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STN-DBS does not change emotion recognition in Parkinson´s disease

Luisa Albuquerque, MD Miguel Coelho, MD Maurício Martins, MD Isabel Pavão Martins, MD,PhD

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All authors and their affiliations:

Luisa Albuquerque,MD [a]

Miguel Coelho,MD [b]

Maurício Martins,MD[a]

Isabel Pavão Martins,MD,PhD [ab]

[a] Language Research Laboratory, University of Lisbon, and Department of Clinical Neurosciences, Santa Maria Hospital, Lisbon, Portugal

[b] Institute of Molecular Medicine and Faculty of Medicine, University of Lisbon, and Department of Clinical Neurosciences, Santa Maria Hospital, Lisbon, Portugal

Corresponding author:

Laboratório de Estudos de Linguagem, Faculdade de Medicina de Lisboa, Hospital de Santa Maria, 1649-028 Lisboa, Portugal.
Tel.: + 351 217934480.
E-mail addresses: lalbuquerque@hospitaldaluz.pt, malbuquerque@fm.ul.pt

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Dear Sirs

We appreciate Péron´s concerns about our study [1], and are glad for this opportunity to clarify the following issues.

First, concerning the literature mentioned in our paper, and as it is shown in the Table below, we note that previous studies have a) a short duration of follow-up or a wide variation in follow-up time across patients, and b) some compared different groups of patients pre and post-operatively. Thus a lack of prospective and systematic follow-up studies justifies the present research. Those methodological problems also render any lack of correlations doubtful, and we expressed this doubt as "…potentially related to behavioral correlates".

Secondly, we totally disagree with the comments pointed out by Péron regarding the efficacy of STN-DBS in these patients. As Table 1 in our paper discloses [1], a decrement in the levodopa equivalents daily dose from 1148 mg to 425 mg is a clear-cut indication of the outcome of the motor benefit of the surgery. The aim to report the score of the UPDRS part III in the "medication on pre-DBS" and "stimulation on / medication on" was to show that the patients performed the neuropsychological evaluation in very similar motor states.

The most important variable to assess the efficacy of DBS is the comparison of the UPDRS motor score between the 2 conditions "stimulation off / medication off" and "stimulation on / medication off" and not the comparison of the UPDRS motor score between "medication on pre-DBS" versus "stimulation on / medication on post-DBS" nor the difference of the Hoehn and Yahr score between the "medication on pre-DBS" and "stimulation on / medication on post-DBS" conditions. The difference in the UPDRS motor score of these patients between the conditions "stimulation off / medication off" and "stimulation on / medication off" was 51.5% (data not shown), which means a large effect size. Moreover, the patients had a benefit of 50% in the UPDRS part II (ADL) after DBS and a benefit of 63% in the UPDRS part IV (data not shown). Additionally, there was a decrease of 58.6% in the score of the Modified AIMS scale, which rates the severity of dyskinesias, between the conditions "medication on pre-DBS" and "stimulation on / medication on" (data not shown). Furthermore, according to patients´ diaries of motor complications, there was a 70% reduction in the duration of the off state after DBS (data not shown). These

figures attest the very correct position of the DBS leads. These data were not reported in the paper because that was not its focus.

Finally, regarding the methodology that we used in our study, Péron raises the question of whether our tasks were sensitive enough to capture differences between PD pre-op and post-op groups. On the one hand, Péron argues, this lack of sensitivity could be due to the number of stimuli used, and on the other hand to the use of categorical tasks instead of more sensitive continuous scales.

Regarding the first point, we acknowledge that the low number of stimuli (22 for emotional faces and 18 for emotional prosody) may be associated with a lower sensitivity than tasks using a higher number of stimuli. However it is not true that these tasks are insufficient to capture variability within and between normal and clinical populations. For instance, the visual task used in our study was sensitive enough to capture effects of education within healthy controls [2] and differences between normal participants and schizophrenia patients (mean difference = 10%) [3].

On the second point, Péron concedes that the lack of difference reported in our study may have not been due to the number of stimuli *per se* but to the use of categorical tasks instead of continuous scales. In an interesting study by Péron [4], PD patients were tested with 60 emotional prosody stimuli, which they were asked to categorize. This task failed to show differences between pre- and post-op patients despite using a higher number of stimuli than in our study.

In Peron et al., patients were also tested with continuous scales. They were asked to rate emotional stimuli, for instance ‘Fear’ stimuli, according to their intensity in 6 continuous emotional scales (‘Fear’, ‘Happiness’, ’Surprise’, ’Anger’, ’Neutral’, ‘Sadness’). A response was deemed correct when subjects rated the ‘target’ scale (e.g. the ‘Fear’ scale when the stimulus was ‘Fear’) higher than all the other scales. Using continuous scales, Perón et al. found interesting differences between pre- and post-op groups. For instance, pos-op patients were more likely than pre-op patients to give nontarget ratings to ‘Happiness’, ‘Fear’, and ‘Sadness’. For example, they gave higher ‘Happiness’ ratings to ‘Fear’ stimuli. From these results, Péron et al. concluded that post-op patients were impaired in emotion recognition. However, in the same study, post-op patients also gave higher target ratings than pre-op patients, i.e., they

rated ‘Fear’ *more* intensely in the ‘Fear’ scale, ‘Anger’ *more* intensely in the ‘Anger’ scale, and ‘Sadness’ *more* intensely in the ‘Sadness’ scale. The most parsimonious explanation to these results is that post-op patients give in general higher ratings than pre-op patients (14.5 vs. 10 mean rating per scale per stimulus) in both target and nontarget scales. Thus, although PD pre-op and post-op groups seem to have different patterns of response, it is at minimum arguable whether this study provides strong proof that post-op patients are impaired relative to pre-op in identifying emotions.

From this discussion we thus consider that it is difficult to sustain that our results are due to lack of sensitivity alone. It is clear that different methods tap into different aspects of emotional processing, rather than simply one being more sensitive than the other. However, we are sympathetic with the concern that experimental results and interpretations might be critically influenced by the particular method and analyses employed. For instance, it is possible that post-op patients have a tendency to perceive emotional traits as more intense than pre-op patients, but that these differences do not necessarily lead to categorization errors. If this were the case, then would need to inquire whether the perception of emotional intensity is a better marker of daily life socio-affective impairment than emotional categorization *per se*.

We propose that future research needs to bind experimental results with clinical and daily life behavioral markers. Only using external validation can we assess whether certain statistical effects (or lack of effects) are artifacts of particular experimental procedures and analyses, or whether they tap into impairments relevant to socio-affective decision-making, and if yes, which.

Luisa Albuquerque MD [ab], Miguel Coelho MD [b], Mauricio Martins MD [a], Isabel Pavão Martins MD, PhD [ab]

[a] Language Research Laboratory, University of Lisbon, and Department of Clinical Neurosciences, Santa Maria Hospital, Lisbon, Portugal

[b] Institute of Molecular Medicine and Faculty of Medicine, University of Lisbon, and Department of Clinical Neurosciences, Santa Maria Hospital, Lisbon, Portugal

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Table – Comparison of studies on emotional recognition after STN-DBS for APD

Article	PD patients (n)	Study design	Post-op F-up(months)
Dujardin et al	12	EF, DBS *on*	3
Schroder et al	10	EF, DBS *on* vs *off*	3 to 24
Biseul et al	15	EF, independent groups pre vs post-op	1 to 48
Péron et al	24	EF, DBS *on* vs apomorphine vs C	3
Péron et al	21	EP, independent groups pre vs post-op vs C	3 to 72
Albuquerque et al	30	EF and EP, prospective pre vs post-op	12 in all patients

APD-advanced Parkinson disease, STN-DBS-subthalamic nucleus deep-brain stimulation, F-up-follow-up, EF–emotional faces, EP–emotional prosody, C-healthy controls.