Archives of Psychiatry and Psychotherapy, 2007; 3 : 25–34

Hypnosis and analgesic suggestions in fMRI

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Summary

Aim: To verify data concerning the influence of verbal analgesic suggestions on the signal of pain and the hypothesis of hypnotic state neurophysiological specificity.

Material and method: Brain activity of 14 volunteers under various conditions was measured using fMRI: 1. (basic experiment) – pain stimulation only; 2. pain stimulation after analgesic suggestion; 3. pain stimulation during hypnosis; 4. pain stimulation during hypnosis after analgesic suggestion. Activity of the whole brain and in particular regions of interest (ROI) was analysed.

Results: The verbal suggestion of analgesia, with or without hypnosis, decreased the pain signals in most ROI analyzed, especially the L-thalamus. Reception of analgesic suggestion seems to be connected with an increase of activity in the Anterior Cingulate Gyrus (ACG), especially in the right hemisphere. Hypnosis seems to be connected mainly with increasing activity of orbitofrontal regions, especially in the left hemisphere.

Conclusions: The reaction to analgesic suggestion is independent of hypnosis. In neuroimaging procedures, hypnosis presents mainly an activity in orbitofrontal regions.

hypnosis / **analgesic suggestion** / **fMRI**

INTRODUCTION

The modern explanations for the phenomenon named "hypnosis" oscillate between the search for specificity of the neurophysiological processes (connected with the idea that hypnosis is a unique, 'third state of consciousness', different from wakefulness and sleep) and specificity of interaction between the persons engaged. It still remains uncertain what decides on the appearance of 'hypnotic' behaviour, nor what is their link to the phenomenon of 'suggestion'.

Suggesting, the action leading to the induction of hypnosis as well as to the appearance of various spectacular phenomena (within or independently of hypnosis), is an interactive process in its nature. It pertains to the subjectivity of the person, the psychic functions connected with the imaginative processes. The possibility of reducing hypnosis to suggestion alone has been discussed since the time of Bernheim [1, 2, 3].

Similarities and differences between the phenomena of suggestion and hypnosis are still amongst the crucial research problems. Even though the induction of hypnosis, connected with suggestions that concentrate one's attention on only one source of stimuli, causes an increased susceptibility to suggestion (suggestibility), suggestion and hypnosis appear to be phenomena of a different quality. Differences between individual suggestibility and susceptibility to hypnosis seem to confirm this opinion [1, 2, 3, 4].

Many hypotheses aimed at explaining the phenomenon of hypnosis were found to be false and resulted from taking the effects of open or indirect (hidden) suggestion as phenomena specific for the hypnotic state. Amongst them are a feel-

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ing of sleepiness and relaxation, a sense of losing control, experiencing one's own reactions as automatic and independent from one's own will, as well as losing sense of time and place orientation. This undermines the possibility of evaluating the "depth"[1] (intensity) of hypnosis, measured mainly by the strength and type of reaction towards such suggestions.

Noticing the significance of the interactive processes changed the view of the hypnotised person as a passive subject of the hypnotist's action, underlining the role of his own activity in the "hypnotic situation". This supports a hypothesis that hypnosis is a special form of inter-human relationship which arises between the hypnotised and the hypnotist. The key issue of this specificity appears to be the concentration of attention and concentrating the hypnotised person's perception towards a single narrow field, limiting the possibility of receptivity (or at least minimizing conscious perception) of the signals appearing outside this area [1, 4].

Theories advocating the model of a hierarchical structure of the central nervous system and its function looked for signs of a disruption in this structure in hypnotic phenomena (dissociation), placing hypnosis in an area of pathology, analogous especially to "hysteria" and "multiple personality disorder". Independently of the meaningfulness of the roots of this model, its' application to hypnosis does not appear to be justified. Also, theories of hypnosis as specific states of brain neurophysiological processes were not confirmed in any research performed in the second half of the last century. Those studies, however, enabled the separation of hypnosis from sleep and relaxation [1, 2, 4, 5].

In spite of these results, a conviction of the existence of a 'specific psychic process' persisted. Recently, by applying the PET and fMRI methods, attempts have been made to verify this hypothesis. These studies considered that the presence of the hypnotic state would be shown by the intensiveness of local changes in blood flow, this being a sign of activity of certain areas of the brain. The research of Rainville [6, 7]; Crawford, De Pascalis, Wiloch [7]; and Derbyshire [8], was mainly concerned with the modification of a specific activity, e.g. pain perception, auditory stimuli perception [7] and visual stimuli [8] in hypnosis. At the same time, to a large extent these scientists relied on the presence of objective changes registered e.g. by functional Magnetic Resonance Imaging, along with the subjective evaluation of the degree of discomfort when experiencing pain, degree of being "absorbed" and relaxed, sense of being in control, experiencing oneself and one's sense of identity, etc., hence phenomena which seem to be secondary towards the very phenomenon of hypnosis itself [6, 7, 8, 9, 10].

This causes significant difficulties in the interpretation of results, mainly due to the problem of differentiating changes in brain function imaging connected with the type of stimuli (task) & the changes which are the result of suggestions, from the functions of the brain connected with the very state of hypnosis. Therefore, the results of these studies did not bring about any really convincing answers.

AIM OF THE STUDY

Taking into account those methodological difficulties and defining hypnosis as intense concentration of attention, [2, 11, 12], we had undertaken research aimed at verification of the hypothesis of hypnotic state neurophysiological specificity using the fMRI method. Our studies were also aimed at confirming the observation that the subjective reduction of pain perception, by consecutive analgesic suggestions, is accompanied by functional changes on the neurophysiologic level.

MATERIAL AND METHOD

Functional imaging of the brain is based on the measurement of relative differences between brain activity observed during the resting state and the active state (i.e. when an experimental task is being applied). This would mean that

[1] The idea of "depth" of the hypnotic state pertains to the degree of difficulty of reacting towards suggestions given during hypnosis – declared subjectively by the experimenters. Henceforth it is at least imprecise (if not misleading) to determine as intensiveness of this specific experience in this manner.

functional imaging of the phenomenon of hypnosis would require induction and disappearance of intense hypnosis in very short time intervals (30 seconds) in an alternating fashion. This is practically infeasible during a standard fMRI scanning session. Therefore, an approach was chosen which involved pain stimulation (pricking of the palm) as an experimental manipulation.

For every subject, each session consisted of five phases. Two of them were active conditions, which were preceded by, intertwined with, and followed by resting conditions. Each condition lasted for 30 seconds. During four sessions, the active condition involved pricking the right palm with a sharpened piece of wood and the resting condition involved withholding the palm stimulation for 30 seconds. During the fifth session, the active condition was focusing of attention and the resting condition was deviating attention (e.g. free associations).

Every subject underwent five experimental sessions in a fixed order:

Session 1. Pain stimulation (palm pricking);

Session 2. Pain stimulation (palm pricking) preceded by a verbal suggestion of analgesia;

Session 3. Pain stimuli (palm pricking) preceded by hypnosis induction;

Session 4. Pain stimuli (palm pricking) preceded by a verbal suggestion of analgesia during a state of hypnosis;

Session 5. Focusing and de-focusing of attention, in an alternate fashion.

Functional images were acquired using a gradient-echo echoplanar sequence sensitive to blood oxygenation level dependent (BOLD) contrast, with the following parameters: TR = 3000 ms, TE = 60 ms, FOV = 28 x 21 cm, matrix 96 x 96, 1 NEX. During each functional scanning session, 50 sets of 10 contiguous, 9-mm-thick axial images were acquired parallel to the anterior-posterior commissure plane. High-resolution anatomical images were acquired in the same locations as the functional images.

Region of interest analysis (ROI) was performed in the regions where changes evoked by pain stimulation could be expected. Statistical analysis of the data was done using SPM2 and MarsBaR software. Results of whole-brain activity and in particular regions of interest (ROI) were analysed. The ROIs were comprised of brain regions known to participate in pain processing, namely: anterior cingulate gyrus (ACG), insula, thalamus, primary somatosensory cortex (postcentral gyrus), secondary somatosensory cortex (S2). ROI analysis used a 2-way ANOVA design with the independent factors of hypnotic state & verbal analgesic suggestion and the percent BOLD signal change as the dependent variable.

The differences between the level of activity in the first session and that of the second were considered as indicative of the influence of the suggestion of analgesia, whereas the differences between the first and third session were indicative of the reaction of hypnotic induction. The difference between the level of activity in the first and fourth session was regarded as additional information on the effect of suggestion (which, due to a higher susceptibility to suggestion in hypnosis, is stronger than during the second session) and on the effect of hypnosis itself. Differences between the second and fourth session were expected to reveal the effects of the hypnotic state.

There were 14 participants in the study – 7 females and 7 males, 13 persons aged 21–26 years old and 1 person (male) 68 years old. The majority of them were students of the 4th and 5th year of medicine, who were broadening their knowledge in a scientific study group organized by the Department of Psychotherapy. All participants had experienced hypnosis many times and themselves had induced the hypnotic state on others.

The susceptibility to hypnosis induced by the experimenter was evaluated preceding the studies. In all these trials, the reaction of inducing hypnosis was assessed by the participants as being similar to their previous experiences ("deep" state of hypnosis).

Placing the participant in the MRI apparatus gantry commenced the experiment. The headphones and microphone were tested. The first session included application of pain stimuli (pricking the right palm). The second session involved the same conditions, however the stimulus was preceded by a verbal suggestion that the subject was not going to feel any pain.

Induction of hypnosis began after dimming the lights in the scanner room, followed by having the subject focus on a point of light, as well as on the voice of the person conducting the procedure, which was heard in participants' headphones, and on the suggestion of the change in shape, colour and placement of the light-point. Following the information that there was a change of perceptiveness, it was recommended that the participant close her/his eyes and breathe deeply, in a rhythm directed by the person conducting the procedure. At this moment the lights in the room were turned on.

The subject was commanded to imagine that all other stimuli except the hypnotist's voice had disappeared, or at least to ignore these stimuli. Following this, heaviness and loosening of the left, and then the right arm, was suggested. In all the experiments, a non-verbal confirmation of these suggestions was obtained.

After another suggestion: "And now you will remain for a few minutes in silence, loosening, resting, gathering strength. You will remain in a state of hypnosis, intense focusing of attention, although you will not hear my voice", another registration of the reaction to pain was made. Then contact was regenerated, suggesting the participant remain further in a state of hypnosis and that he/she will not feel pain during the next phase of the experiment (the text of the suggestion of analgesia was identical in all the cases where it was used: "And now the right palm will stop perceiving the pricking, as though it is placed in a thick glove, through which the needle cannot penetrate. It is so thick, that the needle's pressure or touch will not be felt".)

After ending the hypnotic procedure (by counting from 1 to 6, along with suggestions of the heaviness dissipating and returning to the "normal" state) the participants were directed to close their eyes once again, and then when they heard the signal aired through the microphone by the experimenter, alternately to disperse their attention (e.g. free association) and to concentrate their attention on an earlier chosen task (experimental condition).

Immediately after the experiment, the participants gave an account of their subjective experiences, describing them in detail (especially the pain receptiveness). These accounts were recorded on audio-tape, and then the level of pain receptiveness, reactions towards the suggestions of analgesia introduced before hypnotic induction & during hypnosis, hypnosis intensiveness, concentration of attention, type of task on which they concentrated their attention etc., were all determined.

Owing to its significant variation, when evaluating the pain perception in the first phase of the experiment, a seven-degree scale was considered to be necessary to evaluate it. A five-degree scale was used for all the other experiences studied.

As shown by these descriptions, in most of the subjects, there was a significant reaction towards the first suggestion of analgesia (before induction of hypnosis), as well as to the second analogous suggestion, during hypnosis. The lowering of pain perception after the suggestion of analgesia during hypnosis was more significant than before inducing hypnosis. Some of those persons reported reduced pain perception during the pricking of the palm following induction of hypnosis (session 3), even without any suggestion of analgesia.

The subjective evaluation of hypnosis intensity correlates at 0.75 with the susceptibility to suggestion (effect of anaesthesia) and 0.78 with the effect of anaesthesia with hypnosis. The correlation between the effect of anaesthesia after a suggestion without hypnosis and with hypnosis was 0.64.

RESULTS

Brain activity correlated with the hypnotic state

The analysis of contrast in the selected ROIs comparing pain stimulation during hypnotic state and pain stimulation in the beginning of the experiment (difference between session 1 and session 3) revealed a significant decrease of pain-related activation in the beginning of the experiment within the following areas: insula (bilaterally), secondary somatosensory cortex (S2), left hemisphere, and within the left postcentral gyrus (primary somatosensory cortex, S1). We did not observe any differences in the intensity of activation when we compared results of subjects who rated the intensity of their hypnotic state as high and those who rated it as relatively low neither between female or male subgroups.

The whole-brain analyses for this contrast revealed activation within the orbitofrontal cortex both in the in the right and the left hemisphere, as well as the middle occipital gyrus, and deactivation was observed in the left hemispheric superior temporal gyrus and the postcentral gyrus.

In almost all subjects (11 in the left and 9 in the right hemisphere) applying pain stimulation (i.e. session 1) was correlated with a decrease of activity within the bilateral orbitofrontal cortex when compared to other sessions. For example, the comparison of activity observed during session 1 and during session 3 (pain stimulation during hypnotic state) revealed an increase in activity during session 3 in this region in both hemispheres for most subjects, irrespective of the subjective ratings of the intensity of the hypnotic state. Bilateral increase was observed in 9 out of 15 subjects.

The whole-brain comparison of activity acquired during session 4 (pain stimulation after analgesic suggestion in hypnotic state, likely associated with the intensity of hypnosis) with that acquired during session 2 (pain stimulation after analgesic suggestion, before hypnotic induction) revealed several significant differences. The changes were observed in the left orbitofrontal cortex and middle frontal gyrus and were manifested as an increase in activity between session 2 and session 4. The reverse direction, i.e. a significant decrease between session 2 and session 4, was observed within the left precentral gyrus. The change of activity in the left orbitofrontal region was more significant than in the previous comparison of session 1 and session 3. This increase was observed in 11 out of 14 subjects.

Individual effect sizes within the left orbitofrontal region in the aforementioned comparisons are depicted in the Tab. 1.

The whole-brain comparison of activity during session 1 (pain stimulation) with session 3 (pain stimulation in hypnotic state) revealed an increase of activity in bilateral orbitofrontal regions and a decrease within left postcentral region (S1) and the left S2 cortex (Fig. 1).

Comparison of the whole-brain activity associated with pain stimulation after analgesic suggestion during hypnotic state (session 4) with the effects of pain stimulation after analgesic suggestion only (session 2) revealed an increase of activity within the left orbitofrontal region and a decrease within the left precentral gyrus (Fig. 2).

Table 1. Individual effect sizes

	left orbitofrontal region (spm)		intensity of hypnosis	right orbitofrontal region (spm)	
ss nr	(3–1)	(4–2)		(3–1)	4–2
1	1.654129	5.10513*	**3**	2.818821*	2.220163
2	1.248554	1.022064	**3**	0.996205	–0.20901
3	0.243321	0.773539	**3**	0.645073	–0.10666
4	0.222239	0.289936	**2**	0.064248	–0.01009
5	–0.22435	–0.21583	**4**	0.611996*	0.077011
6	2.36484*	1.43917*	**4+**	1.262957*	0.79763*
7	3.86509*	–0.01490	**5**	5.748962	0.233295
8	–0.53412	0.391949	**5**	–1.18218	0.024239
9	5.35728*	2.81366*	**3+**	7.831519	1.911659
10	0.690351	0.021576	**2**	0.560335	0.147804
11	0.248023	–0.27999	**4+**	–0.24600	–0.18779
12	–0.49576	0.161356	**5**	–0.50280	–0.03444
13	–0.04681	0.53037*	**3**	–0.50604	–0.82385
14	–0.59752	0.184539	**4**	–0.00605	–0.07081

* Statistically significant $p<0.05$

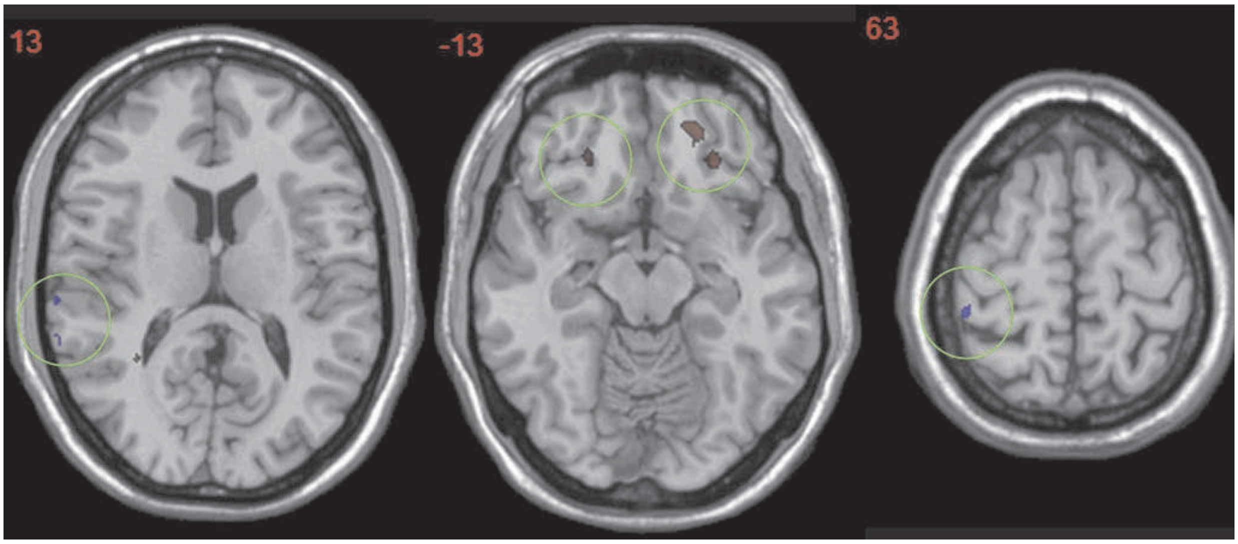

Fig. 1

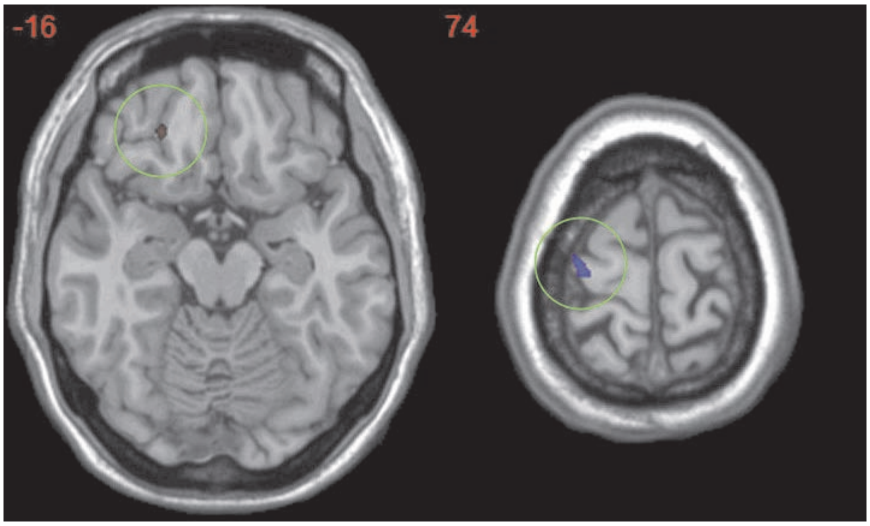

Fig. 2

The voxels that survived the inclusive masking procedure performed on the results of both comparisons (i.e. session 3 – session 1 and session 4 – session 2) were located only in the left orbitofrontal region (Fig. 3). We consider this effect as specifically correlated with the hypnotic state.

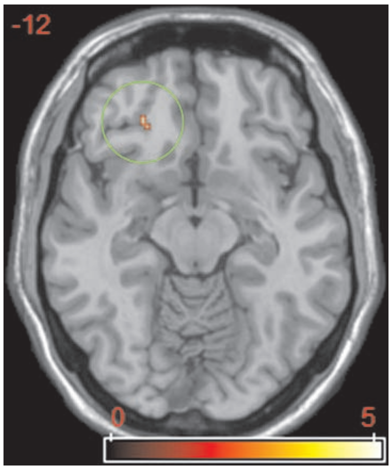

Fig. 3

Brain activity correlated with the reception of analgesic suggestion

The ROI analysis revealed a trend toward a decreased thalamic activation observed specifically after analgesic suggestion both before and after hypnotic induction (i.e. session 2 and session 4). In the remaining ROIs, decreases of activity were observed (some of them were insignificant) after analgesic suggestion during the hypnotic state only (i.e. session 4).

The whole-brain analysis contrast between session 2 (pain stimulation after analgesic suggestion) and session 1 (pain stimulation only) revealed an increase of activity within the middle frontal gyrus in the left hemisphere.

Lastly, the ROI analyses also revealed an increase in activity level within the anterior cingulate gyrus in the right hemisphere (R-ACG) between session 1 and session 2 (Fig. 4).

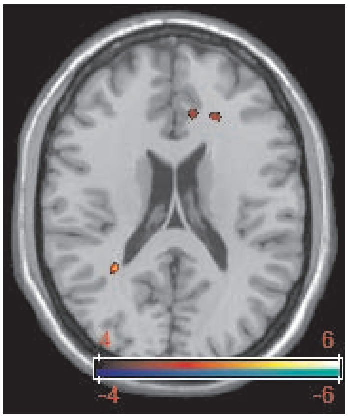

Fig. 4. R – ACG, difference session 1 – session 2

This level did not change substantially during the remaining sessions.

In the majority of subjects this increase corresponded to reduced pain sensation (Tab. 2).

Table 2. Individual effect sizes

ss. no	L-ACG (2–1)	R-ACG (2–1)	effect of the first analgesic suggestion
1	–0.39517	–0.20661	0
2	0.11152	1.03883	2
3	0.07629	0.08322	1
4	0.12053	0.09095	0
5	0.46485	0.11641	4
6	0.87020	*0.72576	4
7	1.89090	*2.17619	4
8	0.17312	0.13446	2
9	0.46864	0.69644	2
10	0.33189	0.11877	0
11	0.08536	*0.58536	4
12	–0.02590	0.12890	4
13	–0.62851	0.01290	2
14	–0.34109	–0.14494	2

* Statistically significant $p<0.05$

The figures below illustrates the effects of pain stimulation after analgesic suggestion (before hypnotic induction) in subject 7 (Fig. 5) who responded to analgesic suggestion and another subject 1, who did not (Fig. 6). Note differences in the right anterior cingulate activation.

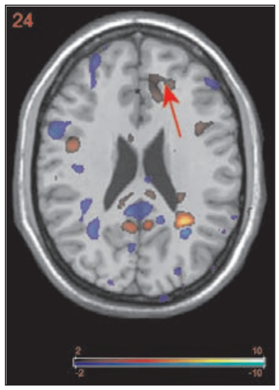

Fig. 5. ss. no 7

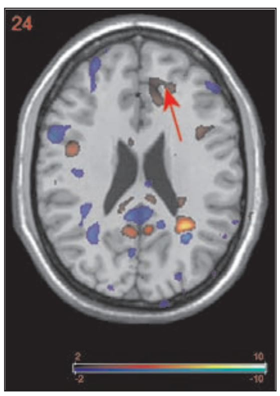

Fig. 6. ss. no 1

Differences between focusing and de-focusing of attention

The effects of alternate focusing and de-focusing of attention were observed principally in the inferior parietal lobule and within the regions of angular, middle and superior occipital gyri (bilaterally). In the anterior parts of the brain some activity was observed within the orbitofrontal gyri and Rolandic operculum in the left hemisphere. Despite considerable inter-subject variability, most of the subjects also displayed activity within the right insula and the left S2.

DISCUSSION

Former research of hypnotic state neurophysiological specificity used a similar methodology. In 2002, Pierre Rainville compared the results of PET before and after inducing hypnosis. The left palm of the participants was exposed to pain (hot water). Derbyshire used the fMRI technique during pain perceptions suggested during hypnosis (with no actual pain stimuli).

In the Rainville study, the most evident changes were observed in the anterior cingulate gyrus (ACG) and in the thalamus. The results of the experiments were correlated mainly with the level of relaxation and absorption during the course of hypnosis [7]. The Derbyshire study revealed significant changes in the insula, the ACG, the thalamus as well as the prefrontal and parietal cortex [8].

Results of such studies present changes in brain function at the time of perceiving pain and their localisation as a relationship between the subjective perception of pain reduction due to the suggestion of analgesia and further changes in certain regions of the brain.

Heightened activity connected with a reaction towards suggestion noted in these areas (but not with the hypnosis itself) is also seen in our observations. This contradicts the Rainville and Derbyshire interpretations of the activity of certain areas (e.g. ACG) as correlated with the very state of hypnosis itself.

Results of our study cannot give a definite answer to questions of whether a specific activity of the anterior cingulate gyrus, especially in the right hemisphere, is related to the phenomenon of suggestion itself, or to the analgesia – meaning the content of suggestion. However, the probability seems to be high that the suggested analgesia provokes changes in pain reception responses (mainly their weakening) and that the observed activity in ACG is associated with the reception of these suggestions.

The changes of activity in those regions where one would expect reactions connected with pain perception confirms that neurophysiological phenomena evoked by pain stimulation are modified by the suggestion of analgesia [13, 14, 15, 16]. The effect of the suggestions during a state hypnosis was stronger than the suggestions alone (preceding hypnosis), which can be seen in the fMRI results.

The suggestions of analgesia not only reduce the activity caused by pain stimuli, but are correlated with increased activity in other areas, e.g. R-ACG. This could mean that the reception of verbal suggestion is an active process and not only a passive reaction of the subject. This, however, requires further research, especially regarding the question of whether the described phenomena are present along with every suggestion or only with the suggestion of analgesia.

Analysis of the activity changes during the remaining sessions (pain stimulation alone, pain stimulation following analgesia suggestion, pain stimulation following induction of hypnosis and analgesia suggestion in the hypnotic state) also showed the inhibitory effect of hypnosis on activity caused by the pain stimuli. Perhaps this is caused by hypnotic induction, but it seems rather more probable that these activity changes (as well as the subjective experience of analgesia after hypnotic induction itself) are the effect of adaptation to pain or a “hidden” suggestion of analgesia related to the participants’ expectation that being hypnotised will reduce perception of pain caused during the experiment.

The most important observation seems to be higher activity in the orbitofrontal gyrus (bilaterally, but more significant in the left hemisphere) correlated with the state of hypnosis. Activity in this area cannot be explained solely by pain stimulation (the effect of which was rather lowered basic activity in the left hemisphere in almost all of those studied) nor by effect of suggestion.

This allows us to formulate a hypothesis that in the functional state of the brain during hypnotic induction, besides a modification of the signal of pain, a specific type of activity appears. It seems interesting that activity in a similar area (however lower) was also noted during any voluntary concentration of attention. This could confirm the conviction that hypnosis is a state of specifically intense concentration of attention (definition of the British Royal Society, 1955 [2]).

It seems reasonable to consider such a state of attention as a specific "functional state" of the central nervous system. This concept was not fully confirmed in our study, however. The discrepancy of the measurement effects of focusing versus de-focusing of attention may result from the variety of tasks (imagined picture, mathematical operations, etc.), as well as distortions brought about by stimuli that attract attention (especially auditory stimuli). This should be a subject of further research attempting to answer the question of whether the state of hypnosis is identical to the state of intense attention concentration or whether it is an independent phenomenon.

The problem of interpretation of fMRI brain activity changes is also related to methodological difficulties. They are caused, amongst others, by technological conditions. For example, the noises of the machinery, especially their variability as well as awaiting for the pain stimuli, can distract the subject's attention from the suggested task. The probability of experiencing tension in the experimental situation and possible defense mechanisms used also complicate interpretation of the relationship between variables such as hypnosis, suggestion, analgesia, etc. and the observed functional state of the brain.

CONCLUSIONS

1. Changes of activity in areas correlated with pain reception are the effect of suggestion of analgesia and are based on lowering of the activity evoked by the pain stimuli (especially in the thalamus, on the left side).
2. The influence of suggestion (and precisely – the reception of its contents) could be connected with the heightened activity of certain areas of the brain, especially the right hemisphere anterior cingulate gyrus (R-ACG).
3. The induction of hypnosis is correlated with higher activity in the orbitofrontal areas, especially in the left hemisphere.

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