PAIN PERCEPTION AND HYPNOSIS:  
Findings From Recent Functional Neuroimaging  
Studies

ANTONIO DEL CASALE

University of Rome, “La Sapienza,” Italy; and P. Alberto Mileno Onlus Foundation,  
Vasto (CH), Italy

STEFANO FERRACUTI

University of Rome, “La Sapienza,” Italy

CHIARA RAPINESI AND DANIELE SERATA

University of Rome, “La Sapienza,” Italy; and Sisters of the Sacred Heart of Jesus Hospital,  
Viterbo, Italy

SAVERIO SIMONE CALTAGIRONE, VALERIA SAVOJA, DARIA PIACENTINO,  
GEMMA CALLOVINI, GIOVANNI MANFREDI, GABRIELE SANI, AND  
GEORGIOS D. KOTZALIDIS

University of Rome, “La Sapienza,” Italy

PAOLO GIRARDI

University of Rome, “La Sapienza,” Italy; and Sisters of the Sacred Heart of Jesus Hospital,  
Viterbo, Italy

Abstract: Hypnosis modulates pain perception and tolerance by affecting cortical and subcortical activity in brain regions involved in these processes. By reviewing functional neuroimaging studies focusing on pain perception under hypnosis, the authors aimed to identify brain activation-deactivation patterns occurring in hypnosis-modulated pain conditions. Different changes in brain functionality occurred throughout all components of the pain network and other brain areas. The anterior cingulate cortex appears to be central in modulating pain circuitry activity under hypnosis. Most studies also showed that the neural functions of the prefrontal, insular, and

Manuscript submitted December 2, 2013; final revision accepted January 9, 2014.
Address correspondence to Antonio Del Casale, NESMOS Department  
(Neurosciences, Mental Health, and Sensory Organs), School of Medicine and Psychology,  
University of Rome, “La Sapienza,” Sant’Andrea Hospital, Via di Grottarossa 1035-1039,  
00189 Rome, Italy. E-mail: antonio.delcasale@uniroma1.it

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somatosensory cortices are consistently modified during hypnosis-modulated pain conditions. Functional neuroimaging studies support the clinical use of hypnosis in the management of pain conditions.

One field where the efficacy of hypnosis has been best evaluated and validated is pain perception and pain tolerance modulation; however, the neural mechanisms underlying such hypnotic modulations remain unclear. Hilgard (1973) first formulated a theory to explain pain reduction in hypnosis (neodissociation interpretation). He and his group also showed a direct correlation between the degree of hypnotizability and an obtainable level of analgesia (Hilgard, 1967, 1975, 1986; Hilgard, Cooper, Lenox, Morgan, & Voevodsky, 1967), and that hypnosis can reduce clinical or experimental pain perception by elevating the perceptual threshold (Hilgard, 1986). Hypnotic analgesia was opiate-independent because it was not reversed by the opiate antagonist naloxone (Goldstein & Hilgard, 1975). McGlashan, Evans, and Orne (1969) supposed that two components were involved in hypnotic analgesia, that is, nonspecific (or placebo) effects of using hypnosis as a method of treatment and specifically induced perception distortion during deep hypnosis. In brief, hypnotic analgesia was shown to possess a specific neurophysiological effect.

Hypnoanesthesia and hypnoanalgiesia showed some advantages in specific types of surgical patients (Van Sickle, 1992). In preoperative anesthesia, hypnosis combined with local anesthesia and minimal conscious sedation (hypnosedation) may reduce patient discomfort, anxiety, pain, and intraoperative requirement for antianxiety and analgesic drugs, ensuring better surgical conditions and faster recovery (Faymonville et al., 1998). A meta-analysis pointed to the efficacy of hypnotic techniques for pain management and their effectiveness in reducing both clinical and experimental pain (Montgomery, DuHamel, & Redd, 2000). A recent meta-analysis comparing hypnosis for chronic pain to standard care and other psychological interventions confirmed the effectiveness of hypnosis (Adachi, Fujino, Nakae, Mashimo, & Sasaki, 2014).

Painful stimuli activate several brain regions, resulting in multidimensional pain perception (sensory discrimination and affective, cognitive, and motor components). The "pain matrix," also called the "homeostatic afferent processing network," mainly includes the primary (SI) and secondary (SII) somatosensory cortices, the insular cortex (IC), the anterior cingulate cortex (ACC), and thalamic nuclei (Apkarian, Bushnell, Treede, & Zubieta, 2005; Tracey & Mantyh, 2007).

Hypnotic modulation of pain can relate to functional changes in this network and other brain areas, but the specific correlates of
hypnoanalgesia and other hypnosis-modulated pain conditions are only partly understood. Functional neuroimaging studies may help in understanding the mechanisms of hypnotic pain matrix modulation. By reviewing the main functional neuroimaging studies on the subject, we aimed to identify the brain activation-deactivation patterns during hypnosis-modulated pain conditions.

**Method**

We searched the PubMed, Embase, and PsycInfo databases using terms such as *hypnosis, trance, pain, pain perception, analgesia, hypnotic analgesia, functional magnetic resonance imaging* (fMRI), *magnetoencephalography* (MEG), *near-infrared spectroscopy* (NIRS), *magnetic resonance spectroscopy* (MRS), *positron emission tomography* (PET), and *single photon emission computed tomography* (SPECT). Papers were included if they satisfied standards for adequate methodology, included population criteria and had focused on pain perception during hypnosis or in highly hypnotizable people. Exclusion criteria comprised inadequate methodology (method unspecified and/or inadequately described), no report of pain perception data, and unspecified inclusion of subjects.

Papers published in peer-reviewed journals dealing with functional neuroimaging during hypnosis-modulated pain conditions were included. Most of these studies were published in the last 10 years. Further papers that did not appear in the above databases were searched from reference lists of retrieved papers.

At the end of the selection, we subdivided the included studies according to the procedures they adopted—namely, the quality and type of hypnotic suggestion—into three main types:

- Type 1: Procedures with hypnotic suggestions to alter an experimental, physically induced (PI) pain condition;
- Type 2: Procedures with hypnotic suggestions to alter a chronic pain condition;
- Type 3: Procedures with hypnotically induced (HI) pain.

Here we discuss the main results of the studies included in each of these types.

**Results**

magnetic resonance imaging [title/abstract] OR fMRI [title/abstract] OR magneto-encephalography [title/abstract] OR MEG [title/abstract] OR near infrared spectroscopy [title/abstract] OR NIRS [title/abstract] OR magnetic resonance spectroscopy [title/abstract] OR MRS [title/abstract] OR positron emission tomography [title/abstract] OR PET [title/abstract] OR single photon emission computed tomography [title/abstract] OR SPECT [title/abstract]),” carried out on November 20, 2013, yielded 30 papers, of which 26 were relevant but eight were reviews, hence leaving 18 original papers for our analysis. The same search in Embase on the same day, without the title/abstract specified, yielded 59 papers, adding four further reviews but no new original papers. The same search as in Embase yielded 62 papers in PsychInfo, with one new original paper. Reviews were not used for the present study but were commented upon when appropriate, and their reference lists were further searched for relevant undetected papers; through this search, two more papers were identified. The final selection included 21 papers for review. Eleven studies used PET (52.38%), nine of which were performed with H$_2^{15}$O (81.82% of PET studies and 42.86% of all studies), one only was carried out with 99mTc-HMPAO SPECT (4.76%), and nine studies used blood-oxygen-level-dependence (BOLD) fMRI (42.86%). It is noteworthy that the first study appeared in 1993 and was the only study to use $^{133}$Xe PET, while the only SPECT study was published 4 years later, along with another PET study; PET studies spanned from 1993 to 2003 and a late addition in 2011, while the first fMRI study appeared in 2004, followed by a series of eight papers that appeared relentlessly until 2010.

We aimed to carry out a comprehensive review of all included studies and divided the studies included in three different types:

- **Type 1 (Procedures with hypnotic suggestions to alter an experimental PI-pain condition).** The results showed hyperactivation of different brain areas under hypnotic-modified pain conditions, as compared to control conditions, mainly including the ACC, IC, SI, SII, prefrontal cortex (PFC), and other brain areas; much less frequently they showed hypoactivation of the thalamus, parietal cortex (PC), and other brain areas.
- **Type 2 (Procedures with hypnotic suggestions to alter a chronic pain condition).** These procedures showed hyperactivation of different brain areas under hypnosis, as compared to control conditions, mainly including the ACC, PFC, IC, SI and SII, thalamus and other basal ganglia, cerebellum, and other brain areas.
- **Type 3 (Procedures with HI pain).** These procedures underlined the role of different brain areas, mainly including the ACC, PFC, IC, SI, SII, basal ganglia, and other brain areas.
DISCUSSION

Procedures With Hypnotic Suggestions to Alter an Experimental PI Pain Condition

The majority of the studies included in this review aimed at analyzing the main functional changes in brain activity occurring with hypnotic suggestions to alter a PI pain condition (see Table 1).

Anterior and middle cingulate cortices. Several studies point out that there are significant cerebral blood flow or blood oxygenation changes in the ACC during the experimental conditions of physical pain and hypnoanalgesia (see below). Current knowledge suggests that ACC regulates or modulates the interaction between cognition, sensory perception, and motor control in relation to changes in attentional, motivational, and emotional states. This paralimbic cortex is involved in assessing the motivational content of internal and external stimuli and in regulating context-dependent behavior (Devinsky, Morrell, & Vogt, 1995) and constitutes a major component of the pain network (Neugebauer, Galhardo, Maione, & Mackey, 2009). Both external and internal (self-administered noxious tactile stimulation) stimuli activate distinct ACC areas according to a rostrocaudal pattern, thus allowing for their distinction (Mohr, Binkofski, Erdmann, Büchel, & Helmchen, 2005). Right ACC hyperactivation occurs during PI pain even with simply receiving suggestions (Mohr et al., 2005).

Reported cerebral blood flow or blood oxygenation changes in the cingulate cortex during PI pain have been specifically related to hypnotic analgesic or hyperalgesic suggestions or both. Rainville and colleagues (Rainville, Duncan, Price, Carrier, & Bushnell, 1997; Rainville et al., 1999) investigated changes in brain activity during pain perception under hypnosis and normal waking through regional cerebral blood flow (rCBF) PET. Pain thermal stimuli (hot [47°C] vs. neutral [35°C] water) under hypnotic state (HS) have been associated with higher rCBF levels both in ACC and occipital cortical areas. The ventral part of the ACC partly modulates this activation with rCBF increasing proportionally to pain sensation (Rainville et al., 1997, 1999). The absence of changes in the sensory component of pain perception and the lack of a similar modulation within other pain-related cortical structures point to a significant involvement of the ACC in the affective component of pain (Rainville et al., 1997). In this line, hypnotic suggestions for increased and decreased pain intensity did not affect the extent of thermal pain-related ACC activation, pointing to the ACC being mostly, but not exclusively, involved in the affective component of pain perception (Hofbauer, Rainville, Duncan, & Bushnell, 2001).
Table 1
Functional Neuroimaging Studies About Pain Perception and Hypnosis: Hypnotic Suggestions Altering an Experimental Physically Induced (PI) Pain Condition

**Study:** Crawford et al., 1993
**Technique:** PET [133Xe]; PI pain (Ischemic); Hypnotic analgesia-hypoalgesia
**Participants:** 11 healthy subjects: 6 LHS, 5 HHS; 11 m, 0 f; Age range = 20–34 y; All right-handed
**Design:** Three rCBF measurements each counterbalanced waking and HS.
Within waking state and HS, there were three conditions: (1) RS with eyes closed; (2) ischemic procedure up to 15 min; (3) ischemic procedure with analgesia suggestions. Ischemic pain was produced for both arms simultaneously.
**Main findings:** Attended pain increased rCBF in the SSC, relative to surrounding regions. During hypnotic analgesia, HHS showed rCBF increase over the SSC, while LHS showed decreases. As compared to LHS, HHS group showed a significant increase in overall rCBF and highly significant bilateral OFC rCBF only during hypnotic analgesia.

**Study:** Heinrichs et al., 1997
**Technique:** SPECT [99mTc-HMPAO]; PI pain; Hypnotic analgesia-hypoalgesia; Hypnotic hyperalgesia
**Participants:** 8 healthy subjects: 0 m, 8 f
**Design:** rCBF measurements after HI modifications of perceived experimental pain stimulation. 4 subjects received normalgetic and hypoalgesic hypnosis and 4 received normalgesia and hyperalgesia.
**Main findings:** Increase of pain during HS correlated with activity in the SI, gyrus postcentralis.

**Study:** Rainville et al., 1997
**Technique:** PET [H215O]; PI pain (Thermal); Hypnotic analgesia-hypoalgesia; Hypnotic hyperalgesia
**Participants:** 8 healthy, MHS–HHS; 5 m, 3 f; age range = 19–53 y
**Design:** PET scans during conditions of the following: (1) alert control; (2) hypnosis control; (3) hypnotic suggestion for increased unpleasantness; or (4) decreased unpleasantness. During each scan, tonic stimuli were presented to the left hand by passive immersion in “neutral” (35°C) or “painfully hot” (47°C) water (10). After each scan, the perceived intensity and unpleasantness of the stimulation were rated.
**Main findings:** Hypnotic suggestions for increased or decreased unpleasantness, altered both the perception of pain affect and the activation within some but not all of these pain-related cortical regions. A comparison of rCBF changes between hypnotic suggestion and hypnosis control conditions revealed significant pain-related activations in SI, ACC, and IC, during both ↑UNP and ↓UNP conditions. Within the vicinity of SII no significant pain-evoked activity was observed in either the ↑UNP or ↓UNP conditions.

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Table 1  
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Study: Rainville et al., 1999
Technique: PET [H_2^{15}O]; PI pain (Thermal); Hypnotic analgesia-hypoalgesia; Hypnotic hyperalgesia
Participants: 8 healthy, HHS: 5 m, 3 f; Mean ± SD Age: 28.5 ± 11.2 y, Range = 19–53 y; 7 right- and 1 left-handed
Design: In the first two conditions (Baseline and Hypnosis), the subject’s left hand was immersed in neutral (35°C) or painfully hot (47°C) water for the duration of each scan. Stimulus order (35 or 47°C) was counterbalanced within sessions and reversed across subjects and sessions to minimize order effects. In the Hypnosis-with-Suggestion condition, suggestions for high or low pain unpleasantness were given before each of two scans, and the painful stimulus was applied during each scan. The order of the suggestion conditions was reversed across subjects and sessions. After each scan in all conditions, subjects rated the intensity and the unpleasantness of the pain sensation on separate scales.

Main findings: Hypnosis was accompanied by significant increases in both occipital rCBF and delta EEG activity, which were highly correlated with each other. Peak increases in rCBF were also observed in the caudal part of the right anterior cingulate sulcus and bilaterally in the inferior frontal gyri. Hypnosis-related decreases in rCBF were found in the right inferior parietal lobule, the left precuneus, and the PCC. Hypnosis-with-suggestions produced additional widespread increases in rCBF in the frontal cortices predominantly on the left side. Moreover, the medial and lateral posterior PC showed suggestion-related increases overlapping partly with regions of hypnosis-related decreases.

Study: Faymonville et al., 2000
Technique: PET [H_2^{15}O]; PI pain (Thermal); Hypnotic recalling of PAM
Participants: 11 healthy HHS: 7 m, 4 f; Mean Age = 31.7 y (range: 27–55 y); All right-handed
Design: Factorial design with two factors: (1) stimulation (warm nonnoxious vs. hot noxious) and (2) state ([a] RS and [b] MI in which during the interscan interval the subjects listened to sentences containing pleasant information taken from their own past; [c] HS, when the subjects were invited to re-experience their PAM).

Main findings: In the HS, in response to noxious stimulation, activation in an area encompassing the ACC (both BA 24 and 32), right caudate, left caudate and left putamen, and in a region involving the right thalamus extending to the upper midbrain. Other activations, not predicted a priori: right OFC, right DLPFC (BA 9), right IPC (BA 40). In the HS, as compared to RS and MI, activation in the right extrastriate area (BA 19) and right ACC. A significant interaction between pain sensation ratings and state was observed in a region involving the ACC (BA 24).
Table 1
(Continued)

**Study:** Hofbauer et al., 2001

**Technique:** PET [H\textsubscript{2}\textsuperscript{15}O]; PI pain (Thermal); Hypnotic analgesia-hypoalgesia; Hypnotic hyperalgesia

**Participants:** 10 healthy subjects: 4 m, 6 f; Mean Age = 24.2 y (range: 20–35 y); All right-handed

**Design:** During each scan, the subject’s left hand was immersed up to the wrist in a temperature-controlled circulating water bath for 60 s. The water temperature was either slightly warm (35°C) or painfully hot (46.0–47.5°C). Subjects received two trials each of painful heat and slightly warm stimulation during two conditions (alert control and hypnotic control) and received painful heat during the conditions involving hypnotic suggestions for increased- or decreased-pain intensity. The alert control condition was always presented first, followed by the hypnotic-control condition, and finally by the increased- and decreased-pain-intensity conditions. Noxious thermal stimuli presented during the alert and hypnosis-control conditions reliably activated contralateral structures, including SI, SII, ACC, and IC.

**Main findings:** Hypnotic modulation of the intensity of the pain sensation led to significant changes in pain-evoked activity within SI. Pain-related activity within SI was larger in response to hypnotic suggestions for increased pain intensity, compared with that observed following hypnotic suggestions for decreased-pain intensity. The rCBF levels in SII were significantly lower in the decreased-pain condition compared with those observed in the hypnosis-control condition. Pain-related activity was evident in ACC during hypnotic suggestion conditions for both increased- and decreased-pain intensity. Pain-related activation was observed in IC during suggestions for increased- and decreased-pain intensity: higher rCBF in the middle IC in the increased-pain intensity condition and higher rCBF in the most rostral part of the IC in the decreased-pain intensity condition.

**Study:** Rainville et al., 2002

**Technique:** PET [H\textsubscript{2}\textsuperscript{15}O]; PI pain (Thermal); Hypnotic PF suggestions

**Participants:** 10 healthy subjects: 4 m, 6 f; Mean Age = 24.2 y (range = 20–35 y); All right-handed

**Design:** Instructions included suggestions for the following: (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.

**Main findings:** Occipital increases in rCBF were again stronger in the warm stimulation condition, and prefrontal increases were stronger in the painful stimulation condition.

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Table 1  
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**Study:** Faymonville et al., 2003  
**Technique:** PET \([H_2^{15}O]\); PI pain (Thermal); Hypnotic recalling of PAM  
**Participants:** 19 healthy HHS: 10 m, 9 f; Mean Age = 28 ± 4 y; All right-handed  
**Design:** PET data during three kinds of states (RS, MI, and HS) and during two kinds of stimulation (hot noxious stimulation or warm nonnoxious stimulation). Subjects were scanned twice in each of these six. In the HS condition, each subject was invited to re-experience very PAM. After each scan subjects were asked to rate the noxious stimulus intensity on a scale from 0 (absent) to 10 (most intense imaginable).  
**Main findings:** HS, compared to normal alertness (RS and MI), significantly enhanced the functional modulation between MCC and a large neural network encompassing bilateral insula, pregenual ACC, pre-SMA, right PFC and striatum, thalamus, and brainstem.

**Study:** Schulz-Stübner et al., 2004  
**Technique:** fMRI; Event-related Thermal Stimulation Paradigm; PI pain (Thermal); Hypnotic PF suggestions  
**Participants:** 12 healthy subjects; All right-handed  
**Design:** Group A underwent the following: (1) detection of thermal pain threshold (left forearm, 36.5–43.2°C); (2) baseline anatomic scan; (3) induction of hypnosis; (4) first scan with thermal pain induction under hypnosis; (5) reversal of hypnosis and 10-minute break; (6) second scan with thermal pain induction without hypnosis. Group B underwent the following: (1) detection of thermal pain threshold (left forearm, 36.5–43.2°C); (2) baseline anatomic scan; (3) first scan with thermal pain induction without hypnosis; (4) 10-minute break; (5) induction of hypnosis; (6) second scan with thermal pain induction with hypnosis; (7) reversal of hypnosis. Subjects were asked to rate their pain experience on the VAS after each scan and to describe their experience with and without hypnosis.  
**Main findings:** Under HS, new activation within the anterior basal ganglia was found, whereas there was significantly less activation in the IC, the MCC, and the SI corresponding with decreased functional activity and reduced rCBF. Activation in the left hemispheric ACC was significantly increased under hypnosis, whereas activity in the right hemispheric ACC was unchanged.

**Study:** Aleksandrowicz et al., 2006  
**Technique:** fMRI; Event-related Stimulation Paradigm; PI pain (Pricking); Hypnotic analgesia-hypoalgesia  
**Participants:** 14 healthy HHS: 7 f, 7 m; Mean age = 26.7 y  
**Design:** Cerebral functionality was analyzed during (1) resting state, (2) only nociceptive stimulation, (3) after analgesic suggestion, (4) after hypnotic induction, (5) after consecutive analgesic suggestion in hypnosis, (6) concentration of attention compared to distraction of attention.
Table 1
(Continued)

**Main findings:** Related to analgesic suggestion: hypoactivation of the left thalamus; Related to reception of suggestion: hyperactivation of the right ACC; During hypnotic induction: hyperactivation of the left OFC; During concentration of attention: hyperactivation of the IPC, middle and superior occipital gyri, left OFC, left frontal operculum, and left IC.

**Study:** Röder et al., 2007
**Technique:** fMRI; Block design paradigm; PI pain (Electrical); Hypnotic PF suggestions; HDP
**Participants:** 7 healthy HHS: 5 f, 2 m; Mean Age = 26 y (range = 22–34)
**Design:** Brain activation examined during states of HT, HR, HDP, and NW; HR: standard suggestion in hypnotic pain treatment of leaving the unpleasant and painful presence and referring to a place in the fantasy or memory where one feels comfortable. HDP: a suggestion was modeled after the clinical experience with depersonalized patients and phenomenological and theoretical descriptions. It aimed at the detachment of the self from the body. Subjects were further encouraged to see their body from outside like in autoscopy.

**Main findings:** Noxious stimuli led to an activation contralateral SI and bilateral SII, bilateral IC, cingulate gyrus, and the ipsilateral cerebellum. Activation was markedly reduced in the contralateral SSC, PC (BA40), PFC (BA9), putamen, and the ipsilateral amygdala during HI pain.

**Study:** Vanhaudenhuyse et al., 2009
**Technique:** fMRI; Event-related Laser Stimulation Paradigm; PI pain (Laser); Hypnotic recalling of PAM
**Participants:** 13 healthy HHS: 5 f, 8 m Mean Age = 24 ± 2 y
**Design:** Authors used a thulium-YAG laser to apply computer-controlled brief radian pulses to the dorsum of the left hand of the subjects. Two sessions were performed on two different days: one during NW and one during HS. During each session, 200 laser stimuli were administered with random target intensities with a randomized inter-stimulus interval ranging from 8 to 12 s. After each stimulus, subjects rated their sensory perception.

**Main findings:** The brainstem, right thalamus, bilateral striatum, right SII, bilateral insula, anterior cingulate cortex, right middle frontal gyrus and right premotor cortex) activated significantly less in hypnosis than in normal wakefulness. Hypnosis-related increases in functional connectivity between SI and distinct anterior IC and PFC.

**Study:** Abrahamsen et al., 2010
**Technique:** fMRI; Event-related Stimulation Paradigm; PI pain (Pricking); Hypnotic analgesia-hypoalgesia; Hypnotic hyperalgesia
**Participants:** 19 patients with a long history of myofascial TMD pain, 1 m, 18 f; Mean Age = 40.7 ± 2.3 y

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Design: Three different experimental conditions: hypnotic hypoalgesia, hypnotic hyperalgesia, and a control condition with the patients in their NW without any relaxation or imagery. Repetitive pin-prick stimuli with identical intensity were used as the painful stimulus in all three conditions.

Main findings: Painful stimulation during hypnotic hyperalgesia: increased activity in right posterior IC, premotor cortex and SMA (BA6), and left PC (area supramarginalis, BA40); significant decreases in SI activation. Painful stimulation during hypnotic hypoalgesia: still activity in right posterior IC; hypoactivation in the right posterior IC and MTC (BA21), as well as left PC (BA40), compared to control conditions.

Note. ACC = Anterior Cingulate Cortex; BA = Brodmann Area; DLPFC = Dorsolateral Prefrontal Cortex; EEG = Electroencephalography; fMRI = Functional Magnetic Resonance Imaging; HDP = Hypnotic Depersonalization; HHS = Highly Hypnotizable Subject; HI = Hypnotically Induced; HR = Hypnotic Relaxation; HS = Hypnotic State; HT = Hypnotic Trance; IC = Insular Cortex; IPC = Inferior Parietal Cortex; MCC = Middle Cingulate Cortex; MHS = Middle Hypnotizable Subject; MI = Mental Imagery; LHS = Low Hypnotizable Subject; MTC = Middle Temporal Cortex; NW = Waking Control Condition; OFC = Orbitofrontal cortex; PAM = Pleasant Autobiographical Memory; PC = Parietal Cortex; PCC = Posterior Cingulate Cortex; PET = Positron Emission Tomography; PF = Pleasant Feelings; PFC = Prefrontal Cortex; PI = Physically-Induced; rCBF = regional Cerebral Blood Flow; RS = Resting State; SI = Primary Somatosensory Cortex; SII = Secondary Somatosensory Cortex; SD = Standard Deviation; SMA = Supplementary Motor Area; SPECT = Single Photon Emission Computed Tomography; SRP = Subjective Reality of Pain; SSC = Somatosensory Cortex; TMD = Temporo-Mandibular Disorder; UNP = Unpleasantness; YAG = Yttrium-Aluminium-Garnet.

Other studies showed hypnotic suggestion-related changes in ACC and middle cingulate cortex (MCC) activity when either pleasant autobiographical memory retrieval or depersonalization were induced during PI pain. Faymonville and colleagues (2000, 2003) conducted two PET studies to compare HS to resting state (RS) conditions during normal alertness and to mental imagery (MI) conditions. The first study showed higher activation in response to noxious stimulation during HS in an area comprising the ACC (both BA 24 and 32), the right caudate, and the left striate (Faymonville et al., 2000). The second study showed significantly enhanced functional modulation between MCC and a large neural network including the right PFC, the pre-SMA (supplementary motor area), bilateral insula, pregenual ACC, striatum, thalamus, and brainstem during HS, as compared to normal waking states (Faymonville et al., 2003). Reviewing this evidence, Faymonville, Boly, and Laureys (2006) hypothesized that the MCC activity modulates the hypnosis-induced reduction of affective and sensory responses to noxious thermal stimuli.
In a study conducted by Schulz-Stübner et al. (2004), painful stimuli applied on the left forearm induced activation in the ipsilateral ACC; under hypnosis, a further significant increase occurred. Left cingulate cortex hyperactivation may reflect specialization of the non-dominant hemisphere in the attentional modulation of negative stimuli and emotions, or it may reflect a stream of activation stemming from the frontal/prefrontal areas, or a combination of the two.

In contrast to the above evidence, another study conducted with a similar design did not show ACC activation during a laser-induced-pain condition modulated with hypnotic pleasant autobiographical memory recall; hypnosis dampened the ACC activation response to painful stimuli, compared to normal wakefulness (Vanhaudenhuyse et al., 2009). Methodological differences (type of task employed) may account for the above discrepancies.

Somatosensory system and parietal cortices. Most studies show cerebral blood flow or blood oxygenation changes in the somatosensory system during PI pain modulated by analgesic and/or hyperalgesic suggestions. The SI, which is the main sensory receptive area for the sense of touch, is localized in the lateral postcentral gyrus, within the parietal lobe of the brain. The SII is mostly localized in the parietal operculum (Eickhoff, Schleicher, Zilles, & Amunts, 2006; Penfield & Jasper, 1954). The SI is a component of the pain matrix and its function is central in pain perception and modulation (Neugebauer et al., 2009; Schnitzler & Ploner, 2000).

Crawford, Gur, Skolnick, Gur, and Benson’s (1993) pioneering study had shown rCBF increases in SI during hypnotic analgesic suggestions for ischemic pain in high hypnotizable persons. Conversely, low hypnotizable subjects had shown lower SI rCBF. Activity in the postcentral gyrus positively correlated with increased physical pain perception during HS (Rainville et al., 1997), with both analgesic and hyperalgesic suggestions (Heirichs, Klemm, Scholz, & Biersack, 1997; Rainville et al., 1997). Hofbauer et al. (2001) showed with PET that pain-related SI activations under hypnosis are stronger in response to hyperalgesic suggestions than to hypoalgesic ones. The same study reported SII hypoactivation during the decreased-pain hypnotic condition (Hofbauer et al., 2001).

Other studies showed changes in SI and SII during hypnotic pleasant or depersonalizing conditions and PI experimental pain. Shulz-Stübner et al. (2004) found with fMRI that SI activity in response to pain thermal stimuli is decreased in healthy volunteers under hypnosis with pleasant feeling suggestions. Hypnotic recall of pleasant autobiographical memories were also related to contralateral SI hypoactivation in response to pain laser stimuli (Vanhaudenhuyse et al., 2009). The importance of the somatosensory cortices was confirmed when Röder, Michal,
Overbeck, van de Ven, and Linden (2007) performed an fMRI study during hypnotic depersonalization showing that brain activation in response to nociceptive stimuli was markedly reduced in the contralateral somatosensory cortex, PC (BA40), PFC (BA9), putamen, and in the ipsilateral amygdala, supporting a role for the nondominant hemisphere in the elaboration of pain stimuli, also during HS.

*Frontal and motor cortices.* The frontal and motor cortices participate in executive functions such as planning, flexibility, prepotent response inhibition, and language comprehension and production. Their activation may indicate cognitive appraisal, attention, or memory (Posner & Dehaene, 1994). These areas are strictly involved also in hypnotic pain modulation, as reported by several studies considered in this article. For example, hypnotic induction has been linked to left orbitofrontal cortex (OFC) hyperactivation (Aleksandrowicz, Urbanik, & Binder, 2006), and hypnotic suggestions have been related to frontal cortex hyperactivity (Rainville et al., 1999) or hypoactivation (McGeown, Mazzoni, Venneri, & Kirsch, 2009).

Crawford et al. (1993) studied with $^{133}$Xenon PET the central neural effects of hypnotic analgesia in 11 men, 5 high hypnotizable subjects (HHS) and 6 low hypnotizable subjects (LHS). Compared to LHS, HHS showed a significant increase in overall rCBF and highly significant bilateral orbito-frontal rCBF activation only during hypnotic analgesia. The authors found bilaterally increased rCBF in the OFC among HHS in hypnotic analgesia during ischemic pain and suggested that hypnotic analgesia involved supervisory attentional control systems that cooperate in the regulation of thalamo-cortical activities (Crawford et al., 1993). Rainville et al. (1999) also reported extensive frontal increases in rCBF during the HS and rCBF increases, mainly in the left frontal cortices, correlating with hypnotic suggestions for modulating pain.

Other important data were obtained on prefrontal areas. Faymonville et al. (2000) reported higher activation during pain perception under hypnosis in a right extrastriate area (BA 19), in the right dorsolateral prefrontal cortex (DLPFC, BA 8), as well as bilaterally in the OFC. The right-sided predominance can support the hypothesis that the nondominant hemisphere is preferentially involved in negative pain-related emotion (Davidson, 1992).

Hypnosis, compared to normal wakefulness, increased functional connectivity between SI and distant IC and PFC, possibly reflecting top-down modulation (Vanhaudenhuyse et al., 2009). The hypnosis-induced functional connectivity changes between prefrontal areas and ACC, which were also shown by Faymonville et al. (2003), may indicate a shift toward another state of functioning of the whole brain during hypnotic analgesia, involving state-dependent cognitive appraisal, newly redirected attention, and state-specific memory function related to perceived noxious stimuli.
Insula, thalamus, and other brain areas. Most data show that limbic and paralimbic areas are involved in hypnotic PI pain modulation. The IC is also involved in this context. Regional cerebral blood flow (rCBF) changes between hypnotic suggestion and hypnosis control conditions revealed significant pain-related activations also in IC, during both increased and decreased suggestions for pain (Rainville et al., 1997). Increased MCC-insular modulation has been reported during hypnosis, reflecting IC function in pain affect (Rainville et al., 1999) and pain-amount coding (Oertel et al., 2012). As stressed in a review conducted by Faymonville et al. (2006), the right IC is involved in the mental generation of an image of one’s physical state underlying the attribution of emotional attributes to external and internal stimuli, and the observed increases in functional connectivity between the MCC, thalamus, and midbrain during hypnosis could be associated with pain-relevant arousal or attention. Abrahamsen et al. (2010) found that during hypnotic hypoalgesia only the right insula remained activated with the painful stimulation, while comparing the control and hypoalgesia conditions, significant decreases were shown in the posterior middle temporal cortex (BA21), posterior insula, and inferior PC (BA40). Schulz-Stübner et al. (2004) in an fMRI study conducted according to an event-related thermal stimulation paradigm showed activation within the anterior basal ganglia during hypnosis and significantly less activation in the SI, SII, insula, and MCC. The authors hypothesized that the reduced activation in the insula under hypnosis could be attributed to the analgesic or sedative effect of the hypnotic state, although it does not seem to be distinguishable from a response to placebo treatment (Schulz-Stübner et al., 2004).

Hofbauer et al. (2001) reported in a PET study pain-related activation in IC during experimental physical pain and suggestions for increased and decreased pain intensity. The direct contrast of the different suggestion-related cerebral blood flow changes revealed an assorted activation pattern with higher middle IC rCBF in the increased-pain-intensity condition and higher rostral IC rCBF in the decreased-pain-intensity condition. Faymonville et al. (2000) conducted a PET study with a two-factor design (stimulation—warm nonnoxious vs. hot noxious—and state—HS, RS, and MI). Hypnotic modulation of pain was mediated by the ACC. The main effect of pain, as compared with nonnoxious stimulation, consisted of activation in both thalamic nuclei (predominantly on the right side), in the right caudate nucleus, and in a region encompassing the left insula and the ACC. Further activation was found in a region comprising the right thalamus and extending caudally to the upper midbrain (Faymonville et al., 2000). The same group of authors, in a later PET study conducted in patients with PI pain and hypnotic recalling of pleasant autobiographical memories, confirmed that HS, compared to resting state in normal waking and mental
imagery, enhanced the functional modulation between MCC and a network comprising bilateral insula, pregenual ACC, presupplementary motor area, right PFC, striatum, thalamus, and brainstem (Faymonville et al., 2003). Regarding the role of the thalamus, left-sided hypoactivation has been related to simple analgesic suggestions (Aleksandrowicz et al., 2006).

The role of the insula was also underlined by Vanhaudenhuyse et al. (2009), who used an fMRI pain stimulation task during RS and HS. This study showed that hypnosis-related increases in functional connectivity between the SI and the anterior insula and PFC probably reflect top-down modulation.

Röder et al. (2007) investigated pain perception in three different mental states, including waking state, hypnotic relaxation, and hypnotic depersonalization. In this study, pain was induced with electrical stimulation to the median nerve at the right wrist, and fMRI measurements were performed during all states. Noxious stimuli led to significant activation of the insula, bilaterally. Pain perception during hypnotic depersonalization was associated with markedly reduced activity in the putamen and ipsilateral amygdala (Röder et al., 2007).

Procedures With Hypnotic Suggestions to Alter a Chronic Pain Condition

Different studies (see Table 2) were conducted with the aim of analyzing the main changes in brain functions occurring with hypnotic suggestions to modify a chronic pain condition (e.g., low-back pain, fibromyalgia, phantom limb pain).

Anterior and middle cingulate cortices. The involvement of the cingulate cortices appears to be central also in this type of study. An fMRI study by Derbyshire, Whalley, and Oakley (2009) reported greater anterior MCC responses during hypnosis, both with analgesic and hyperalgesic suggestions directed to a preexisting chronic pain condition in patients with fibromyalgia. Nusbaum et al. (2011) in an H$_2^{15}$O PET study carried out in patients with chronic low-back pain showed ACC and insular activations during hypnotic analgesic suggestions. Another PET study by Wik, Fischer, Bragée, Finer, and Fredrikson (1999), which confirmed subgenual ACC hyperactivation with HS, showed bilateral PCC and posterior ACC hypoactivations in patients with chronic pain due to fibromyalgia subjected to hypnoanalgesia. This points to differential roles of the rostral anterior portions compared to more posterior portions of the cingulate in hypnotic pain analgesia, similar to what occurs with nonhypnotic analgesia.

The extent of phantom limb pain sensation under hypnosis correlated positively to higher rCBF in the ACC and posterior cingulate cortex (PCC; Rosén, Willoch, Bartenstein, Berner, & Røsjø, 2001; Willoch et al., 2000).
Table 2
*Functional Neuroimaging Studies About Pain Perception and Hypnosis: Hypnotic Suggestions Altering a Chronic Pain Condition*

**Study:** Wik et al., 1999  
**Technique:** PET [15O]-Butanol; Hypnotic analgesia-hypoalgesia  
**Participants:** 8 HHS with fibromyalgia: 8f; Mean Age = 47 y (range = 42–56 y); All right-handed  
**Design:** During RS, patients were told to be comfortable and to watch relaxing videotapes. Hypnosis was induced by gently talking to the subjects, instructing them to be relaxed and to go into a deep trance, to watch the videotapes, and not to feel any pain whatsoever. After each scan, pain was rated on a visual analogue scale that spanned from 0 (no pain) to 10 (unbearable pain).  
**Main findings:** As compared to the RS, hypnotic analgesia increased rCBF bilaterally in the subcallosal ACC (BA 25), right thalamus, and left IPC (BA 39 and 40). A separate analysis of 4 patients revealed increased OFC activation during hypnotic analgesia. Decreases in rCBF during hypnotic analgesia bilaterally in cluster, including PCC (BA 23/31) and posterior ACC (BA 24).

**Study:** Willoch et al., 2000  
**Technique:** PET H215O; Hypnotic analgesia-hypoalgesia  
**Participants:** 8 patients with PL pain: 6 m, 2 f; Age range = 25–68 y  
**Design:** The study used four different conditions under hypnosis: (1) CP: the subject imagined the limb as immobile and in a comfortable position; (2) PP: the subject imagined the limb in a position causing pain; (3) PM: the subject imagined moving the limb in a painful way; (4) CM: the subject imagined moving the limb in a comfortable manner.  
**Main findings:** PL movement sensation related to activity in the SMA and the SI. Painful PL movement activated the same brain areas but was weaker and less extended in the SMA. In contrast to the sensation of movement, pain was significantly related to activity in the thalamus, ACC, and lateral PFC. Subjectively rated PL pain sensation correlated positively to activations in the ACC and PCC.

**Study:** Rosén et al., 2001  
**Technique:** PET H215O; Hypnotic analgesia-hypoalgesia  
**Participants:** 2 patients with PL pain: 1 m, 38 y; 1 m, 22 y  
**Design:** The study used four different conditions under hypnosis: (1) CP: the subject imagined the limb as immobile and in a comfortable position; (2) PP: the subject imagined the limb in a position causing pain; (3) PM: the subject imagined moving the limb in a painful way; (4) CM: the subject imagined moving the limb in a comfortable manner.  
**Main findings:** PP was associated with highest pain rating and higher ACC and thalamic rCBF; CM was least painful and showed lower rCBF increases.

**Study:** Derbyshire et al., 2009  
**Technique:** fMRI; Block design paradigm; Hypnotic analgesia-hypoalgesia; Hypnotic hyperalgesia

(Continued)
Table 2
(Continued)

**Participants:** 13 HHS with fibromyalgia: 13 f; Mean Age = 51.4 y; Medication: 6 on meds, including antidepressants, benzodiazepines, and opiates

**Design:** fMRI scans during suggested changes in fibromyalgia pain experience with and without hypnosis. Following the hypnotic induction, patients received suggestions for increasing and decreasing the subjective experience of fibromyalgia pain. The order of these suggestions was counterbalanced across patients. Seven patients were hypnotized upon entering the fMRI scanner using the same induction as during screening (Hypnosis condition). After the collection of two blocks of fMRI data, hypnosis was terminated and two further blocks of data were collected (No-Hypnosis condition). For the remaining, the order of the two conditions was reversed. Patients were told to visualize the dial labeled from 0 to 10 representing their current level of fibromyalgia pain.

**Main findings:** During HS the BOLD responses were significantly greater in several regions including the cerebellum, anterior MCC, and anterior and posterior IC compared to the unhypnotized condition. Activation of the midbrain, cerebellum, thalamus, and midcingulate, SI and SII, IPC, IC and PFC correlated with reported changes in pain with hypnotic and nonhypnotic suggestion. These activations were greater when suggestions followed a hypnotic induction in the cerebellum, anterior midcingulate cortex, anterior and posterior insula, and the inferior parietal cortex.

**Study:** Nusbaum et al., 2011

**Technique:** PET H₂¹⁵O; Hypnotic analgesia-hypoalgesia

**Participants:** 14 patients with chronic low-back pain: 14 m, 0 f; Mean Age = 40.9 y (SD = 12.5); All right-handed

**Design:** Five sequential conditions: three resting conditions of 20 minutes each alternating with the analgesic suggestions of 30 minutes each, in NW and in HS. Subjects were divided in two groups (Groups A and B). Subjects of Group A were given a direct suggestion, referring to the pain itself, its location, and relief. Subjects of Group B were given an indirect suggestion, referring to the subject’s well-being without mentioning the pain itself or its location.

**Main findings:** Brain activities were observed during analgesic suggestions (1) in normal alertness state in STC (BA38), cerebellum, IFC (BA47), medial PFC (BA10), and OFC (BA11) and (2) in hypnotic state in anterior IC and ACC (BA32). During hypnotanalgesia activations in the medial PFC, anterior IC, and the lenticular, caudate, and accumbens nuclei.

**Note.** ACC = Anterior Cingulate Cortex; BA = Brodmann Area; BOLD = Blood-Oxygenation-Level-Dependent; CM = Comfortable Movement; CP = Comfortable Position; fMRI = Functional Magnetic Resonance Imaging; HHS = Highly Hypnotizable Subject; HS = Hypnotic State; IC = Insular Cortex; IPC = Inferior Parietal Cortex; NW = Normal Wakefulness; OFC = Orbitofrontal cortex; PCC = Posterior Cingulate Cortex; PET = Positron Emission Tomography; PFC = Prefrontal Cortex; PL = Phantom Limb; PM = Painful Movement; PP = Painful Position; rCBF = regional Cerebral Blood Flow; RS = Resting State; SI = Primary Somatosensory Cortex; SII = Secondary Somatosensory Cortex; SD = Standard Deviation; SMA = Supplementary Motor Area; STC = Superior Temporal Cortex.
Somatosensory system and frontal and motor cortices. An fMRI study conducted in patients with fibromyalgia during hypnotic analgesia and hyperalgesia showed greater activation in bilateral SI in normal wakefulness than under HS with suggestions for altered pain (Derbyshire et al., 2009). The involvement of the SI and supplementary motor area is also stressed by other studies, even if they were conducted with different designs. Willoch et al. (2000) conducted a PET study to measure rCBF of patients with phantom limb pain under hypnosis; they found that phantom limb movement was significantly related to activity in these areas.

The supervisory activity of the frontal cortices was confirmed by the results of a PET study conducted by Wik et al. (1999) in patients with fibromyalgia, during HI analgesia and resting wakefulness. They showed that hypnoanalgesia increased rCBF in the orbitofrontal and subcallosal cingulate cortices, bilaterally, in the right thalamus, and in the left inferior PC. Cingulate cortices showed bilateral rCBF decreases. Another recent PET study by Nusbaum et al. (2011) found medial PFC activations during hypnotic hypnoanalgesia in patients with chronic low-back pain. Derbyshire et al. (2009) also found BOLD activations of the PFC to correlate with reported changes in chronic pain due to fibromyalgia with hypnotic and nonhypnotic suggestion.

Insula, thalamus, and other brain areas. The importance of the limbic system in this respect was stressed by a recent PET study of chronic low-back pain patients, investigating brain activity during analgesic suggestions (Nusbaum et al., 2011). During hypnoanalgesia, activations in the frontolimbic network emerged, including the medial PFC, the anterior IC, and the lenticular, caudate, and accumbens nuclei. In the same study, the analysis of the relationships between visual analog scale ratings (used by patients to estimate their pain perception), state of consciousness (normal alertness or hypnosis), and type of suggestion (direct or indirect) suggested that normal alertness only had a significant effect on chronic pain when the suggestion used cognitive processes (direct suggestion), whereas hypnosis showed strong effects with either direct or indirect suggestion (Nusbaum et al., 2011). The fMRI study by Derbyshire et al. (2009) observed various modifications during suggested changes in fibromyalgia pain experience with and without hypnosis. BOLD responses during hypnosis were significantly greater in the insula and other brain regions, as compared to nonhypnotized conditions. Wik et al. (1999) found that hypnotic analgesia increased right-thalamic rCBF, and they hypothesized a precise role in pain defense for the thalamus, which could be linked to analgesic processes. The same authors hypothesized that a prerequisite for pain control by descending pathways in hypnoanalgesia is that mental activity may mark the pace of thalamic and spinal mechanisms modulating
nociception. Thalamic activations were also related to phantom-limb pain intensity under hypnosis in the PET studies conducted on patients with chronic phantom limb pain (Rosén et al., 2001; Willoch et al., 2000).

*Procedures With HI Pain*

Three studies (Derbyshire, Whalley, Stenger, & Oakley, 2004; Raij, Numminen, Närvänäen, Hiltunen, & Hari, 2005, 2009) aimed to analyze the brain functional changes occurring through hypnotic suggestions for pain (see Table 3). These studies reported changes in the neural function of different brain areas of the pain network.

*Anterior and middle cingulate cortices.* The ACC is involved in pain evoked through hypnotic suggestion, without physical induction. ACC activity is different in HI pain, compared to the PI pain setting. Derbyshire et al. (2004) conducted an fMRI block design study with a double pain-inducing task (PI and HI pain), showing greater activation in the PI condition relative to HI in the contralateral ACC, orbitofrontal cortex (OFC), and thalamus, and in the ipsilateral PC and perigenual ACC. Raij et al. (2005) reported that activation of PCC adjacent to caudal ACC is stronger during HI than PI pain. Another study from the same group showed that ACC and IC activations during HI pain are linked with secondary somatosensory cortex activation (Raij et al., 2009).

*Somatosensory system and parietal cortices.* OFC, PC (Derbyshire et al., 2004), and SII (Raij et al., 2005) showed greater activation during PI-than HI-pain conditions. Raij et al. (2009) subsequently showed that SII activation can be predicted by activations of the ACC and IC. Derbyshire et al. also reported that HI pain also significantly related to activations of the PC. Furthermore, activation strengths during initiation of suggestion for pain in several brain regions (mostly in medial thalamus, premotor and motor cortices, cerebellum, bilateral ACC, insula, right DLPFC, and midbrain) were related to maximum activation strengths in the contralateral SII, during subsequent HI pain (Raij et al., 2009).

*Frontal and motor cortices.* Prefrontal activations have been reported also during experimental HI pain. The fMRI study by Derbyshire et al. (2004) showed that HI pain significantly correlated with PFC activation. The fMRI study by Raij et al. (2009) showed significant changes within the PFC and PC, in addition to the ACC. The authors found right DLPFC activation due to initiation of suggestions for pain to positively correlate with subjective intensity of HI pain. They hypothesized that the right DLPFC is related to functional modulation in the modality-specific target areas of given suggestions. The study also showed that both IC and ACC activations predicted pain-related SII activation (Raij et al., 2009).
Table 3
Functional Neuroimaging Studies About Pain Perception and Hypnosis: Hypnotically Induced (HI) Pain

| Study: Derbyshire et al., 2004 |
| Technique: fMRI; Block design paradigm |
| Participants: 8 healthy HHS: 3 m, 5 f; Age range = 21–50 y |
| Design: The subjects were fitted with the thermal stimulator and told to expect noxious heat pulses to the palmar surface of their right hand interspersed by 30 seconds rest over 6 min. A single tap to the foot indicated arrival of the stimulus, and two taps indicated the beginning of the rest. Actual noxious heat pulses (48.5°C) were delivered following only three of the six single taps. The other three single taps and all six double taps were accompanied by nonnoxious heat (37.0°C). |
| Functional data were collected in two blocks of 6 min. each to derive 3 min. of PI pain, 3 min. of HI pain, and 6 min. of rest. The conditions (PI and HI pain) were alternated within blocks, and the alternation was counterbalanced across blocks and subjects. Another experiment was conducted during an imagined-pain condition (no HI and no PI pain). |
| Main findings: Significant activation in the PI condition relative to HI in contralateral thalamus, ACC, OFC, and in the ipsilateral PC and the perigenual ACC. HI pain experience: activation in the thalamus, ACC, PFC, IC, and PC. |

| Study: Rajj et al., 2005 |
| Technique: fMRI; Block design paradigm |
| Participants: 14 healthy HHS: 3 m, 11 f; Mean Age = 26 y (range = 20–36 y); 13 right-handed, 1 ambidextrous |
| Design: During each session, the experience of pain alternated with rest periods. During the first session, pain was induced by hypnotic suggestion, and during two other sessions by laser stimulation applied to the left hand. The subject stayed under hypnosis during the second session, whereas a third session was performed in the absence of hypnosis. |
| Main findings: The ACC and the middle insula areas are related to the emotional component of pain and activated similarly during both physically and psychologically induced pain. The SII and the posterior IC are related to the sensory component of pain and were activated more strongly during PI than psychologically induced pain. The PCC, adjacent to the caudal ACC, was more strongly activated during suggestion- than laser-induced pain. |

| Study: Rajj et al., 2009 |
| Technique: fMRI; Block design paradigm |
| Participants: 14 healthy HHS: 3 m, 11 f; Mean Age = 26 y (range = 20–36 y); 13 right-handed, 1 ambidextrous |

(Continued)
Table 3 (Continued)

**Design:** The operator induced hypnosis for the whole imaging period. The subject was asked to signal with a small movement of the right foot when the pain had reached its maximum and when the pain was totally relieved. After a 30-second hypnosis baseline, the operator initiated the suggestion for pain. When necessary, the verbal suggestion was repeated until the subject signaled maximum pain. No new suggestions were given during the subsequent 30-second period of suggestion-induced pain. Thereafter, suggestion was given for pain relief. Subject’s signal for pain relief was followed by a 30-second hypnosis baseline. During this period, no suggestion was given. After the hypnosis baseline, suggestion for pain was repeated. These procedures were repeated throughout the 12-minute scanning session.

**Main findings:** Activation strengths in the right DLPFC during initiation of suggestion for pain correlated positively with the subjective intensity of the subsequent suggestion-induced pain, as well as with the strengths of the maximum pain-related activation in the in the SII. Furthermore, activation of the IC and the ACC predicted the pain-related SII activation.

*Note.* ACC = Anterior Cingulate Cortex; DLPFC = Dorsolateral Prefrontal Cortex; fMRI = Functional Magnetic Resonance Imaging; HHS = Highly Hypnotizable Subject; HI = Hypnotically Induced; IC = Insular Cortex; OFC = Orbitofrontal cortex; PC = Parietal Cortex; PCC = Posterior Cingulate Cortex; PFC = Prefrontal Cortex; PI = Physically-Induced; SII = Secondary Somatosensory Cortex.

*Insula, thalamus and other brain areas.* The studies focused on HI-pain experiences and reported functional changes also in limbic/paralimbic areas. Derbyshire et al. (2004) found that HI-pain experience induced significant BOLD activation of the thalamus, IC, and PC, in addition to the already reported ACC and PFC. Other fMRI studies showed that posterior IC was hyperactive during PI rather than during HI pain (Rajj et al., 2005), and that activation of the IC, along with the ACC, predicted pain-related SII activation (Rajj et al., 2009).

Although three studies do not allow for drawing definite conclusions, they are nevertheless consistent and point to a crucial role for cingulate cortices, PFC, IC, and SII in HI-pain conditions.

**Summary and Future Perspectives**

Several issues emerge from this review. The neuroimaging underpinnings of hypnoanalgesia are quite consistent across the various studies, despite differences in techniques and experimental designs. These data allow for formulating a model in which the central role is taken by the cingulate cortex and its functional connectivity with most pain matrix.
areas, both cortical and subcortical. This activity overlaps with the brain pattern of activity induced by hypnosis, that is, the default mode (a decreased frontopolar/prefrontal activation; McGeown et al., 2009), and findings are consequently compatible with this overlap. However, much needs to be done to understand the events underlying analgesia obtained through hypnosis to identify the neurotransmitters involved in this process and the sequence of events resulting in analgesia. The current picture is a puzzle with many pieces to assign.

Here we summarize the major points of interest:

- Hypnotic pain modulations are associated almost exclusively with brain activations rather than deactivations.
- The ACC is central in reducing pain perception, whatever the stimulus type applied (tonic stimuli: thermal, laser, or pin-prick), and also in the hypnotic desensitization of chronic pain.
- The hypnosis-induced modifications of pain perception are related to functional changes in several brain areas, including the cingulate (mainly in its anterior part), prefrontal, insular, and pregenual cortices, the thalamus, the striatum, and other midbrain areas.
- These findings point to a critical role for the ACC in hypnosis-related modification of sensory, affective, cognitive, and behavioral aspects of nociception.
- The activations found in the lenticular nucleus, anterior insula, and ACC also relate to the modulation of the emotional dimension of pain.
- PFC hyperactivation often occurs in hypnotic pain modification phenomena. In particular, all procedures involving hypnotic induction with suggestions to recall pleasurable autobiographic memories or aimed at provoking pleasurable depersonalization experiences invariably caused an increase in prefrontal neuronal activity.
- The hypnotic strategies for modulating pain can influence cortical and subcortical activity in brain regions that are involved in pain perception and modulation. Further studies focusing on functional neuroimaging and hypnoanalgesia can clarify the mechanisms by which hypnoanalgesia is obtained and can help the understanding of other phenomena as well, like placebo or drug effects, by comparing activation/deactivation patterns.
- Functional neuroimaging studies support the clinical use of hypnosis in the management of pain and pain-related conditions.

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Schmerzempfindung und Hypnose: Ergebnisse neuerer funktioneller Neuroimaging Studien

Antonio Del Casale, Stefano Ferracuti, Chiara Rapinesi, Daniele Serata, Saverio Simone Caltagirone, Valeria Savoja, Daria Piacentino, Gemma Callovini, Giovanni Manfredi, Gabriele Sani, Georgios D. Kotzalidis und Paolo Girardi

Abstrakt: Hypnose verändert Schmerzempfindung und Schmerztoleranz durch Affektion der kortikalen und subkortikalen Aktivität derjenigen

Stephanie Reigel, MD

Hypnose et perception de la douleur: résultats d'études récentes de neuro-imagerie fonctionnelle

Antonio Del Casale, Stefano Ferracuti, Chiara Rapinesi, Daniele Serata, Saverio Simone Caltagirone, Valeria Savoja, Daria Piacentino, Gemma Callovini, Giovanni Manfredi, Gabriele Sani, Georgios D. Kotzalidis et Paolo Girardi


Johanne Reynault
C. Tr. (STIBC)

Percepción de dolor e hipnosis: Hallazgos de estudios de neuroimagen funcional recientes

Antonio Del Casale, Stefano Ferracuti, Chiara Rapinesi, Daniele Serata, Saverio Simone Caltagirone, Valeria Savoja, Daria Piacentino, Gemma Callovini, Giovanni Manfredi, Gabriele Sani, Georgios D. Kotzalidis, y Paolo Girardi
Resumen: La hipnosis modula la percepción de dolor y su tolerancia al afectar la actividad cortical y subcortical en las áreas del cerebro involucradas en estos procesos. Al revisar estudios de neuroimagen funcional enfocados en la percepción del dolor bajo hipnosis, los autores procuran identificar patrones de activación-desactivación que ocurren en condiciones de dolor modulado por hipnosis. Distintos cambios en la funcionalidad cerebral ocurrieron a lo largo de todos los componentes de la red de dolor y en otras áreas cerebrales. Al parecer, la corteza del cíngulo anterior es fundamental en la modulación de la actividad del circuito de dolor bajo hipnosis. La mayoría de los estudios también mostraron que las funciones neuronales de las cortezas prefrontal, insular, y somatosensorial consistentemente son modificadas durante condiciones de dolor modulado por hipnosis. Las investigaciones de neuroimagen funcional apoyan el uso clínico de la hipnosis en el manejo de condiciones de dolor.

Omar Sánchez-Armáss Cappello, PhD  
Autonomous University of San Luis Potosi,  
Mexico