THE CHALLENGE OF PAIN: CAN THE HYPNOTIC BRAIN CONTROL YOUR PAIN?

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HYPNOTIC ANALGESIA

• What is pain?
• Recent advances in understanding pain mechanisms: the role of neuroimaging
• Can hypnosis alleviate pain?
• The role of hypnotic susceptibility
• Peripheral Mechanisms
• Spinal Mechanisms
• Cortical / Subcortical Mechanisms
• Hypnosis and Neuroscience: A Cross-Talk
• Clinical Implications
Pain is a perfect misery.

John Milton, Paradise Lost
EPIDEMIOLOGY OF PAIN IN ITALY

<table>
<thead>
<tr>
<th>Chronic Pain Syndromes</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Headache</strong></td>
<td>4,000,000</td>
</tr>
<tr>
<td><strong>Back Pain</strong></td>
<td>2,000,000</td>
</tr>
<tr>
<td><strong>Neuropathic Pain</strong></td>
<td>500,000</td>
</tr>
<tr>
<td><strong>Cancer Pain</strong></td>
<td>200,000</td>
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</tbody>
</table>
### EPIDEMIOLOGY OF CHRONIC PAIN

**META-ANALYSES**

<table>
<thead>
<tr>
<th>Pain Patients</th>
<th>RCT(n=)</th>
<th>(N=)</th>
<th>Mean Prevalence (%)</th>
<th>Range</th>
<th>F/M ratio (%)</th>
<th>Severe Pain (%)</th>
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<tbody>
<tr>
<td>General Chronic Pain</td>
<td>7</td>
<td>35160</td>
<td>35.5</td>
<td>11.5-55.2</td>
<td>F 39.6</td>
<td>M 31.4</td>
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<tr>
<td>Pediatric Chronic Pain (age 6-18 yrs)</td>
<td>1</td>
<td>5423</td>
<td>25.0</td>
<td></td>
<td>F 30.4</td>
<td>M 19.6</td>
</tr>
<tr>
<td>Chronic Pain in the Elderly (&gt;65 yrs)</td>
<td>2</td>
<td>1731</td>
<td>50.2</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
DEFINITION OF PAIN

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such pain.

IASP Classification of Pain, 2nd edn., 1994
PAIN IS A "PRIVATE" EXPERIENCE.
THE MULTIDIMENSIONAL CONSTRUCT OF PAIN

- Sensory-Discriminative
  (stimulus localization, intensity and quality of pain)
- Motivational - Affective
  (anhedonic quality and negative emotional resonance)
- Cognitive

Melzack & Casey, 1968; Wade et al., 1996
NOCICEPTIVE ASCENDING SYSTEMS

Diagram illustrating the nociceptive ascending systems with labels and connections.

- Perception of Pain
- Neurotransmitters at Dorsal Horn Level: Nonpeptide, Enkephalins
- Primary Afferent Neurotransmitter Candidates: Substance P, L-Glutamate, GABA, VIP, CCK-B, Somacation
- Spinothalamic Tract
- To the Limbic System
- Descending Inhibitory Pathway
- Trauma, Capillary
- Release of: Substance P, Histamine, Serotonin, Endoylektin, Prostaglandins
- Release of Norepinephrine
- Motor of Other Effluent Nerve
- Segments Reflexes: Increased Skeletal Muscle Tension, Decreased Chest Compliance, More Nociceptive Input, Increased Sympathetic Tone, Decreased Gastric Mobility, Ileus, Nausea, Vomiting
PAIN INTENSITY-RELATED STRUCTURES

Coghill et al., 1999
THE NEUROMATRIX OF PAIN

- Thalamic Nuclei
- Insular Cortex
- Frontal Areas (e.g. lateral orbitofrontal cortex)
- Anterior Cingulate Cortex (ACC)
- Cerebellar Vermis
- S1 / S2 Cortices
- Inferior Parietal Cortex (Brodman’s area 40)
- Periaqueductal Gray (PAG)

Petrovic & Ingvar, 2003
PAIN PERCEPTION AND PET

MORE PAIN

LESS PAIN

Coghill et al., 2003
PAIN-INTENSITY RELATED BRAIN AREAS

Coghill et al., 2003
The role of the Anterior Cingulate Cortex (ACC) modif. from Petrovic & Ingvar, 2002
NEUROIMAGING STUDIES ON PAIN

- Taken together, the convergence of neuroimaging findings on pain processing is remarkable, given the diversity of experimental noxious stimulation and experimental conditions used in these studies, and despite minor discrepancies.

- This combined evidence suggests that the concurrent activation of this network of brain structures constitutes the *Signature of Pain* in the brain, and may reflect the multidimensional complexity of the subjective experience of pain.
The same structure may both respond to pain and participate to pain control.

Peyron et al., 2003
Franz Anton Mesmer (1734-1815)
MESMERISM IN INDIA,

AND ITS

PRACTICAL APPLICATION IN SURGERY
AND MEDICINE.

BY

JAMES ESDAILE, M.D.,

CIVIL ASSISTANT SURGEON, H. C. S., BENGAI.

"I rather choose to endure the wounds of those darts which envy casts at
novelty, than to go on safely and sleepy in the easy ways of ancient
mistakings."—Raleigh.

HARTFORD:
SILAS ANDRUS AND SON.
1851.
More than 150 papers on hypnosis published yearly in peered scientific journals (Larkin, 1999; De Benedittis, 2004).

The American Medical Association (AMA) and other medical institutions formally recognize hypnosis as a viable and effective tool for medical treatment.

Since 1994, IASP (International Association for the Study of Pain) has included hypnosis in the Core Curriculum for professional training of pain therapists.
Efficacy of Hypnotic Analgesia

Hypnosis is a viable and effective intervention for alleviating pain with cancer and other chronic pain conditions.

*NIH Technology Panel Report, 1996*
HYPNOTIC ANALGESIA
Clinical (Acute/Chronic) & Experimental Pain

- Meta-analysis of 18 RCT studies (n= 933)
- Substantial pain relief in 75% of the population
- Positive correlation with hypnotic susceptibility
- Hypnotically-suggested pain reduction can be classified as “well-established treatment”.

Montgomery et al., 2000
• Meta-analysis of 20 RCT studies (n= 1624)
• Better outcomes than 89% of patients in control groups.
• Patients in hypnosis group reported significantly more satisfaction than those in control groups.

Montgomery et al., 2002
HYPNOTIC ANALGESIA

Pain Relief in Labour and Childbirth

• Meta-analysis of 5 RCT studies (n= 224)
• Fewer parturients having hypnosis required analgesia as compared with controls.
• Women using hypnosis rated their labour pain less severe than controls (<.01).
• Hypnosis reduced opioid (meperidine) requirements and increased the incidence of not requiring pharmacological analgesia in labour (<.001).

Cyna et al., 2004
“There is sufficient clinical evidence, of sufficient quality, for several high-quality reviews to have concluded that hypnosis has demonstrated efficacy in the treatment of pain”.

Large et al., 2003
MECHANISMS OF HYPNOTIC ANALGESIA
E.R. & J.R. HILGARD

Hypnosis in the Relief of Pain

ERNEST R. HILGARD
JOSEPHINE R. HILGARD
The Hidden Observer (Hilgard, 1984)

WAKING

- Communication Channels
  - Normal Cognition
    - "Pain Felt"
  - Voluntary Indicators (grimacing)
  - Involuntary Indicators (ANS)

HYPNOSIS

- Communication Channels
  - System A
    - Overt Hypnotic Cognition
      - "No Pain Felt"
  - Voluntary Indicators (grimacing)
  - Involuntary Indicators (ANS)

- Communication Channels
  - System B
    - Covert Hypnotic Cognition
      - "Pain Felt"
NEO-DISSOCIATIVE THEORY
(Hilgard, 1977)

Executive Ego

Egoic Substructure 1
(Hypnosis)

Egoic Substructure 2

Input
Output
Input
Output
PAIN & DISTRESS TOLERANCE IN HIGH (HHS) AND LOW (LHS) HYPNOTIZABLE Ss

Hypnosis vs Waking

De Benedittis et al., 1989
PAIN TOLERANCE IN HIGH HYPNOTIZABLE Ss

*Hypnosis vs Waking*

**De Benedittis et al., 1989**

VAS Mean Scores

Time in minute of ischemia

Waking

Hypnosis
DISTRESS TOLERANCE IN HIGH HYPNOTIZABLE Ss

*Hypnosis vs Waking*

De Benedittis et al., 1989
BETA-ENDORPHIN PLASMA LEVELS IN HIGH (HHS) AND LOW (LHS) HYPNOTIZABLE Ss

Hypnosis vs Waking

De Benedittis et al., 1989
ACTH PLASMA LEVELS IN HIGH (HHS) AND LOW (LHS) HYPNOTIZABLE Ss

Hypnosis vs Waking

De Benedittis et al., 1989
CHARACTERISTICS OF HYPNOTIC ANALGESIA

- It involves both sensory pain and distress, the latter being reduced significantly more than pain.
  (De Benedittis et al., 1989; Hilgard & Hilgard, 1994)

- The dissociative effect seems positively correlated with hypnotic susceptibility.
  (De Benedittis et al., 1989; Dahlgren et al., 1995; Rainville et al., 2000)

- The differential modulation of components of pain is dependent upon the structure of hypnotic suggestions.
  (Barabasz et al., 1999; Rainville et al., 1999; Faymonville et al., 2000)
Highly Hypnotizables demonstrate greater cognitive flexibility than Lows, as they possess stronger filter abilities. (Crawford & Gruzelier, 1992; Crawford, 1994)

These attentional skills seem to be associated with inhibitory functions of the frontal lobe and limbic system. (Crawford, 1994; 1998)

Consequently, hypnotic analgesia can be seen as an active process of enhanced attention/disattention that requires an inhibitory effort, dissociated from conscious awareness, where the far frontal cortex participates as a Supervisory Attentional System (SAS). (Shallice, 1988; Crawford, 1994)
BISPECTRAL ANALYSIS: AN OBJECTIVE METHOD FOR ASSESSING AND MONITORING TRANCE DEPTH.

Preliminary results.

World Congress of Hypnosis, Acapulco (Mexico), 2006

Giuseppe De Benedittis

Pain Research & Treatment Unit, Institute of Neurosurgery, Dept. of Neurological Science, University of Milan, Italy
Awake
- Responds to normal voice

General Anaesthesia
- Low probability of explicit recall
- Unresponsive to verbal stimulus

Deep Hypnotic State
- Burst suppression

Flat Line EEG
- Responds to loud commands or mild prodding/shaking
MEAN BIS INDEX VALUES
Waking vs Hypnosis (Lows & Highs)

- Waking: 95.47
- Lows: 90.57
- Highs: 85.24

p < .05  
p < .01
MEAN BIS INDEX PROFILES
Waking vs Hypnosis (Lows & Highs)

BIS Index

- C (n=20)
- Lows (n=7)
- Highs (n=13)

$p < .05$
$p < .01$

T0 Time T30
BIS INDEX vs. HYPNOTIC SUSCEPTIBILITY (SHSS)

$\text{SHSS}$ vs. $\text{BIS Index}$

$r = -0.83$
BISPECTRAL ANALYSIS: IN SEARCH OF THE HYPNOTIC ZONE

Upper Level
Controls = Mean-2SD

HYPNOTIC ZONE

Lower Level
Hypnosis= Mean-2SD
THE HYPNOTIC BIS-SPECTRUM

BIS Index

Waking (n=20)  Hypnosis (n=20)

THE HYPNOTIC SPECTRUM
BIS INDEX: COGNITIVE-EMOTIONAL MODULATION
Waking vs Hypnosis (Lows vs. Highs)

Units

Baseline Mean % Change

Pain

Stress

Waking
LHS
HHS

0.4
p < .05

0.2

0.1
0.9

1.1
p < .05

De Benedittis, 2008
HYPNOTIC ANALGESIA

Peripheral Mechanisms

- Hypnosis increases heat detection and heat-pain threshold in healthy volunteers.
- Postulated modulation of A-delta and C fibers activity.

Langlade et al., 2001
HEAT PAIN THRESHOLD

Benhaiem et al., 2001
AUTONOMIC CHANGES IN HYPNOSIS

The sympatho-vagal balance of the Autonomic Nervous System (ANS) can be studied by means of a heart rate variability spectrum analysis (R-R interval).

De Benedittis et al., 1994
POWER SPECTRUM DENSITY ANALYSIS

- RR INTERVALS
- TACHOGRAM
- HISTOGRAM
- SPECTRAL COMPONENTS
- POWER SPECTRAL DENSITY
Low Frequency (LF) (0.10 Hz) as a marker of Sympathetic Activity (S. N. D.)
High Frequency (HF) (0.25 Hz) as a marker of Vagal Activity (V. N. D.)
<table>
<thead>
<tr>
<th>Subjects</th>
<th>Condition</th>
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<th>HFp</th>
<th>LF / HF</th>
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</thead>
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<tr>
<td>Total Sample</td>
<td>waking</td>
<td>39.3</td>
<td>22.5</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td>hypnosis</td>
<td>50.1</td>
<td>25.9</td>
<td>1.4**</td>
</tr>
<tr>
<td>Lows</td>
<td>waking</td>
<td>39.5</td>
<td>19.0</td>
<td>2.9</td>
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<td>hypnosis</td>
<td>53.1</td>
<td>29.9</td>
<td>1.6*</td>
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<tr>
<td>Highs</td>
<td>waking</td>
<td>33.4</td>
<td>27.1</td>
<td>2.6</td>
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<tr>
<td></td>
<td>hypnosis</td>
<td>39.9</td>
<td>27.1</td>
<td>1.2***</td>
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</table>
POWER SPECTRUM DENSITY OF A HIGHLY HYPNOTIZABLE SUBJECT IN WAKING AND NEUTRAL HYPNOSIS

De Benedittis et al., 1994
PAIN INTENSITY, R-III & H REFLEX

Waking vs Hypnosis

Kiernan et al., 1995
HEMISPHERIC SPECIALIZATION IN HYPNOSIS
Task-Dependent Asymmetry during Hypnosis in Lows (LHS) and Highs (HHS)

LHT : Left Hemisphere Tasks
RHT : Right Hemisphere Tasks

De Benedittis, 1994
HYPNOTIC ANALGESIA

Neurochemistry

- Hypnotic analgesia is not dependent upon opioid and ACTH modulation.
  (De Benedittis et al., 1989)

- Highly hypnotizable subjects are associated with high levels of CSF HVA (Vanilmandelic Acid), major catabolite of dopamine (Spiegel & King, 1992) and of COMT (Co-Methyl-Transferase), enzyme involved in dopamine metabolism (Lichtenberg et al., 2004). Dopamine is the neurotransmitter more involved in attentional mechanisms.
NEUROIMAGING
fMRI FUNCTIONAL NEUROANATOMY OF NEUTRAL HYPNOSIS

Maquet, 1999; Rainville & Price, 2000; Faymonville et al., 2000; Rainville et al., 2002
## CEREBRAL BLOOD FLOW (rCBF) CHANGES IN HYPNOTIC ANALGESIA

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Method</th>
<th>rCBF Increase</th>
<th>rCBF Decrease</th>
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<tbody>
<tr>
<td>De Benedittis et al.</td>
<td>1988</td>
<td>SPECT</td>
<td></td>
<td>S1</td>
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<td>Crawford et al.</td>
<td>1993</td>
<td>PET</td>
<td>Orbito-Frontal S1</td>
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<td>Wik et al.</td>
<td>1999</td>
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<td>Orbito-Frontal Subcallosal Cingulate</td>
<td>Inferior Parietal</td>
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<td>Rainville et al.</td>
<td>1999</td>
<td>PET</td>
<td>ACC Frontal-Dorsolateral</td>
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<td>Hofbauer et al.</td>
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<td>S1</td>
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<td>Faymonville et al.</td>
<td>2001</td>
<td>PET</td>
<td>ACC - S1</td>
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<tr>
<td>Faymonville et al.</td>
<td>2003</td>
<td>PET</td>
<td>Increased connectivity of pain-related structures to Mid-Caudal Cingulate Cortex</td>
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SPECT rCBF CHANGES

Waking vs Hypnotic Analgesia

De Benedittis, 1988
SPECT rCBF CHANGES IN A HIGHLY HYPNOTIZABLE SUBJECT

De Benedittis, 1988
CHANGES IN PAIN-RELATED ACTIVITY ASSOCIATED WITH HYPNOTIC SUGGESTIONS OF HIGH AND LOW UNPLEASANTNESS

Rainville et al., 1997
HYPNOTIC COGNITIVE FLEXIBILITY

(a) Hypnotic suggestions for pain sensation modulation

(b) Hypnotic suggestions for pain affect modulation

Rainville et al., 2002
REGIONS OF INCREASED FUNCTIONAL CONNECTIVITY WITH ANTERIOR MID-CINGULATE CORTEX IN HYPNOSIS AS COMPARED WITH WAKING STATE

Faymonville et al., 2003
PUTATIVE MECHANISMS OF HYPNOTIC ANALGESIA

Sensory-Affective Modulation

Descending Noxious Inhibitory Control (DNIC)

Peripheral (A-delta and C fibers) & Autonomic Modulation

Attentional Filter

Spinal Modulation (R-III Reflex)

De Benedittis, 2003
HYPNOTIC ANALGESIA : WHERE ARE WE NOW ?

- Taken together, the degree of consistency across all these studies is remarkable.

- This combined evidence suggests that the concurrent activation of this network of central and peripheral neural structures might constitute the NEUROSIGNATURE of Hypnotic Analgesia.

- However, the dynamics of these complex, functional patterns need to be further elucidated.
A COPERNICAN REVOLUTION?

- Hypnosis is no longer a disputed and controversial issue for the scientific community.
- Hypnosis has not only been established as a viable, valid and reliable intervention for controlling both acute and chronic pain, but it has been eventually recognized as a real psychobiological state and process that deserves increased scientific interest and attention.
- Mostly important, neuroscience research has beginning to consider and use hypnosis as a physiologically effective tool for studying the normal, human brain.

De Benedittis, 2003
Mercy pour votre attention!

Thank you!