

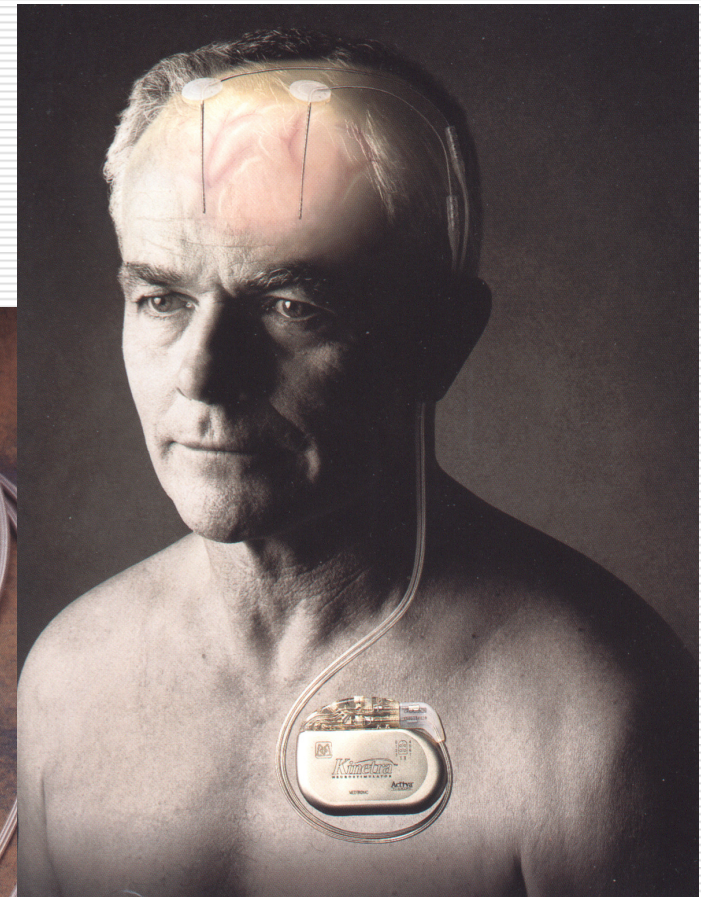
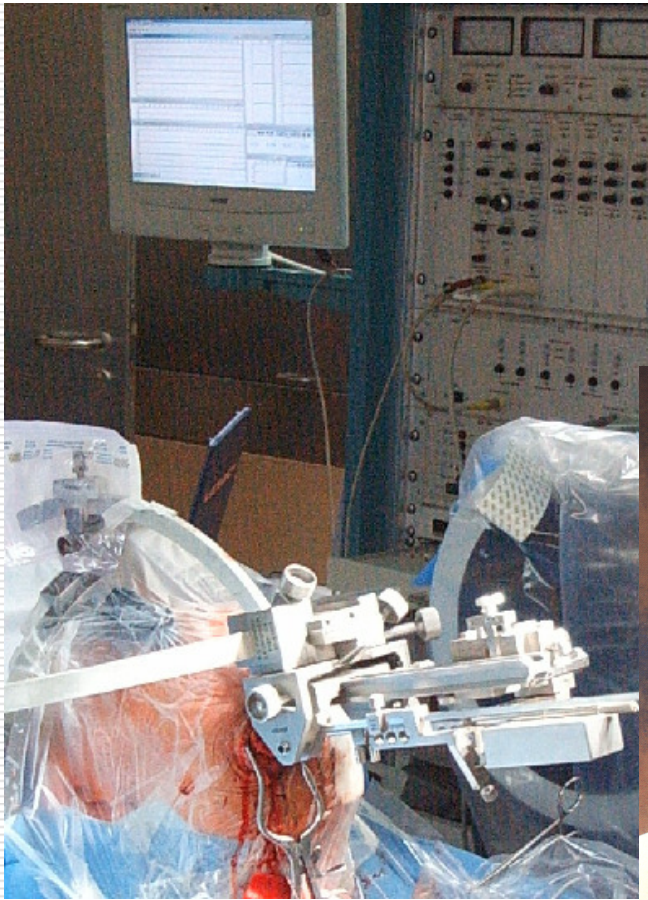
Human Enhancement: Moral, Religious and Ethical Aspects from a European perspective



Deep Brain Stimulation and
Human Enhancement:
clinical cases and future
prospect

Henriette Krug
Department of Neurology
Charité Berlin

Deep brain stimulation: The device



Indications and Targets of DBS

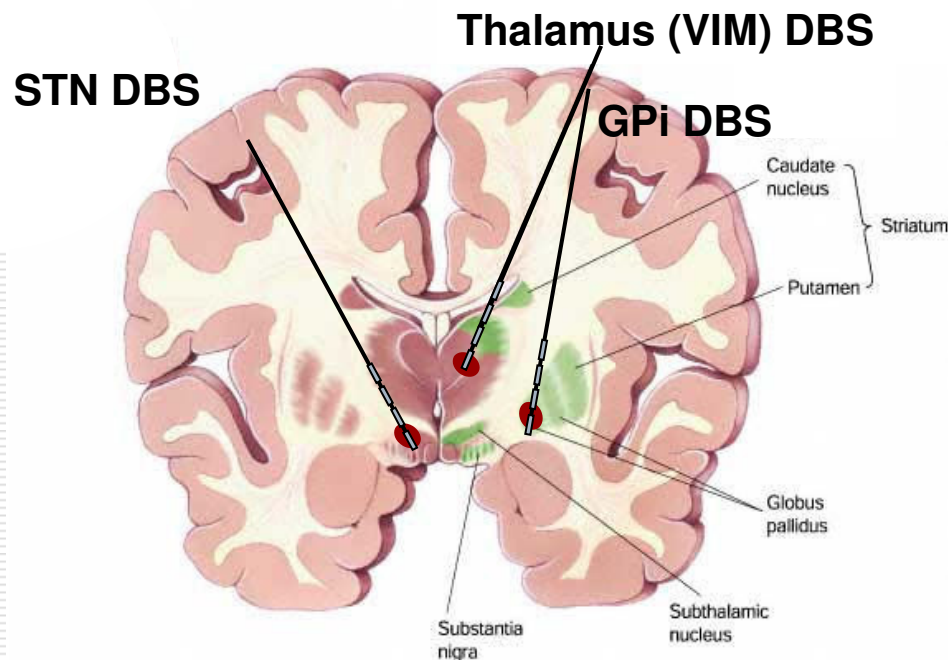
Established indications

Essential Tremor
Parkinson's Disease
Generalised Dystonia

New indications

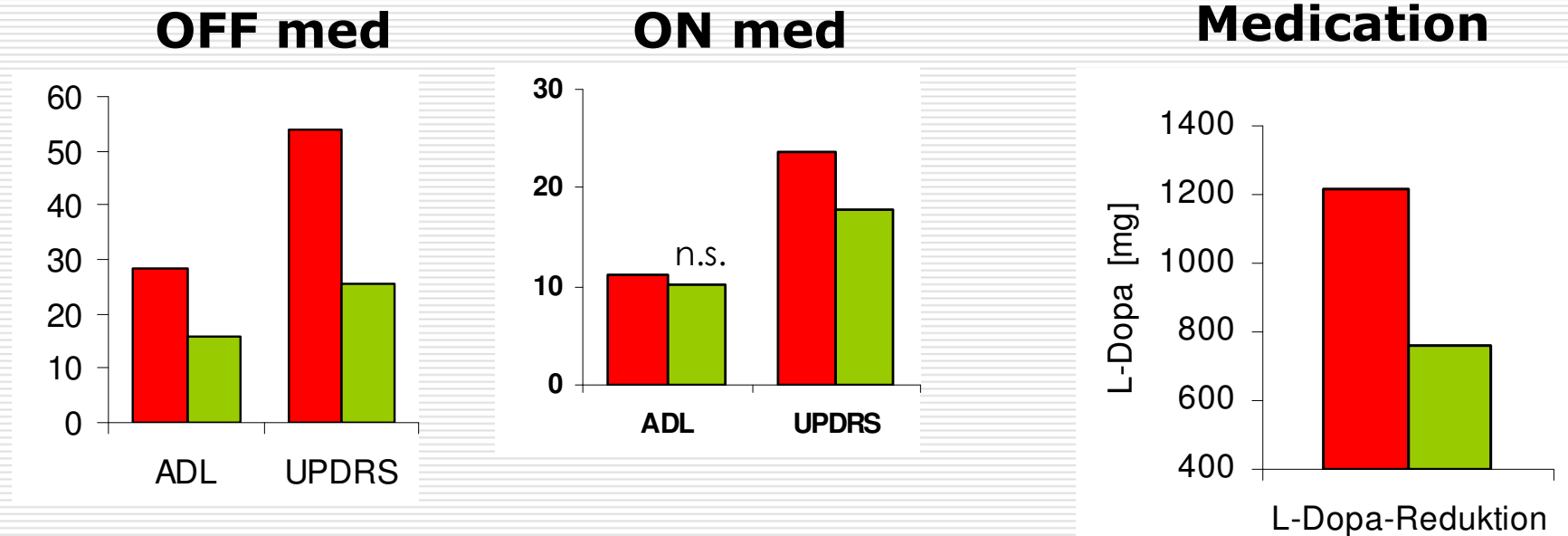
Cervicale Dystonia
Tardive Dystonia
M. Huntington
Gille de la Tourette
Obsessive-compulsive Disorder
Depression

Epilepsy
Cluster Headache



The effect of STN-stimulation in Parkinson's disease(PD)

91 patients, 6 months post-op, 18 centers



Improvement 6 months after surgery

- Motoric symptoms (UPDRS) ~52 %
- Activities of daily living (ADL): ~44 %
- Reduction l-dopa-dose: ~36.5 %

The effects of DBS in Parkinson's Disease



The motoric side-effects of STN-DBS in PD

- Eyelid-opening apraxia: 19 %
- Disabling dyskinesia: 16 %
- Weight gain (mean 3kg): 92%
- Dysarthria: 9 %
- tetanic muscle contraction: 5 %

Non-motor effects of STN-DBS in PD

STN-HFS is associated with non-motor effects related to cognitive functioning, emotion and behaviour

- *acute* induction of
 - mirthful laughter** (Krack 2001)
 - depression** (Bejjani 1999)
 - aggressive attack** (Bejjani 2002)
 - euphoria** (Funkiewiez 2003)
 - *chronic* STN stimulation may result in
 - resolution or development of **depression** (Kumar 1999; Ardouin 1999; Krack 2000; Berney 2002; Houeto 2002)
 - enhanced emotional lability** (Krack 2000)
 - manic episodes** (Herzog 2003; Romito 2002)
 - impulse control disorder**, e.g. pathological gambling, hypersexuality (Krause 2001; Romito 2002)
-

Psychiatric side effects of STN-DBS: Case report I



Affective lability induced by STN-DBS

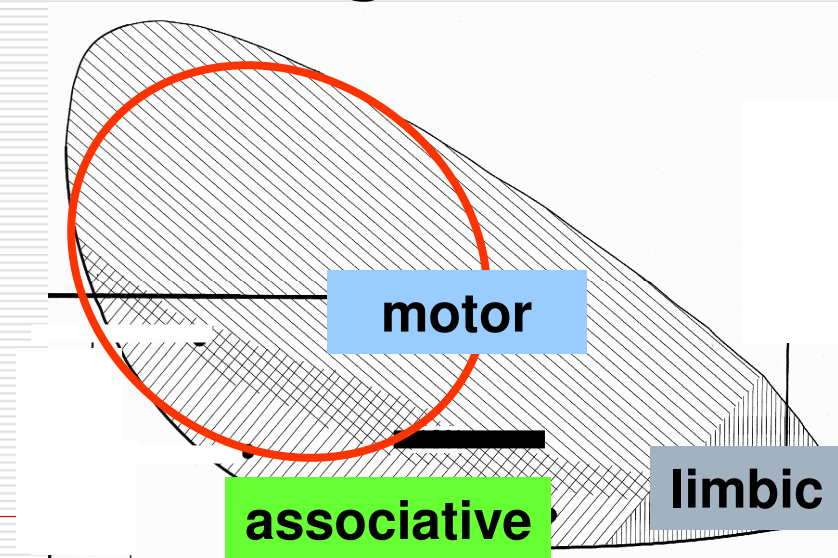
Wojtecki et al.

Psychiatric side effects of STN-DBS: Case report I

Mirthfull laughter induced by STN-DBS

Non-motor effects of STN-DBS

- parallel basal-ganglia cortical circuits mediating movement, cognition and emotion
- STN involved in processing of limbic information



Deep brain stimulation and its capacity of neuroenhancement



„Practically no intervention in the structure or functioning of the human brain can be undertaken in complete certainty that it will not affect mental processes, ...“

Enhancing side effects of STN-DBS: Case report III

“This has been the best adjustment of
my life.”

Enhancing side effects of STN-DBS: Case report IV

“When I turned on the device after such a long time, I immediately felt somewhat of a jar. Everything went dark, I felt dizzy, and I was unable to speak. After several minutes, I gradually got better and my condition normalized. Concerning the sensation: my general condition quickly improved and my endurance got much better and get this, my mind made a quick jump into the positive, like I would have never imagined before. In this situation, we can certainly debate if and how much the procedure changes personality and how far it even changes character traits. However, the fact of the matter for me is this: I feel much better, yes I feel good. If my personality did in fact change, I think I will cope.”

DBS and emotional enhancement

□ Emotional enhancement as a side effect of DBS in established indications:

■ How should we deal with?

■ need of criteria

DBS and enhancement

□ Enhancement by DBS as a future scenario:

- What seems to be feasible?
 - enhancing mood?
 - enhancing cognition?
 - enhancing body shape?
 - enhancing ?
-

Case report: Treatment of obesity led to memory enhancement

Memory Enhancement Induced by Hypothalamic/Fornix Deep Brain Stimulation

Clement Hamani, MD, PhD,¹
Mary Pat McAndrews, PhD,² Melanie Cohn, PhD,²
Michael Oh, MD,¹ Dominik Zumsteg, MD,³
Colin M. Shapiro, MD, PhD, FRCPC,⁴
Richard A. Wennberg, MD, FRCPC,³
and Andres M. Lozano, MD, PhD, FRCSC¹

Bilateral hypothalamic deep brain stimulation was performed to treat a patient with morbid obesity. We observed, quite unexpectedly, that stimulation evoked detailed autobiographical memories. Associative memory tasks conducted in a double-blinded “on” versus “off” manner demonstrated that stimulation increased recollection but not familiarity-based recognition, indicating a functional engagement of the hippocampus. Electroencephalographic source localization showed that hypothalamic deep brain stimulation drove activity in mesial temporal lobe structures. This shows that hypothalamic stimulation in this patient modulates limbic activity and improves certain memory functions.

Ann Neurol 2008;63:119–123

Case report: Treatment of obesity led to memory enhancement

A Phase I Trial of Deep Brain Stimulation of Memory Circuits in Alzheimer's Disease

Adrian W. Laxton, MD,¹ David F. Tang-Wai, MDCM, FRCPC,^{2,5} Mary Pat McAndrews, PhD,³
Dominik Zumsteg, MD,⁴ Richard Wennberg, MD, FRCPC,⁵ Ron Keren, MD, FRCPC,²
John Wherrett, MD, FRCPC,^{2,5} Gary Naglie, MD, FRCPC,² Clement Hamani, MD, PhD,²
Gwenn S. Smith, PhD,⁶ and Andres M. Lozano, MD, PhD, FRCSC¹

Objective: Alzheimer disease (AD) is characterized by functional impairment in the neural elements and circuits underlying cognitive and memory functions. We hypothesized that fornix/hypothalamus deep brain stimulation (DBS) could modulate neurophysiological activity in these pathological circuits and possibly produce clinical benefits.

Methods: We conducted a phase I trial in 6 patients with mild AD receiving ongoing medication treatment. Patients received continuous stimulation for 12 months. Three main lines of investigation were pursued including: (1) mapping the brain areas whose physiological function was modulated by stimulation using standardized low-resolution electromagnetic tomography, (2) assessing whether DBS could correct the regional alterations in cerebral glucose metabolism in AD using positron emission tomography (PET), and 3) measuring the effects of DBS on cognitive function over time using clinical scales and instruments.

Results: DBS drove neural activity in the memory circuit, including the entorhinal, and hippocampal areas and activated the brain's default mode network. PET scans showed an early and striking reversal of the impaired glucose utilization in the temporal and parietal lobes that was maintained after 12 months of continuous stimulation. Evaluation of the Alzheimer's Disease Assessment Scale cognitive subscale and the Mini Mental State Examination suggested possible improvements and/or slowing in the rate of cognitive decline at 6 and 12 months in some patients. There were no serious adverse events.

Interpretation: There is an urgent need for novel therapeutic approaches for AD. Modulating pathological brain activity in this illness with DBS merits further investigation.

Deep Brain Stimulation and Human Enhancement: future prospect

?!
