

Antidepressant-like effects of Deep Brain Stimulation in rats and the hypothalamic, pituitary, adrenal axis

Luciene Covolan



Clement Hamani



Steps in the search for ideal treatment to neurological dis

- ✓ Conventional drugs
- ✓ Surgical treatment
- ✓ Deep Brain Stimulation (DBS)



Innovation:

DBS at present represents a promising alternative for patients with major depression who are refractory to other treatments. Though initial clinical trials have been extremely encouraging, numerous fundamental questions remain unanswered.

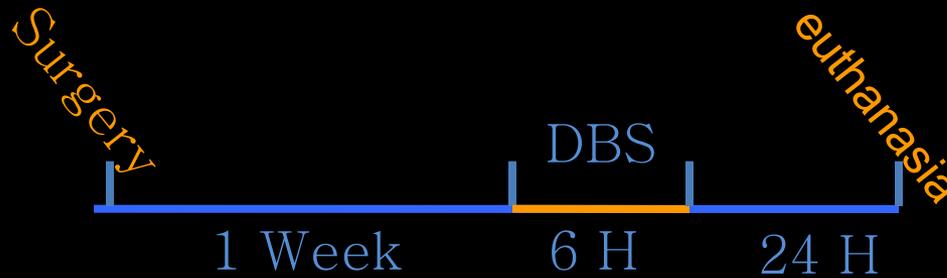
We aim to model an existing, clinical intervention in order to help perfect it by gaining insight into its possible underlying mechanism of effectiveness.

We will assess whether chronic vmPFC DBS normalizes stress-induced HPA axis changes that are often deleterious from a health perspective. Chronic stress is associated with a higher incidence of cardiovascular diseases, reduced immunologic resistance and disruption of brain plasticity .

If DBS is shown to reverse stress-induced HPA changes, it may, at long-term, comprise an important strategy to improve some of the deleterious consequences of chronic stress.

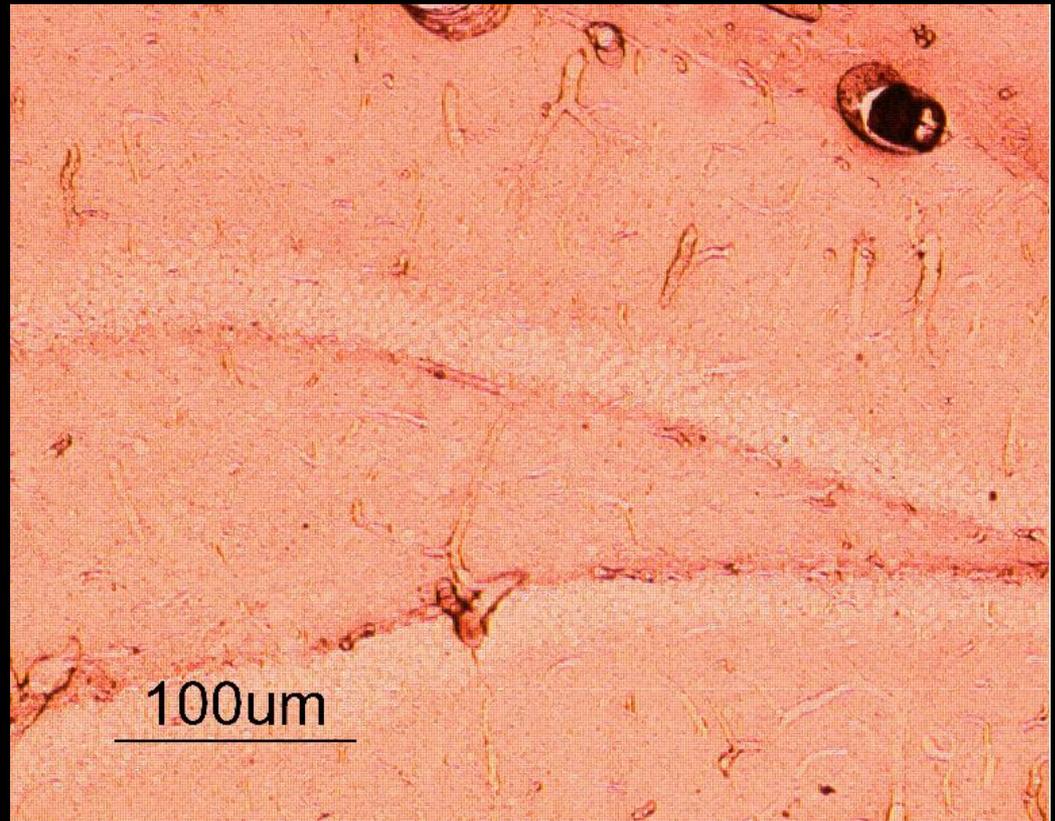
Does DBS cause cell injury?

Dark Cell



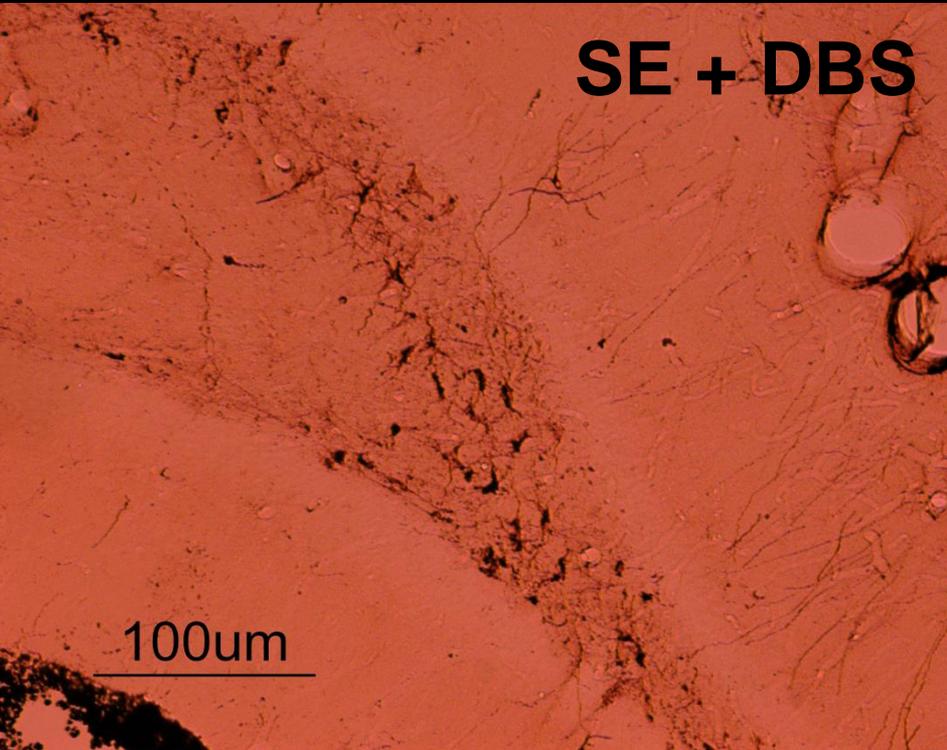
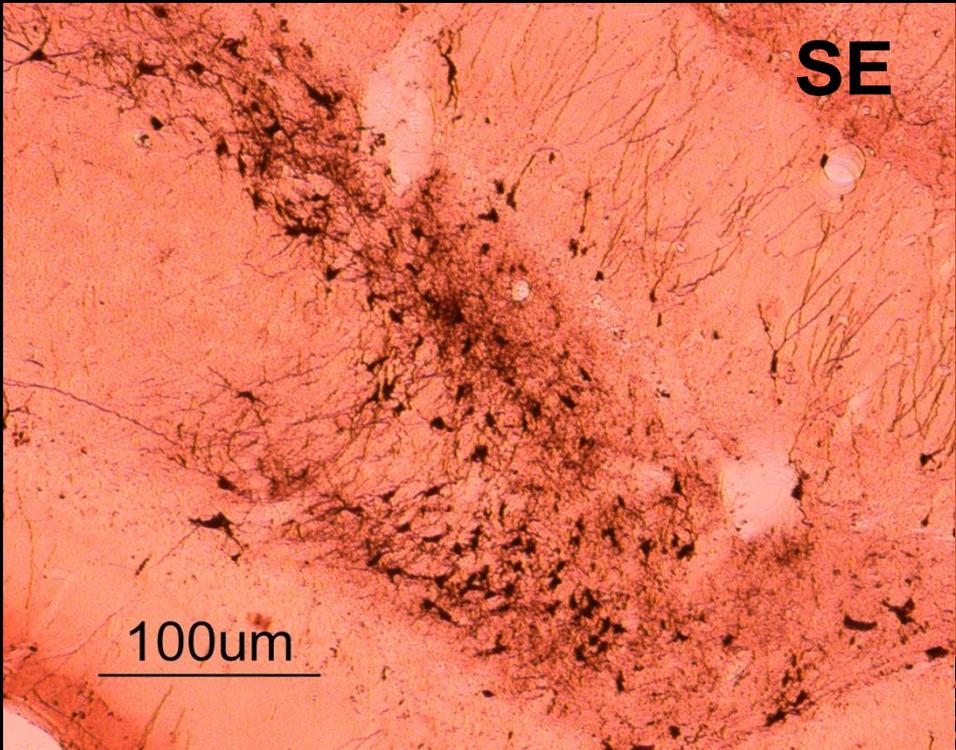
(St Jude Medical, TX)

DBS:
500 μ A
90 μ s
130 Hz



Dark Cell

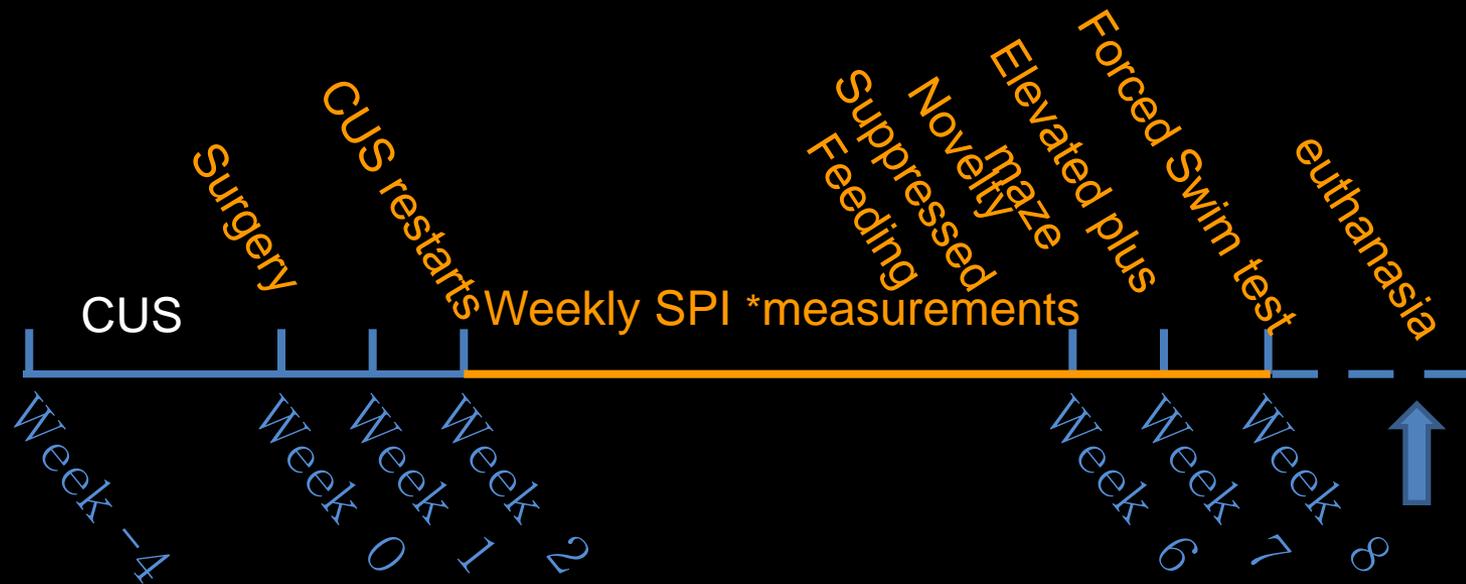
DBS is able to reduce neuronal injury induced by response to status epilepticus?



Experimental Hypothesis

- ✓ DBS will improve a series of tests to measure depressive- and anxiety-like behavioral in animals undergoing CUS ;
- ✓ DBS will reverse stress-induced changes in the hypothalamic-pituitary adrenal (HPA) axis.

Time frame for experimental procedures



Non stressed Sham (n=15)
Non stressed DBS (n=15)
Non stressed Controls (n=15)
Stressed Sham (n=15)
Stressed DBS (n=15)

✓ Brains processed for in situ hybridization
✓ Blood samples assayed for corticosterone

* Sucrose preference index

Investigators

Luciene Covolan

Clement Hamani

Deborah Suchecki

Jose N. Nobrega

Debora Hipolide

PhD students

Proposed collaboration (2012):

Prof. Covolan: UNIFESP

- ✓ Is conducting the chronic mild unpredictable stress experiments in São
- ✓ Came to Toronto to teach it to Dr. Hamani's research team (September 20

Dr. Hamani; University of Toronto

- ✓ Is conducting the chronic mild stress model experiments in Toronto
- ✓ Is going to São Paulo to conduct/supervise DBS procedures to Dr. Covolan's research team (November 2012)

Proposed collaboration (2013):

UNIFESP

- ✓ CUS procedures
- ✓ DBS procedures
- ✓ behavioral tests

University of Toronto

- ✓ PhD students from UNIFESP will visit the UT to learn and conduct in situ hybridization and autoradiographic techniques
- ✓ in situ hybridization analyses
- ✓ the PhD student will give seminar to show her own results

Expected gains

- ✓ Strengthen the already established collaborative effort between two researchers teams
- ✓ Generate novel and important data to be published in high impact journals
- ✓ Open various lines of research on the mechanisms and effects of DBS
- ✓ Get additional fundings from FAPESP and University of Toronto (and other research funding agencies)
- ✓ Bring benefits to both Universities and PhD programs