaks were also found in both the right and left lateral parietal cortices and in the precuneus (see Table 2). These

effects were largely independent of thalamic activity as indicated by the absence of significant effects at these locations in the covariation analysis (Table 3). The right posterior parietal cortex has been suggested to constitute a vigilance/orientation system (Pardo, Fox, & Raichle, 1991) and hypnosis-related decreases in this area may reflect a relative disengagement toward external sources of stimulation. Right and left posterior parietal cortices at the precise sites of relaxation- and absorption-related decrease in rCBF have been suggested to contribute to the monitoring of external space and time, respectively (Gitelman et al., 1996, 1999; Kim et al., 1999; Coull & Nobre, 1998; Nobre et al., 1997). Although these functions were not directly assessed in this experiment, the hypnotic induction procedure includes specific instructions for decreased orientation to, and interest in, irrelevant external sources of stimulation, and previous observations suggest that hypnotic relaxation and absorption are precursors to some alterations in spatio-temporal orientation and monitoring (Price, 1996). Thus, we speculate that those additional experiential changes may be consequent to relaxation- and absorption-related decreases in posterior parietal activity.

Relaxation- and Absorption-Related Effects on Occipital rCBF

The subtraction analysis confirmed the reliability of the hypnosis-related increase in occipital rCBF reported in our previous study (Rainville, Hofbauer, et al., 1999). We now show that this effect was associated with the subjective experience of hypnotic relaxation (see Table 2; relaxation-specific). Consistently, our previous study demonstrated a coupling between occipital increases in rCBF and increases in slow (delta) EEG activity during hypnosis. Similar increases in occipital rCBF and/or slow EEG activity had been observed in another study on hypnosis (Maquet et al., 1999) and in states of decreased vigilance (Paus et al., 1997), meditation (Lou et al., 1999), and slow wave sleep (Kajimura et al., 1999; Hofle et al., 1997). These effects are consistent with our previous proposition that hypnotic induction produces a global decrease in cross-modality suppression in unattended sensory channels leading to a relative disinhibition of cortical activity (see Paus et al., 1997; Kawashima, O’Sullivan, & Roland, 1995).

In contrast, negative correlations between rCBF and mental absorption were observed over both occipital lobes (Table 2; Figure 3B). Consistently, occipital rCBF was correlated negatively with thalamic rCBF at the absorption-specific site (Table 3). These contrasting effects imply that variations in occipital rCBF are associated with separate portions of the variance in relaxation and absorption. (Note that, although absorption and relaxation were significantly correlated, the variance in absorption was largely independent of relaxation; see

Methods). For a given level of relaxation, the increase in hypnotic absorption could reflect the concurrent engagement of the “executive attentional network,” which exerts an opposite effect over brain areas subserving unattended sensory channels (i.e., a relative facilitation of cross-modality suppression).

Hypnosis as a State of Consciousness

The representation of the body-self is central to the neurophenomenology of consciousness (Metzinger, 2000). In the Introduction, we have proposed that the induction of hypnosis produces global changes in subjective experience reflecting a modulation of basic aspects of the body-self representation. Consistently, the PET results indicate that hypnosis involves changes in activity within brain structures essential for the basic regulation of states of consciousness, self-monitoring, and self-regulation. Furthermore, changes in relaxation and absorption are precursors (although they may not be essential) to other hypnosis-related effects such as the diminished tendency to judge, monitor, and censor; the suspension of usual orientation toward time, location, and/or sense of self; and the experience of one’s own response as automatic or extra-volitional (Price, 1996). These dimensions of experience also rely critically on self-representation and may depend at least partly on cerebral areas shown here to be involved in hypnosis. Among those changes, the increased feeling of automaticity, an altered feeling of agency, may be the most distinctive aspect of hypnotic phenomenology (Weitzenhoffer, 1980). Interestingly, the sense of agency has recently been suggested to involve areas that display consistent changes in activity during hypnosis, such as the right inferior parietal cortex, the precuneus, and the somatosensory cortices (Blakemore & Decety, 2001; Ruby & Decety, 2001). The modulation of activity observed here within those areas is consistent with the interpretation that hypnosis produces changes in self-representation construed as an essential element for conscious experience.

Conclusion

The present study used self-ratings of subjective feelings of mental relaxation and mental absorption to map brain areas involved in hypnosis. We replicated previous findings and further demonstrated that hypnotic relaxation and absorption reflect changes in brain activity within regions involved in the control of consciousness states and in self-regulation, such as the brainstem, the thalamus, and the ACC. The coordinated activity within these structures and other absorption-related areas, such as the ventrolateral frontal and right posterior parietal cortices, has been previously shown to underlie the regulation of the content of consciousness through mechanisms of executive attention. We must recognize

that our findings are correlative in nature and are relevant to hypnosis to the extent that mental relaxation and absorption are conceived as basic experiential dimensions that characterize hypnotic phenomena. We further speculate that these changes in subjective experience and brain activity may contribute to other hypnosis-related effects such as the altered feeling of agency experienced during hypnosis. These findings are consistent with the notion that hypnotic states are achieved through the modulation of activity within a distributed network of cerebral structures involved in the regulation of consciousness states.

METHODS

Subjects

Ten right-handed subjects (4 men, 6 women) were selected from a group of 22 volunteers as a part of a study on the hypnotic modulation of pain (Hofbauer et al., 2001). Hypnotic susceptibility was assessed using the SHSS-A administered between scans (range: 1/11–10/11; mean \pm SD: 6.9 \pm 2.8). The Ethics Committee of the Montreal Neurological Institute (MNI) approved all procedures, and subjects signed a consent form describing the procedure and affirming their right to withdraw from the experiment without prejudice.

Experimental Procedure

We report the results obtained in eight scans acquired in a restful baseline and hypnosis condition. Hypnotic induction started immediately after Scan 4 and was sustained in the remaining scans by repeating induction instructions between scans. Instructions included suggestions for (1) increased physical and mental relaxation; (2) comfortable feeling of warmth, heaviness, and drowsiness; (3) sustained passive attention to the experimenter’s voice and to the instructions; and (4) decreased concern with, and orientation to, external and internal (mental) sources of distraction. No specific instruction for visual imagery was included. During all scans, the subjects’ eyes were closed and their left hand was immersed in warm or painfully hot water. Pain-related activation and four additional scans performed with suggestions for pain modulation are reported elsewhere (Hofbauer et al., 2001).

Self-Ratings of Mental Relaxation and Absorption

After each scan, subjects were instructed to rate (0–10): (1) their level of tension–relaxation with “10 being the most relaxed and at ease you can be” and (2) their level of sustained focus of attention, with “10 being the most absorbed and the largest amount of sustained focused attention you can gather.” Ratings of relaxation and absorption were transformed using the rank within subjects to (1) control for individual differences, (2) prevent

scaling biases, and (3) parallel the analysis of rCBF data. Subjects rated pain on separate scales (0–100). Hypnosis-related increases in relaxation and absorption did not interact with the stimulation condition (pain vs. warm stimulation; p 's > .10), neither relaxation nor absorption correlated significantly with pain ratings (all p 's > .10), and pain was not altered by hypnosis alone [$t(9) = 0.69$, $p = .51$].

PET Imaging Methods

rCBF was measured using the H₂¹⁵O bolus injection method (10 millicuries/scan) without arterial blood sampling (Herscovitch, Markham, & Raichle, 1983), with a high-resolution PET scanner operated in 3-D acquisition mode (Siemens ECAT HR⁺, 63 slices). Stimulus onset was simultaneous with bolus injection and 1-min acquisition scans started about 15 sec postinjection (interscan interval of 12–15 min). Data from the first 40 sec of acquisition were reconstructed and analyzed. Each subject also underwent a high-resolution anatomical MRI (160 1-mm sagittal slices acquired on a Philips 1.5-T Gyroscan system). Each PET and MRI volume was aligned and transformed using software developed at the MNI to match the MNI standardized Talairach space (Collins, Neelin, Peters, & Evans, 1994; Talairach & Tournoux, 1988). PET volumes were smoothed (FWHM = 14 mm) and normalized to the average brain count. Peak and cluster analyses were performed (Friston, Worsley, Frackowiak, Mazziotta, & Evans, 1994; Worsley, Evans, Marrett, & Neelin, 1992).

Reliability of Hypnosis-Related Effects

A first analysis was performed using the subtraction method (Hypnosis minus Baseline) to evaluate the reliability of the effects reported in our previous study (Table 2 in Rainville, Hofbauer, et al., 1999). We considered that hypnosis-related changes in rCBF were replicated when a significant peak was observed within one resel (Worsley et al., 1992) of the peak sites reported in our previous study, or when the peak sites were within a significant cluster.

Regression of rCBF on Self-Ratings of Relaxation and Absorption

Regression analyses were used to test the relation between ratings and rCBF (GLM). Subject- and stimulus-related effects were removed first (ANCOVA), and the significance of the regression slope between the covariate of interest and rCBF was estimated using t tests. Relaxation-specific and absorption-specific effects were further tested using ANCOVAs to remove the variance shared between absorption and relaxation ($R^2 = .42$, $p < .001$). The statistical criterion was set to $t > 2.58$ (two-tailed uncorrected $p < .01$) in the

directed searches restricted to the brainstem, the thalamus, and the ACC (Table 1; Figure 2). Global search effects are significant ($p < .05$) based on peak (t value > 4.20) and/or clusters analysis, after a correction for multiple comparisons over the gray matter volume (uncorrected $p < .0001$) (Table 2; Figure 3).

Thalamic Covariations

A covariation analysis was performed in which the rCBF measured in the thalamus was used as the covariate of interest, after accounting for subject- and stimulus-related variance (ANCOVA; see Tables 1 and 3). Because we were mainly interested in the relationship between the activity in the thalamus and other absorption-related sites, the threshold for statistical significance was set to $t = 3.70$ ($p = .05$, uncorrected $p < .0008$) based on the volume defined by the sum of clusters of voxels showing significant absorption-specific effects (186 cm³; see Worsley et al., 1992).

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