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Focused hypnotic analgesia: Local and remote effects

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Abstract

Suggestion for hypnotic analgesia aimed at a specific body area is termed "focused hypnotic analgesia". It is not clear, however, whether this analgesia is limited to a specific body location or spread all over the body. Focused hypnotic analgesia was studied, in response to ascending electrical stimuli, when analgesia and stimulation were applied to the same area (local), and when analgesia was applied to one location and stimulation was delivered to a different area (remote). The face or leg served alternately as the local or remote areas, and the effect was tested in 12 high-hypnotizable (HH) and 13 low-hypnotizable (LH) subjects. Hypnotic analgesia in the local site produced a significant pain reduction compared to the remote site in HH subjects ($P < 0.0001$) but not in LH subjects ($P = 0.68$). As stimuli increased in intensity the reduction in pain as a result of hypnosis was larger both in HH and LH subjects ($P < 0.0001$). Nevertheless, significant analgesia occurred in the 3 highest intensities in the local and remote location of HH subjects, but only in 2 highest intensities in the local and 1 in the remote of LH subjects. We conclude that in HH subjects focused hypnotic analgesia is mostly confined to the area aimed at, but some spread of analgesia to remote areas cannot be dismissed all together. Alternatively, this "spread" of analgesia could be due to a placebo effect in the remote area. Focused hypnotic analgesia requires increased attention to the body area aimed at, unlike analgesia achieved by distraction of attention.

Keywords: Hypnotic analgesia; Hypnotic location; Local hypnotic analgesia; Remote hypnotic analgesia; Attention; Stimulus intensity

1. Introduction

Focused hypnotic analgesia is a mode of hypnotic suggestion when the subject is instructed to concentrate on a specific body area and to imagine that this area is anesthetized. It was shown that suggestions for focused analgesia were superior to other modes of hypnotic instructions such as deep relaxation or dissociated imagery (Zachariae et al., 1998; De Pascalis et al., 1999, 2004; Sharav and Tal, 2004), but only in high-hypnotizable subjects (De Pascalis et al., 2004; Sharav and Tal, 2004). Thus, pain reduction is strongest when the hypnotized subjects specifically attend to the stimulated area, in contrast to the use of distraction and attention directed away from the stimulated area in order to reduce pain not under hypnosis (Bushnell et al., 2004). Focused hypnotic analgesia and generalized relaxation produced different stimulus-response curves to stimuli of ascending intensity. Under relaxation, there was no clear relationship to hypnotic susceptibility. Under focused analgesia, there was a change in slope, showing a positive relationship to hypnotic susceptibility (Sharav and Tal, 2004).

Whereas the effect of generalized relaxation is not limited to any specific body area, focused analgesia is aimed at a specific location. It is not clear, however, whether instructions for "focused" analgesia produce analgesia confined to a certain location, as demonstrated in response to placebo analgesia, target-directed to a specific body location (Benedetti et al., 1999). Benhaiem

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et al. (2001) showed, on the other hand, that heat pain thresholds increased modestly in both local and remote locations in response to hypnotic analgesia aimed at only one location, with no significant difference between locations. However, their results are difficult to interpret since the subjects were not pre-selected for hypnotic susceptibility, and a placebo effect associated with generalized relaxation was possibly more dominant in these subjects than hypnotic analgesia. Additional studies are, therefore, needed in subjects pre-selected for hypnotic susceptibility.

The aim of this study was to determine in high-hypnotizable (HH) and low-hypnotizable (LH) subjects the effect of hypnotic analgesia focused to a defined body location (Local) compared with its effect on a remote location (Remote) in response to ascending electrical stimuli. The following hypotheses were tested: (a) the analgesic effect will be greater in the local than in the remote location in HH subjects, (b) no difference in the analgesic effect will be observed between locations in LH subjects, (c) analgesia in the HH local location will be greater than that in LH local location, (d) no difference in the analgesic effect will exist between HH remote and LH remote, (e) the analgesic effect will increase in response to ascending stimuli, in the local location of HH subjects, (f) the analgesic effect will not increase in response to ascending stimuli in the remote location of HH subjects, (g) the analgesic effect will not increase in response to ascending stimuli in local or remote locations of LH subjects.

2. Methods

2.1. Subjects

Paid volunteers were recruited through an announcement on the campus of The Hebrew University in Jerusalem. All subjects were healthy and were not taking any medications during the month prior to the experiment. The Ethical Committee of The Hebrew University-Hadassah Medical Center, approved the study, and subjects freely consented to partake in the experiments. Hypnotic susceptibility was tested by the 'Stanford Hypnotic Arm Levitation Induction and Test (SHALIT): 6-min arm levitation hypnotic induction and measurement scale (Hilgard et al., 1979). Twenty-five (14 males, 11 females) subjects were selected out of 61 that were screened. Subjects were rejected for various reasons, such as being on medication or displaying extremely anxious behavior during screening. The 25 selected subjects were divided into "low-hypnotizable" (LH) and "high-hypnotizable" (HH) groups, based on "elbow-raising" during the SHALIT test (Hilgard et al., 1979). "Elbow-raising" meant that during the 6 min induction of hypnotic arm levitation, HH subjects lifted their elbow from the table. This elbow-raising criterion correctly classified 85% of the subjects into upper or lower hypnotizable groups according to the Stanford Hypnotic Susceptibility Scale, Form A (SHSS:A, Hilgard et al., 1979). It was also found suitable in our previous studies to differentiate between HH and LH subjects, and very convenient in not being language dependent (Sharav and Tal, 1989; Sharav and Tal, 2004; Tal and Sharav, 2005). The LH group consisted of 13 subjects (8 males, 5 females; mean age 24.1, range 18–32), and the HH group – of 12 subjects (6 males, 6 females; mean age 21.5, range 20–30). The subjects were informed that they were suitable for the study, but were not advised as to which group they were allocated. This was done so as not to bias their expectation for hypnotic analgesia.

2.2. Pain stimuli

Painful stimuli were delivered via a pair of surface electrodes placed 2 cm apart on scrubbed, degreased skin. Subjects were given stimuli of ascending and descending intensity and sensory and pain thresholds were determined according to the Method of Limits. Ascending stimuli were then delivered up to a point tolerated by the subject, this point established as the pain tolerance. Stimuli were delivered at two sites: (a) The right mental nerve was stimulated on the skin overlying the mental nerve at the antero-lateral third of the mandible, (b) The right sural nerve was stimulated at the ankle on the skin overlying the nerve at the retromaleolar area. Stimuli consisted of a train of 10 pulses, each pulse 0.8 ms with a 0.2 inter-pulse-interval, from a constant current stimulator (Iso-Flex AMPI).

Four ascending stimulus values were determined for each subject: (A) pain threshold, (B) one-third of the way between pain threshold to pain tolerance, (C) two-third of the way between pain threshold to pain tolerance, and (D) Pain tolerance. Each of the stimulus intensities was delivered 4 times in random order for a total of 16 stimuli per site. The experimenter who delivered the stimuli was blind to the hypnotic susceptibility of the subjects.

2.3. Assessment of sensation and expectation

After each stimulus was delivered, the subject graded the intensity and unpleasantness of the sensation evoked on two 100 mm visual analog scales (VAS). The end points on the line were marked "no sensation" and "strongest possible sensation" for sensory intensity, and "not felt" and "most unpleasant sensation" for sensory unpleasantness.

Subjects were asked, at the beginning of each session, to estimate on a scale of 0–10 how much pain relief they expected to feel under hypnosis.

2.4. Experimental design

Each subject was tested twice, once when the face served as the local area of focused analgesia and the leg as the remote one, and once when the leg served as the local area and the face as the remote one. Sessions were held one week apart and the order of locations was counterbalanced.

Each session consisted of the following stages with the subject seated in an armchair with legs lifted up and both locations attached to the stimulating electrodes:

Thresholds. Sensory and pain thresholds and pain tolerance levels were identified, and stimulus intensities were established.

Familiarization. One trial using 4 stimuli delivered in ascending order to familiarize the participants with the range of stimulus intensities and the use of the visual analog scale

(VAS). This was followed by two trials each of 4 ascending stimuli that were randomly presented, the participants being blind to the order of the stimuli. The stimuli were separated by ~30–60 s, and the participants rated pain intensity and unpleasantness on the VAS immediately following each stimulus. As the stimuli chosen spanned a broad range of intensities, from pain threshold to pain tolerance, participants learned to use the VAS ratings across most of its range.

Expectation. The subject was asked to evaluate his/her expectation by answering the question: "On a scale of 0–10, how much pain relief do you expect under hypnosis?".

Pre-hypnosis. A total 16 consecutive electrical stimuli, 30–60 s apart, were delivered at each of the two stimulation sites. The order of the sites was reversed, and stimuli were delivered randomly. This session lasted about 12–15 min.

Hypnosis. Under hypnosis, focused analgesia was delivered to the face or to the leg in a counterbalanced manner. Under "focused analgesia," the hypnotic suggestions were to "concentrate on the right side of the face (or the right leg), and to feel it becoming numb" (see below). Instructions for focused analgesia were given in separate sessions for the face and for the leg. The order of the sites was reversed. Stimuli were then delivered in a way similar to that during the pre-hypnotic stage. Hypnotic induction lasted for 10–12 min. Suggestions were given throughout administration of the stimuli since continuous suggestion has been found to be more effective than one time suggestion (Price and Barber, 1987).

Post hypnosis. The subject was instructed to terminate hypnosis. The stimuli were then delivered in a way similar to that during the pre-hypnotic stage.

2.5. Hypnotic induction and suggestion for analgesia

Induction of hypnosis included the following:

> (1) *Physical relaxation*: "you start to feel relaxed and loosen up, your feet... your legs... your knees... belly... shoulders... head... all your muscles are loosening up. You have a feeling of warmth, heaviness and deep relaxation all over your body, you sit relaxed... calm".
> (2) *A feeling of tranquility and restfulness*: "and although you are aware of my voice, you are now more aware of the feeling of tranquility... you feel calm and peaceful, as you continue enjoying the restfulness of not having to do anything in particular right now".
> (3) *Relaxing guided imagery*: "you are now taking a short, relaxed walk, you are on a path in the countryside leading to the gate of a beautiful garden. You enter the gate and go down five stairs into the garden, you become more calm and relaxed with each step; 5... 4... 3... 2... 1... you are now in the garden and face a lawn with trees. Under the trees there are reclining chairs, you choose one and sit, you look upward, you can see the leaves moving in the wind and glittering in the sun, and through the leaves you can see the blue sky, you feel totally relaxed... calm... secure and in harmony."
> (4) *Normalization of analgesia*: "and it is interesting to notice that while you are listening to me you have forgotten that you have a right hand... and yet now you can feel it. We've all had a great deal of experience in developing anesthesia in all parts of our body".
> (5) *Creating focused anesthesia*: "Concentrate now on your right leg (face), and you can imagine a curious tingling in your right leg (face), similar to that you might have experienced after an injection of a local anesthetic... something you may enjoy now, as you feel that your right leg (face) is becoming more and more numb, as the stimulus dial is turned up, you can just turn down the dial of your own sensation. You might enjoy letting your right leg (face) become more and more numb... more and more numb".

2.6. Data analysis

All data were analyzed using SAS® (SAS Institute, Cary, NC). Pain intensity and unpleasantness were measured on a 100-point visual analog scale and were considered continuous variables. We modeled each of the two dependent variables, pain intensity and unpleasantness, using the SAS procedure PROC MIXED for repeated measure analysis of variance with interactions. The fixed-effect parameters modeled were: location of stimulation (local, remote), time (before, during, after hypnosis), site (face, leg), intensity level (A,B,C,D). Since there were two groups of subjects, based on hypnotizability (HH and LH), we modeled them separately, and combined the data only to formally test for differences between the groups. In the combined model, an additional fixed-effect was type (HH, LH). We tested for differences between the coefficients of variation for pain intensity and unpleasantness of the hypnotized location versus the non-hypnotized location using analysis of variance. The post hoc *t*-tests, Bonferroni adjusted for multiple testing, were applied as well. The Mann–Whitney Test was used to test differences in expectations between the HH and LH groups. $p < 0.05$ was considered statistically significant.

3. Results

There was no evidence that the effect of hypnotic analgesia (3 states: before, under, and after hypnosis) differ between hypnosis locations (face and leg). Specifically, the state by hypnosis–location interaction was nonsignificant for HH and LH subjects ($F[2,22] = 2.23$, $p = 0.13$; $F[2,24] = 0.86$, $p = 0.44$, respectively). Therefore the variable for hypnosis location was included as a factor in the ANOVA design, but the effects from this variable were removed from the model, effectively treating the data as the average of the two values. Hypnotic analgesia significantly decreased pain intensity and pain unpleasantness in HH ($F[2,22] = 173.74$ $P < 0.0001$, $F[2,22] = 163.09$ $P < 0.0001$, respectively) as well as in LH subjects ($F[2,24] = 49.25$ $P < 0.0001$, $F[2,24] = 46.23$ $P < 0.0001$, respectively), Table 1. As there was no difference in the effect on pain intensity or unpleasantness, the results are presented for pain intensity.

3.1. Effect of location and hypnotic susceptibility

The effect of relative location (local versus remote) depended on hypnotizability. This hypothesis was tested separately for each of the hypnotizability groups (HH and LH) as we initially modeled each of the groups separately. We found that in the HH group the local site produced a significant pain reduction compared to the remote site ($F[1,23] = 1.12$, $p < 0.0001$), there was no such difference in the LH group ($F[1,12] = 0.17$,

Table 1
The effect of hypnotic susceptibility on pain intensity at different states of hypnotic induction

Pain intensity				
State	Hypnotic susceptibility	*N*	Mean	SD
Before hypnosis	HH	768	44.91	28.5035275
	LH	832	46.85	28.3220713
Under hypnosis	HH	768	30.11	24.6411749
	LH	832	39.31	25.5943702
After hypnosis	HH	768	38.34	28.5873391
	LH	832	42.38	27.5131400

$p = 0.68$), Fig. 1. In addition the interaction between relative location and hypnosis state was statistically significant only for HH subjects (HH: $F[2,22] = 6.43$ $P = 0.006$ versus LH: $F[2,24] = 2.09$ $P = 0.15$), supporting this pattern, Table 2. Bonferroni adjusted post hoc *t*-tests showed that a statistically significant difference exists only between HH local and HH remote locations (in favor of HH local $P < 0.0001$), but not between any of the other combinations; HH-remote, LH-local, LH-remote (Fig. 2) Table 2. Thus a larger analgesic effect of focused hypnotic analgesia aimed at the local location was observed in HH subjects only.

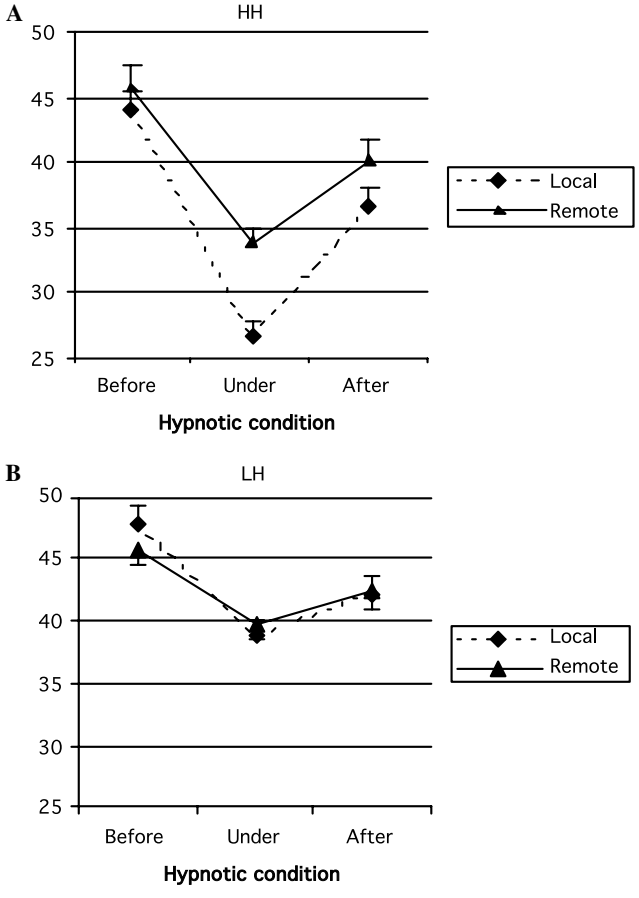

Fig. 1. Effect of location on pain intensity under focused hypnotic analgesia. (A) In high-hypnotizable (HH) subjects, the analgesic effect under hypnosis is significantly higher in the local than in the remote location ($P < 0.01$). (B) In low-hypnotizable (LH) subjects there is no difference between the local and the remote location ($P = 0.68$).

3.2. Effect of ascending stimuli

Hypnotic analgesia was found to be dependent upon stimulus intensity. As stimuli increased in intensity the reduction in pain as a result of hypnosis was larger (Figs. 3 and 4), this effect was true for both HH and LH subjects since the intensity by hypnosis state interaction was statistically significant in both groups (from the individual models: HH: $F[6,66] = 16.38$, $P < 0.0001$ LH: $F[6,72] = 5.46$, $P = 0.0001$). The difference between LH and HH subjects was not statistically significant as seen from the 3-way interaction term from the combined model, hypnotizability group by intensity by hypnosis state ($F[6,138] = 2.06$ $P = 0.0618$).

We examined the impact of stimulus intensity and location (local and remote) on the analgesic response to hypnosis whilst looking for possible differences between the hypnotizability groups. For this purpose we assessed both 3-way interaction terms (hypnosis state × hypnotizability group × location) and (hypnosis state × hypnotizability group × stimulus intensity) from the combined model. Neither of these terms was found to be statistically significant.

Nevertheless, Bonferroni post hoc analysis showed significant reduction in pain at the 3 highest intensities (B,C,D) within the HH group for the local ($t = 8.75$, 11.45, 13.26; respectively, $P < 0.0001$) as well as for the remote locations ($t = 5.23$, 6.98, 8.46; $P < 0.0003$) (Fig. 3). In the LH group, there was a significant reduction in pain at the 2 highest intensities in the local area (C,D) ($t = 5.54$, 6.38; $P < 0.0001$), but only at the highest intensity in the remote location (D) ($t = 5.43$; $P < 0.0001$) (Fig. 4).

3.3. Expectation

In order not to bias expectation, subjects did not know whether they were in the HH or LH group. No difference was found between HH (5.91 ± 0.366) and LH (5.06 ± 0.594) groups in their expectation to achieve analgesia (Mann–Whitney; $Z = 1.246$, $P = 0.2$).

4. Discussion

The analgesic effect of focused hypnotic analgesia was studied in response to ascending electrical stimuli. The effect was studied when analgesia and stimulation were applied to the same area (local) or when analgesia was applied to one location and stimulation delivered to a different area (remote). The face or leg served alternately as the local or remote areas for inducing "focused"

Table 2
The effect of location and hypnotic susceptibility on pain intensity at different states of hypnotic induction

Pain intensity					
State	Location	Hypnotic susceptibility	*N*	Mean	SD
Before hypnosis	local	HH	384	44.05	27.59
		LH	416	47.88	28.74
	Remote	HH	384	45.77	29.40
		LH	416	45.83	27.90
Under hypnosis	Local	HH	384	26.45	22.72
		LH	416	38.87	25.62
	Remote	HH	384	33.77	25.94
		LH	416	39.73	25.60
After hypnosis	Local	HH	384	36.54	26.01
		LH	416	42.21	27.98
	Remote	HH	384	40.13	30.88
		LH	416	42.56	27.07

hypnosis. The effect was tested in high-hypnotizable (HH) and low-hypnotizable (LH) subjects. Statistically significant differences existed only between HH local and HH remote (in favor of HH local) (Fig. 1), but not between any of the other location-hypnotizability combinations, i.e. HH-remote, LH-local, and LH-remote (Fig. 2). Thus a larger analgesic effect of focused hypnotic analgesia was observed in HH subjects.

Hypnotic analgesia was dependent on stimulus intensity. As stimuli increased in intensity the reduction in pain was greater (Figs. 3 and 4), this was more apparent in the HH group and to a lesser degree in the LH group.

4.1. Effect of focused hypnotic analgesia on local area

Focus hypnotic analgesia was previously found to be more effective than other modes of hypnotic induction, such as deep relaxation or dissociated imagery (Zachariae et al., 1998; De Pascalis et al., 1999, 2004; Sharav and Tal, 2004). It is not clear, however, whether the analgesic effect is confined only to the location on which it is focused. Benedetti et al. (1999) demonstrated that placebo analgesia aimed at a specific area was confined to that area. On the other hand, Benhaiem et al. (2001) showed that heat pain thresholds increased modestly in both local and remote locations in response to

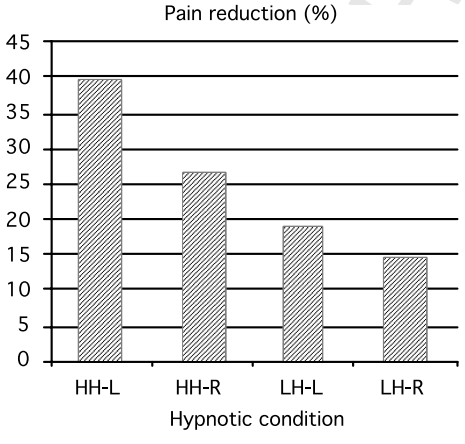

Fig. 2. Percentage reduction in pain intensity under hypnotic analgesia (1) high-hypnotizable local area (HH-L), (2) high-hypnotizable remote area (HH-R), (3) low-hypnotizable local area (LH-L), and (4) low-hypnotizable remote area (LH-R). Pain reduction is significantly higher in HH-L compared with that in the other 3 groups ($P < 0.0001$). There was no significant difference between the other 3 groups.

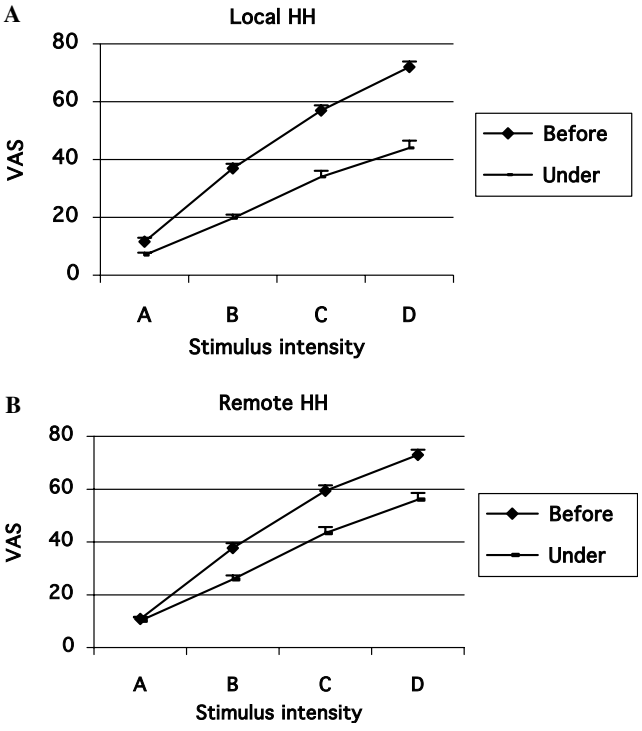

Fig. 3. Pain intensity at four ascending stimulus levels in HH subjects before and under hypnotic analgesia: (A) local location, and (B) remote location. The reduction in pain increased at higher stimuli and was significant for the three highest stimuli ($P < 0.0003$).

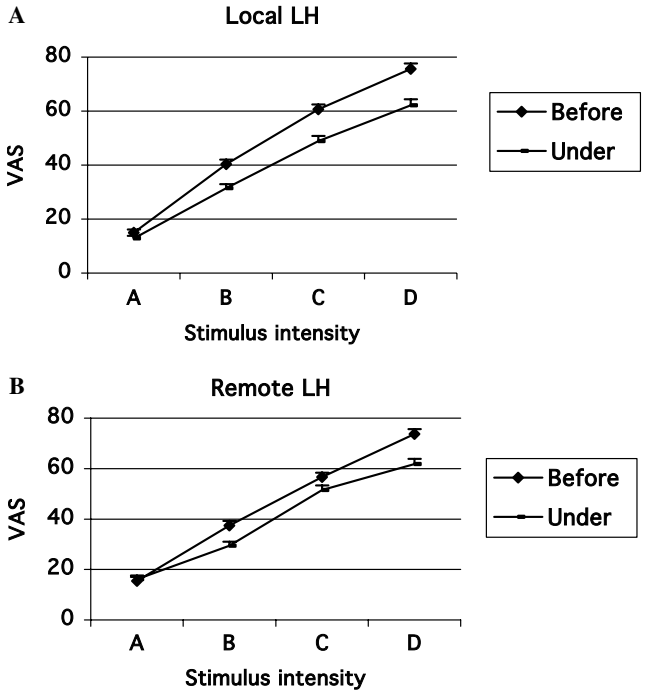

Fig. 4. Pain intensity at four ascending stimulus levels in LH subjects before and under hypnotic analgesia: (A) local location, and (B) remote location. The reduction in pain increased at higher stimuli. It was significant for the two highest stimuli in the local location ($P < 0.0001$), but only for the highest stimulus level in the remote location ($P < 0.0001$).

hypnotic analgesia aimed at only one location, and that there was no difference in pain threshold elevation between the two locations. It could be assumed, therefore, that the effect of "focused hypnotic analgesia" is not confined to a targeted body location, but acts equally on remote body parts. The findings of Benhaiem et al. (2001) are difficult to interpret since subjects were not pre-selected for hypnotic susceptibility, and a placebo effect could possibly be more dominant in these non-selected subjects, rather than hypnotic analgesia. This placebo effect may also explain the modest analgesia achieved in their study. Our results, on the other hand, showed significantly better hypnotic analgesia in the local than in the remote area in HH subjects (a reduction of 39.8% and 26.0% in pain intensity, respectively, Fig. 2). No such difference was observed between local and remote locations in the LH group (19% and 14%, respectively). Furthermore, hypnotic analgesia in the remote location in HH subjects did not differ from that achieved in LH subjects, suggesting that the analgesia in this remote area exhibited a placebo-like effect (and see below). This, therefore, leads to the conclusion that focused hypnotic analgesia may be confined primarily to a local "hypnotized" area and is mediated by hypnotic susceptibility.

What specific changes operate in the area to which focus hypnotic analgesia is directed? We know that electrical stimuli are not blocked peripherally from reaching the central nervous system during hypnotic analgesia (Sharav and Tal, 1989). Locally achieved analgesia in response to placebo, target-directed to a specific body location, was modulated by opioid systems (Benedetti et al., 1999). Such mechanisms would not apply to hypnotic analgesia, not reversed by Naloxone, and therefore not dependent on endogenous opioid pain-inhibitory mechanisms (Goldstein and Hilgard, 1975; Barber and Mayer, 1977; Zachariae et al., 1998).

LH and HH subjects did not differ in expectation rate, as we also demonstrated in a previous study (Sharav and Tal, 2004). Expectation, therefore, does not seem to have affected the differences between the two groups of subjects in their selective site-specific hypnotic analgesia. Additionally, expectation is one of the main mediators of placebo analgesia (Montgomery and Kirsch, 1966; Amanzio and Benedetti, 1999; Price et al., 1999; Pollo et al., 2001), while it may play a minor role in producing hypnotic analgesia (Sharav and Tal, 2004). Although initial evidence suggested that the effects of hypnosis on post-surgical pain and distress were mediated by pre-surgical expectation (Montgomery et al., 2002).

4.2. Effect of focused hypnotic analgesia on remote area

In this experiment, the analgesic effect in the remote area in HH subjects was significantly smaller than that in the local area of these subjects. Additionally, this remote effect in HH subjects did not differ from that achieved in LH subjects in both local and remote areas. It was previously found that the hypnotic effect in LH subjects did not differ from a placebo effect (McGlashan et al., 1969). It seems, therefore, that the hypnotic analgesia achieved in the remote area in HH subjects was no better than a placebo effect. One cannot dismiss however the possibility of a spread, or a generalized hypnotic analgesia that went throughout the body. Our study is limited in this respect by the fact that we did not test directly for this possibility, and a direct comparison between focused analgesia and generalized, whole body, hypnotic analgesia is worthwhile examining. Furthermore, unlike in our previous studies (Sharav and Tal, 1989; Sharav and Tal, 2004) where a "parallel shift" (i.e. a constant reduction of pain intensity at all stimulus intensities) was noticed in response to ascending stimuli under placebo analgesia or under hypnotic relaxation, in this study the remote area in HH subjects did exhibit an increase in pain reduction with ascending stimulus intensity. This may also indicate that the analgesia achieved in the remote area in HH subject could be associated to some extent with a spread of hypnotic analgesia beyond the local area.

4.3. Focused hypnotic analgesia and attention

Focused hypnotic analgesia is intended to replace sensations of pain with others such as numbness or complete absence of sensation, and requires increased attention to the pained body area. This situation is, therefore, totally different from that of redirecting spatial attention away from the stimulated area (Bushnell et al., 1985, 2004). It seems that narrowing attention during hypnosis to the relevant stimuli activates an inhibitory control system, as suggested by somatosensory task-related changes produced by focused analgesia in highly hypnotizable subjects (De Pascalis et al., 1999). Friederich et al. (2001) found that hypnotic analgesia, produced by suggestion of "glove analgesia," and distraction of attention, significantly reduce pain to noxious laser-heat stimuli. However, during hypnotic analgesia the amplitude of the late laser-evoked brain potentials (N200 and P320) was not significantly different from that of the control, while it did reduce during distraction of attention. They concluded that hypnotic analgesia and distraction of attention represent different mechanisms of pain control.

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