Hypnosis Prevents the Cardiovascular Response to Cold Pressor Test

Edoardo Casiglia\textsuperscript{a,b}, Laura Schiavon\textsuperscript{a}, Valérie Tikhonoff\textsuperscript{a}, Hilda Haxhi Nasto\textsuperscript{a}, Mariafrancesca Azzi\textsuperscript{a}, Panagiota Rempelou\textsuperscript{a}, Margherita Giacomello\textsuperscript{b,c}, Monica Bolzon\textsuperscript{a}, Anna Bascelli\textsuperscript{a}, Roberta Scarpa\textsuperscript{a}, Antonio M. Lapenta\textsuperscript{b}, Augusto M. Rossi\textsuperscript{a,b}

Abstract
To highlight the effects of hypnotic focused analgesia (HFA), 20 healthy participants underwent a cold pressor test (CPT) in waking basal conditions (WBC) by keeping the right hand in icy water until tolerable (pain tolerance); subjective pain was quantified by visual scale immediately before extracting the hand from water. The test was then repeated while the participants were under hypnosis and underwent HFA suggestions. Cardiovascular parameters were continuously monitored. Pain tolerance was 121.5±96.1 sec in WBC and 411.0 ± 186.7 sec during HFA ($p < 0.0001$), and visual rating score 7.75 ± 2.29 and 2.45 ± 2.98 ($p < 0.0001$), respectively. CPT-induced increase of total peripheral resistance was non significant during HFA and +21% ($p < 0.01$) in WBC. HFA therefore reduced both perception and the reflex cardiovascular consequences of pain as well. This indicates that hypnotic analgesia implies a decrease of sensitivity and/or a block of transmission of painful stimuli, with depression of the nervous reflex arc.

Keywords: Physiology, peripheral circulation, hypnosis, pain, psychology, cold pressor test.

Address correspondences and reprint requests to:
Prof. E. Casiglia, MD
University of Padova - Dept. of Clinical and Experimental Medicine
Via Giustiniani No. 2
35128 Padova, Italy
E-mail: edoardo.casiglia@unipd.it

\textsuperscript{a} Department of Clinical and Experimental Medicine, University of Padova, Via Giustiniani No. 2, Padova, Italy
\textsuperscript{b} Italian Centre for Clinical and Experimental Hypnosis, Via Medici No. 43, Torino, Italy
\textsuperscript{c} Institute of Anaesthesiology and Intensive Care, General Hospital of Padova, Via Giustiniani No.2, Padova, Italy

Acknowledgments
We thank Miss Jillian Walton for kindly revising the manuscript.
Quantification of hypnotic focused analgesia

Introduction

During hypnosis, it is possible to give special suggestions (thermal, tactile, visual, auditory, coenesthesic) that, due to the high level of attention and to the characteristics of altered consciousness, rise to special relevance and can be experienced as belonging to real world (Bryant & Mallard, 2005; Kaffman, 1981).

It is nevertheless still uncertain whether these experiences are mere hallucinations, or rather are accompanied by real and measurable physiological modifications. Our group is particularly interested in clinically measurable, repeatable, physical consequences of hypnosis (Casiglia et al., 1997; Casiglia et al., 2006).

A very special field of research is represented by the role of hypnosis in modulating pain (Chaves & Dworkin, 1997; Holroyd, 1996). The effect of hypnosis in this respect is well documented (Chaves, 1994; Holroyd, 1996; Howland et al., 1995; Kiernan et al., 1995; Miller & Bawers, 1993; Zachariae & Bjerring, 1994). Nevertheless, a theoretical understanding of the mechanisms of pain control via hypnosis is still lacking, and the chain of events leading to this effect is uncertain. In particular, it is unclear whether hypnotic analgesia represents nothing more than an inhibitory hallucination accompanying dissociation, or when at a certain level, is due to a genuine block of pain.

Although it is difficult to answer this question, cardiologists can give a contribution through research into cardiovascular modifications that are typical of pain.

Quantification of pain is the crucial point. Visual point-rating scales or lines depicting verbal anchors are usually employed, but this subjective way has recently been questioned (Mader, Blank, Smithline, & Wolfe, 2003).

Cold pressor test (CPT) is extensively used by cardiologists to induce pain (Mitchell, MacDonald & Brody, 2004; Sevre & Rostrup, 1999). This method, when applied to participants free to interrupt the test when they want, has three important advantages: 1) it can be standardized, 2) its length reflects tolerance to pain, and 3) its haemodynamic consequences can be easily measured, providing a further demonstration of pain reduction or relief. The combination of visual rating scale and CPT appears therefore to be a good way of obtaining a reliable measurement of pain and analgesia.

The aim of the present study was to quantify the so-called hypnotic focused analgesia (HFA), and to monitor the haemodynamic effects of CPT both in waking basal conditions (WBC) and during HFA, so clarifying whether or not hypnotic analgesia, if any, has to be considered an inhibitory hallucination/dissociation (not accompanied by cardiovascular modifications) or rather a real block of painful stimuli (accompanied by reduction of sympathetic cardiovascular response to pain).

Methods

Study Participants. Twenty healthy, young volunteers, whose general characteristics are summarized in Table 1, were studied. They were recruited among the medical staff of a department of internal medicine, and previously defined as eligible for hypnosis on the basis of a historical questionnaire, a personal interview with the staff, and when necessary, a Minnesota Multiphasic Personality Inventory 2 procedure. This was aimed at screening out participants with borderline personality, more prone to show unwanted effects during hypnotic dissociation. Hypnotizability was also individually determined in each subject by means of the Harvard group scale of hypnotic susceptibility (De Pascalis,
Russo & Marrucci, 2000; Younger, 2005). Highly hypnotizable participants having Harvard Scale score $9.4 \pm 3.1$ (range 7 to 10) were chosen for the present study, as it was previously shown that they tend to experience more evident inhibition of CPT pain when receiving HFA (Horton, Crawford, Harrington & Downs, 2004).

Table 1: General Characteristics of Study Participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>26.9 ± 2.7</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.6 ± 0.1</td>
</tr>
<tr>
<td>Body mass index (kg x m²)</td>
<td>21.0 ± 2.0</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>118.7 ± 11.8</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>72.7 ± 10.1</td>
</tr>
<tr>
<td>Mean blood pressure (mmHg)</td>
<td>88.0 ± 10.0</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>6.0 ± 7.8</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>81.0 ± 13.2</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>60.2 ± 16.7</td>
</tr>
<tr>
<td>Cardiac index (1 x min⁻¹ x m²)</td>
<td>3.2 ± 1.2</td>
</tr>
<tr>
<td>Total peripheral resistance (mmHg x 1⁻¹ x min)</td>
<td>19.1 ± 6.1</td>
</tr>
</tbody>
</table>

Ethical Aspects. This research adheres to the principles of the Declaration of Helsinki. All participants gave written informed consent to the procedure. Each one was preliminary and personally informed about the aims, methods and possible risks of the procedure, and had the opportunity to ask all questions that he/she considered necessary. Local Ethics Committee approved the protocol.

Procedure. The study was performed in three steps.

In the first phase (preliminary setting), participants were screened out, interviewed and individually prepared for hypnosis. In the second phase, some days later, they underwent CPT in WBC, without any hypnotic suggestions. In the third phase, they underwent CPT after receiving hypnotic suggestions of analgesia.

In details, in the preliminary setting all participants in turn individually underwent hypnotic induction through verbal suggestions with cues of relax and well-being. Through the voice of an expert hypnotist (E.C.), each subject was guided towards focusing his/her attention on a single idea, excluding any other external or internal stimuli. A traditional hypnotic induction was used, consisting of a brief enumeration coupled with suggestions of general well-being, eyelid heaviness, regular deep breathing, and staring at a point. After spontaneous eyelid closure was obtained, participants were invited to concentrate on their
own body from their feet to the head, while a feeling of heaviness and muscular relaxation was being suggested. The verification of hypnosis was based on some signals, such as arm levitation, the easing of facial tension, the lower jaw dropping down with a slight opening of mouth, and slowing down of breathing rate. The analysis of these signals enabled a predetermined commission of three hypnotists different from E.C. to verify if the participants were really hypnotized, aimed at allowing E.C. to maintain or modify this condition by means of continuous appropriate suggestions. The aim of this preparatory procedure was to establish a valid interpersonal relationship between the operator and the subject, in order to favor rapid and valid mono-ideism in the occasion of the following experimental sitting. To reduce the time needed for induction, posthypnotic conditioning was predisposed in all participants.

On the day chosen for the experiment, the participants individually underwent CPT in WBC (Mitchell et al., 2004) by immerging their right hand in a tub containing icy water at a temperature of 0°C (32 °F). As known, CPT induces local pain accompanied by cardiovascular effects, such as an increase of total peripheral resistance (TPR) and a decrease of cardiac index (Peckerman et al., 1991; Peckerman et al., 1994; Sevre et al., 1999; Sendowski et al., 2000). The pain reached at the end of CPT was quantified in two ways: 1) by a 0 to 10 subjective rating scale (Dirks et al., 1993), and 2) measuring the time of permanence in icy water (pain tolerance threshold). For this purpose, participants were asked to keep their right hand in the icy water tub until possible. Only when pain became intolerable, they were allowed to interrupt the CPT (Langlade, Jussiau, Lamonerie, Marret & Bonnet, 2002). Pain-induced variations of the cardiovascular parameters described below were recorded as a measure of the reflex consequences of pain.

On the same day, after haemodynamic stabilization was reached, the same participants were asked to repeat the same procedure while undergoing HFA. Once a valid neutral hypnosis was induced, the special suggestions aimed at obtaining hand analgesia were administered. In detail, it was suggested that the right hand was insensitive to pain and that no pain sensation could originate from it. The aim of this procedure was to produce analgesia by focusing attention on the hand receiving painful stimulation. It has previously been demonstrated that this procedure is more effective than dissociated imagery in reducing pain, and the most effective in absolute.

Pain intensity (rating scale) and pain tolerance threshold (time of permanence in icy water) were recorded as previously described, and haemodynamic parameters were continuously monitored both before and during the entire painful procedure.

For patients who developed complete analgesia and resulted in being insensitive to pain during this phase, it was decided a priori to stop the test at the 9th min of immersion to avoid freezing that could have lead per se to reduced perception of pain. During hypnosis, continuous suggestions of well being were given. Particular attention was paid in order to suggest sensations of normal temperature and absence of pain at right hand after de-hypnotization. The subject’s usual consciousness was then gradually restored.

It was decided to perform in all participants first CPT alone and then CPT with analgesia, instead of employing a square-latin random protocol. As no tolerance to CPT has ever been described, counterbalancing the order of presentation could have been redundant and counterproductive, leading to possible confounding residual analgesic effect of hypnosis. A limitation of this open protocol is that expectancy effect and/or non-hypnotic suggestion could have influenced the results, as the participants knew they were going to receive the CPT with or without hypnosis and they could have been more likely to rate the stimulus experienced without hypnosis as more intense than with hypnosis.
On the other hand, the painful and haemodynamic effects of CPT are notoriously so univocal and intense, that it was considered unnecessary and redundant to include a baseline suggestion in the absence of formal hypnosis or to follow a real-simulator design.

**Cardiovascular Monitoring.** Monitoring of cardiovascular parameters was performed before and during CPT, both in WBC and during HFA.

Duration of permanence of the hand in icy water was measured with a Casio 3043 PRW-1200 chronometer, and blood pressure (in mmHg) by an automatic Omron 705 IT device (Omron Europe, Hoofddorp, The Netherlands). Pulse pressure (in mmHg) was calculated as systolic - diastolic, and mean blood pressure (in mmHg) as diastolic +1/3 pulse pressure. The amount of blood ejected from the left ventricle at each systole (stroke volume, in ml) and in one minute (cardiac output, in l x min\(^{-1}\)) was measured with an impedance cardiograph, featuring enhanced bio-impedance signal morphology analysis (PhysioFlow TM-Lab-1, Manatec Biomedical, Ebersviller, France); this device also provided heart rate recording (in beats per minute, bpm) from RR-intervals [Richard et al., 2001]. TPR (in mmHg x min x l\(^{-1}\)) was calculated as usual from mean blood pressure/cardiac output ratio. Cardiac index (in 1 x min\(^{-1}\) x m\(^{2}\)) was calculated by indexing cardiac output by body surface area.

The aim of these measurements was to ascertain whether the CPT procedure was accompanied by a sympathetic drive discharge leading to systemic haemodynamic variations (particularly to increase in TPR), or if, on the contrary, the sympathetic response to CPT was reduced or absent during HFA.

**Statistics.** A priori power analysis based on previous experience of the same laboratory (Casiglia et al., 2000) indicated that 20 participants were sufficient to show cardiovascular effects on TPR, if any, avoiding \(\beta\) error. For this purpose, theoretical mean values in the two conditions (WBC and HFA) were based on previous experience of our laboratory (Casiglia et al., 2000), and mean difference (\(\delta\)) between the two means and its standard deviation (\(\sigma\)) were used to calculate the centrality parameter \(\bar{O} = 5\delta/\sigma\). Linearity assumption was ascertained by the residuals, and normality assumption by the Kolmogorov-Smirnov one-sample test.

Continuous variables were expressed as mean ± standard error and compared with analysis of covariance and the Bonferroni’s post-hoc test; statistics were adjusted for the covariates age, body-weight and baseline values; 95\% confidence intervals (CI) were indicated when proper. The within trend of each curve, as well as the differences between the curves, were evaluated with the analysis of covariance for repeated measures. The null hypothesis was rejected for a \(p\) of 0.05 or less.

**Results**

**General Trend of The Study and CPT-pain Tolerance.** The study was completed in all participants. Duration of the test was 121.5 ± 96.1 sec (CI 76.5-166.5) in WBC without any suggestion of analgesia, and 411.0 ± 186.7 sec (CI 323.6-498.4) during HFA (234\%, \(p < 0.0001\)). Probably due to the limited range of the Harvard scale related to choice of highly hypnotizable participants, increase in CPT tolerance did not correlate with individual hypnotic susceptibility \((r = 0.24, p = 0.3)\).

The test conducted in WBC was always interrupted for hand pain. Thirteen participants tolerated pain for 1 minute, 10 for 2 minutes, seven for 3 minutes, four for 4 minutes and one for 5 minutes (Figure 1). After extraction from the icy water, the hand always appeared vasoconstricted and cold, and the typical postischemic pain was experienced by all participants.
During HFA, 20 participants tolerated CPT for 1 minute, 17 for 3 minutes, 14 for 4 minutes, 13 for 5 minutes, 12 for 6 minutes, 10 for 7 minutes, 10 for 8 minutes, and in nine cases it was necessary to stop the test at the nineth minute in the absence of any tolerance threshold (Figure 1). The reason of interruption - reported after dehypnotization - was never hand pain, but rather feelings like “I am tired”, “there is dripping of cold water”, “my right hand tickles”, and so on. All participants reported to having felt a normally hot hand throughout the procedure and after dehypnotization.

**Subjective Pain.** When CPT was conducted in WBC, the maximum rating score of pain measured immediately before the subject asked interrupting the test was $7.75 \pm 2.29$ (CI 6.68-8.82). When the same procedure was performed having preliminary induced HFA, the score was $2.45 \pm 2.98$ (CI 1.05-3.85) ($p < 0.0001$). Figure 1 shows the trend of the 20 singular cases.

![Figure 1: Quantification of pain at the end of cold pressor test (CPT) through visual rating scale score (upper panel) and through tolerance to cold pressor test (lower panel). The symbol indicates mean trend, $p < 0.0001$ indicates difference between waking basal condition and hypnotic focused analgesia.](image-url)
Subjective visual rating scale score directly correlated with objective increase in pain tolerance measured through time of permanence in icy water ($r = 0.84, p < 0.0001$), while, probably for the same reasons listed on page 10, no correlation was found between rating scale and Harvard scale hypnotic susceptibility ($r = 0.09, p = 0.7$).

*Cardiovascular Monitoring.* When CPT was performed in WBC, blood pressure, heart rate and PR increased (Figure 2), while cardiac index decreased in comparison to baseline (Figure 3), mirroring TPR trend. These variations were due to systemic arteriolar constriction. The maximum variation of TPR was $+21\% (p < 0.01)$. During HFA, TPR (Figure 2) and cardiac index (Figure 3) were unchanged in comparison to baseline, showing nothing more than small and insignificant variations near the line of zero, due to the usual physiological variability. The cardiac index variations - although non significant - perfectly mirrored those of TPR in this phase too, indicating that measurements were reliable.

![Figure 2](image2.png)

*Figure 2.* Pain-induced % variations of total peripheral resistance (TPR) during cold pressor test. In waking basal conditions (WBC, —●—), out of any hypnotic suggestions, participants agree to keep the hand in icy water for not more than 4 minutes on average, and their TPR increases, due to reflex sympathetic discharge secondary to CPT-pain. During hypnotic focused analgesia (HFA, —○—), mean tolerance time is 9 minutes, and TPR is not different from zero, not being influenced by reflex sympathetic discharge. TPR are significantly lower during HFA than in WBC from 2nd to 4th minute.

![Figure 3](image3.png)

*Figure 3:* Pain-induced percent variations of cardiac index (CI) during cold pressor test. Abbreviations as in Figure 2. In WBC, CI decreases (mirroring variation in TPR) due to reflex sympathetic discharge secondary to CPT-pain. During HFA, CI is not different from zero, not being influenced by reflex sympathetic discharge. CI is significantly lower (indicating systemic vasoconstriction) in WBC than during HFA from second to fourth minute.
Discussion

Our results demonstrate that HFA was actually reached. In fact, subjective perception of pain measured through a rating scale decreased by 68% and objective pain tolerance was more than doubled during HFA. Although documented in a modern, instrumental way, this result is not a surprise, as the possibility to induce HFA is well known. The underlying patho-physiological mechanism is, nevertheless, under debate. HFA has been attributed from time to time to dissociation or to the blocking of painful stimuli.

The cardiovascular monitoring performed in the present study seems to indicate that HFA implies a certain degree of painful stimuli blocking along the nervous ways, as the reflex vasoconstriction accompanying CPT-pain was reduced during HFA. As the cardiovascular reflexes that are responsible for vasoconstriction act at a lower level than that of consciousness, dissociation cannot be an explanation for this. Our results are therefore in agreement with the models of HFA that involve at least in part a reduction of nociceptive stimuli (Kiernan et al., 1995; Sandrini et al., 2000).

Gate control is a possible explanation. It is well known that a gating mechanism modulates the transmission of noxious stimuli at the dorsal horn of the spinal cord (Melzack & Wall, 1965). The question is: how can hypnosis modify this mechanism? It has been demonstrated that the gating is modulated by selective cognitive processes transmitted through descending fibres (Melzack, Casey & Sensory, 1968). Such fibres could be activated during HFA. Confirming this hypothesis, Kiernan et al. (1995) reported, during hypnosis, changes in the nociceptive spinal cord reflex R-III.

This is, of course, a simplistic explanation. Pain is a multi-dimensional experience involving sensory, motivational, emotional and cognitive factors, and HFA could act peripherically (by down-regulating the input of painful stimuli), at a spinal level (reducing the poly-sympathetic reflexes), and at a cortical level (modulating directly perception and affective dimension of pain and unpleasantness). A supervising attentional system involving fronto-temporal cortex and the limbic system is probably associated to these multiple, hierarchical chains (Kiernan et al., 1995; Patterson, Adcock & Bombardier, 1997). But in our experiment, a gating mechanism must be involved in HFA as hypnotic suggestion reduced the cardiovascular reflexes to pain.

On the contrary, the results of our studies seem to indicate that dissociation cannot be the only mechanism of HFA. According to dissociative theories, hypnosis could act by dissociating pain experiences from conscious awareness (Croft et al., 2002; Gruzelier, 1990; Gruzelier, 1996; Gruzelier, 1998; Kropotov et al., 1997). Pain would be registered, but remain dissociated from conscious and emotional awareness, being masked by an amnesia-like barrier (Hilgard, 1979; Hilgard, 1986; Pribram, 1991). Using CPT plus HFA, other authors actually observed EEG shifts in hemispheric dominance of high θ frequency band power, confirming an active attentional/inhibitory processing in the anterior temporal cortex, with a shift towards greater power in the right hemisphere (Becker & Yingling, 1998; Crawford, 1990; Crawford, 1990b) and an aspecific inhibition feedback circuit regulating thalamo-cortical activity (Birbaumer et al., 1990; Crawford & Gruzelier, 1992).

The dissociative theory pretends that, when HFA is produced, the far-frontal cortex determines that the incoming painful events are irrelevant (Crawford et al., 1993). Although this evidence is of great importance to demonstrate that a certain degree of dissociation is present during hypnosis, it appears clear from the results of the present study that this cannot be the only mechanism. In fact, if hypnosis merely dissociated painful experience
from consciousness, a normal cardiovascular reflex response to pain would develop, and an increase in TPR would be recorded during HFA like in WBC.

For the same reasons, our results are in disagreement with the social-cognitive theory, stating that HFA depends on cognitive-behavioural strategies, that it is similar to waking analgesia and consists of distracting attention from pain by using goal-directed fantasies (Spanos et al., 1979; Spanos et al., 1984; Spanos, 1986; Turk et al., 1983). In this case too, cardiovascular response to pain, acting at a lower level, should be fully present.

Finally, the constructivist theory affirms that HFA works as a combination of hypnotic obstruction and localization of the analgesia schema in the forefront. As consciousness operates under limited capacity, only one representation of reality— that excluding awareness of pain - can occupy it at a given moment (Chapman & Nakamura, 1998). This may be true, but does not explain why the CPT induced vasoconstriction is depressed during HFA.

In conclusion, during hypnosis it is possible and relatively easy to induce analgesia. Our research, based on recording of cardiovascular parameters in response to pain accompanying CPT, suggests that pain sensation is blocked by HFA at a certain, undefined level of nervous system. Nevertheless, our results are not definitive enough to conclude that the theories other than those invoking a block of painful stimuli are invalid. The gating control theory is not completely antithetical to the other ones, and different mechanisms (gate control, dissociation, distraction of attention) could be involved at the same time in HFA. Further studies involving functional imaging of the brain are mandatory to clarify whether, as likely, superior functions are also responsible for the reduction of subjective feelings of pain.

References


Quantification of hypnotic focused analgesia

