Subthalamic Nucleus Deep Brain Stimulation Combined with Duloxetine Changes Pain Behavior in Parkinsonian Rats

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Introduction

Chronic pain is the most common non-motor symptom in Parkinson's disease (PD) and is undertreated in half of PD pain cases (1). Subthalamic nucleus deep brain stimulation (STN DBS) relieves PD pain temporarily. To optimize STN DBS, we have combined it with duloxetine and shown increased mechanical thresholds indicative of antinociception in the hemiparkinsonian 6-hydroxydopamine (6OHDA) lesion rat model (2). In this study, we advance from investigating STN DBS-duloxetine's effects on nociception to quantifying its effects on pain-related behavior in the place escape/avoidance paradigm (PEAP).

Methods

Male seven-week-old Sprague-Dawley parkinsonian rats were treated with STN DBS, duloxetine, or STN DBS-duloxetine. Rats underwent PEAP testing before and after treatment in a chamber consisting of a bright and dark side that were both easily accessible. When rats spent time in the dark side, they were poked with a suprathreshold (60.0 g) von Frey filament on their left/parkinsonian neuropathy-affected hind paw; in the bright side, rats were poked on their right/non-parkinsonian hind paw.

Results

Percent decrease in bright side time was significantly greater after STN DBS-duloxetine than after STN DBS ($p=0.031$) and duloxetine alone ($p=0.036$). STN DBS-duloxetine decreased bright side time by 32.82 ± 7.62% (n=4), while STN DBS (4.17 ± 11.55%, n=4) and duloxetine (1.22 ± 10.61%, n=5) caused minimal percent bright time changes. Therefore, STN DBS-duloxetine reduced pain-related behavior significantly more than STN DBS and duloxetine alone.

Conclusions

Our project presents STN DBS-duloxetine as a new treatment for PD pain. Because escape/avoidance behavior has been associated with the anterior cingulate cortex (ACC) (3), STN DBS-duloxetine's mechanism may involve altering ACC neuronal activity in the descending inhibitory pain pathway.

Learning Objectives

1) Understand that chronic pain is a prevalent PD non-motor symptom that needs new effective therapies.

2) Describe, in small groups, how to quantify pain-related behavior using the PEAP test.

3) Identify STN DBS-duloxetine as a potential new effective treatment for PD pain.

References

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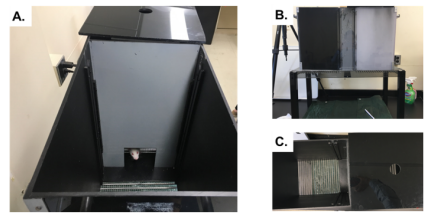
(3) Uhelski ML, Morris-Bobzean SA, Dennis TS, Perrotti LI, Fuchs PN. Evaluating underlying neuronal activity associated with escape/avoidance behavior in response to noxious stimulation in adult rats. Brain Res. 2012;1433:56-61. doi: 10.1016/j.brainres.2011.11.016. PubMed PMID: 22137659.

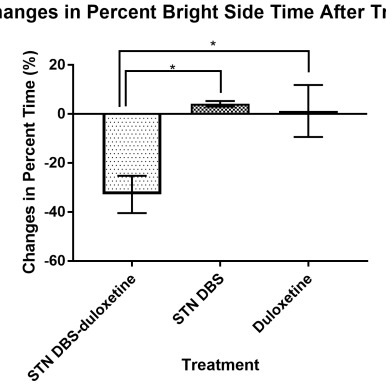
Place Escape/Avoidance Paradigm Test Chamber



PEAP chamber (A) during a test session, (B) from a lateral view, and (C) from a superior view.

Place escape/avoidance paradigm (PEAP) test chamber (A) during a test session, (B) from a lateral view, and (C) from a superior view.

Graph of Changes in Percent Bright Side Time After Treatment



Decreases in percent time spent in the bright side after STN DBS-duloxetine treatment were significantly greater than after STN DBS or duloxetine alone in parkinsonian rats.