Recording and Stimulation of the Pathologic Brain Cavity Wall in a Rat Model for Thalamic Syndrome

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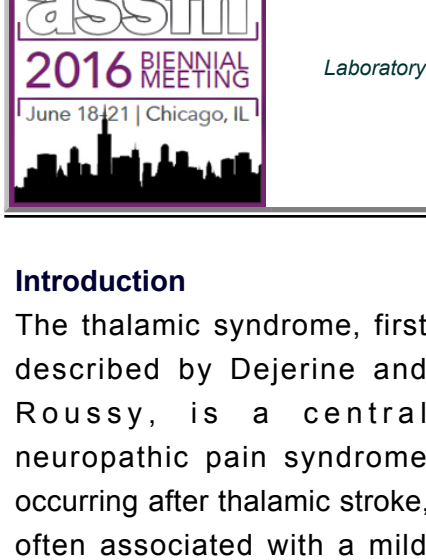
Introduction

The thalamic syndrome, first described by Dejerine and Roussy, is a central neuropathic pain syndrome occurring after thalamic stroke, often associated with a mild paresis. It is a form of central post-stroke pain. Treatment is challenging and often not satisfying.

We propose a novel treatment, based on electrical stimulation of the brain cavity wall to reduce its associated symptoms (fig.1).

Fig.1: General hypothesis.

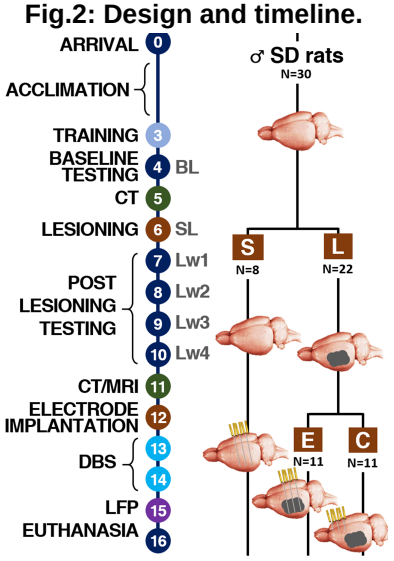


We hypothesize that brain cavities affect brain circuitry, hereby causing symptoms, that can be alleviated by electrical stimulation of the brain cavity wall, anatomically steered by electrical and metabolic characterization.

Methods

30 rats were tested for thermal and mechanical pain and motor performance, and were then randomly allocated into a lesion group (L; electrolytic thalamic lesioning; n=22) and a sham group (S; sham surgery; n=8). Pain and motor tests were repeated weekly over the next 4 weeks (fig.2).

Fig.2: Design and timeline.

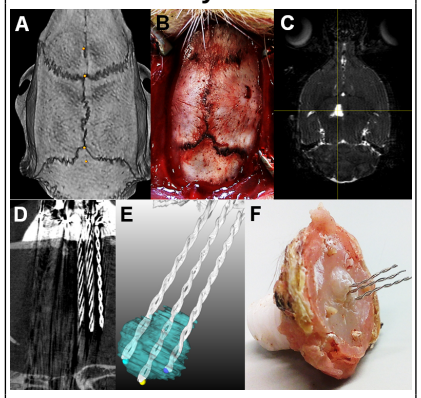


Time is shown in weeks (w).

Next, after CT and MR imaging (fig.3), 3 bipolar electrodes were implanted. L was randomly divided into a cavity wall electrode group (E; electrodes aiming for the ventral cavity wall; n=11) and a random electrode group (C; electrodes aiming for a random brain target not related to motor or pain behavior; n=11). In S, electrodes were implanted at the same coordinates as in W.

Motor tests were then repeated during deep brain stimulation (DBS; biphasic, 130Hz, 200µs at 0%-50%-75%-100% of the highest tolerated amplitude (HTA; amplitude above which side effects are observed)). Finally, local field potentials (LFPs) were recorded in resting state.

Fig.3: Implanting and localizing electrodes lining the brain cavity wall.

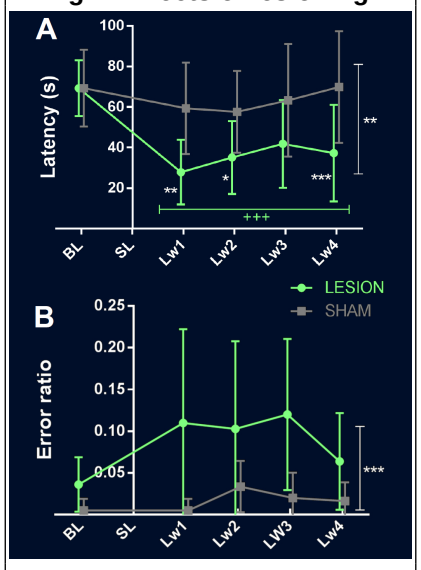


(A) CT to plan surgery, (B) with a good intra-operative correlation. (C) Pre-implantation surgery MR demonstrating the cavity. (D) Post-implantation CT showing the electrodes. (E) MR-CT fusion showing the electrode tips with respect to the cavity wall. (F) Head stage after removal, showing the 3 twisted bipolar electrodes.

Results

After but not before lesioning, motor scores were significantly (P<.05) worse in L vs. S, while pain scores did not differ (fig.4). In C, DBS at 50%, 75% or 100% HTA did not improve motor scores significantly as compared to 0% HTA in W or to DBS in C or S (fig.5).

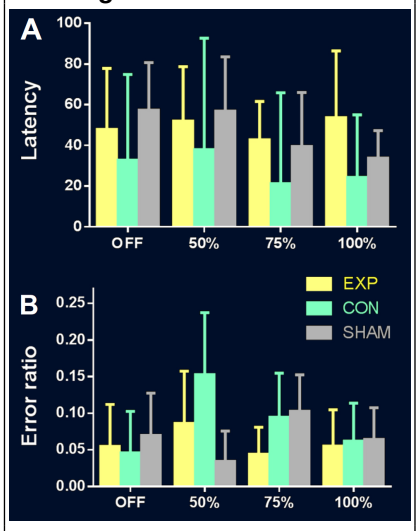
Fig.4: Effects of lesioning.



(A) Rotarod. Average latency ± SD. *: significant difference between left and right, +: significant difference from baseline. (B) Ladder rung walking test. Mean error ratios per paw ± SD. *: significant difference between groups, +: significant difference from baseline. */+:P<0.05; **/++:P<0.01; ***/+++:P<0.001.

LFPs recorded from the same anatomical locations differed significantly between E and S groups.

Fig.5: Effects of DBS.



(A) Rotarod. Average latency ± SD. (B) Ladder rung walking test. Mean error ratios per paw ± SD. % of HTA (highest tolerated amplitude).

Conclusions

In a thalamic syndrome rat model with motor deficits but no mechanical or thermal hyperalgesia, the tested DBS parameters did not alleviate the symptoms.