Clinical Neurophysiology 130 (2019) 877–878

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Letter to the Editor

Disease-specific patterns of basal ganglia neuronal activity in Neurodegeneration with Brain Iron Accumulation type I (NBIA-1)

We read with interest the paper by Huebl et al. (2019) on subthalamic and pallidal oscillatory activity in six patients with Neurodegeneration with Brain Iron Accumulation type I (NBIA-1). NBIA-1 is one of the most distressing dystonic disorders and we welcome further research aiming to better understand its underlying pathophysiology.

As the authors state, intracranial recordings from patients with "dystonia-plus" syndromes are rare. We have previously published intra-operative single cell and multi-unit neuronal recordings from the Globus pallidus internus (GPi) and externus (GPe) in eight young people with NBIA-1 as part of a larger cohort of 44 children with dystonia undergoing Deep Brain Stimulation (DBS) (McClelland et al., 2016). A novel finding in our study was that although GPi neuronal firing frequencies were generally low across the cohort as a whole, the mean firing frequency in NBIA-1 patients was significantly higher than in isolated idiopathic/genetic or acquired (non-degenerative) dystonia. Although we did not record local field potentials (LFPs) in our study, GPi LFPs are likely to reflect, at least in part, GPi neuronal discharge (Chen et al., 2006). Thus Huebl and colleagues' observation in patients with NBIA-1 of prominent LFPs in not only the low frequency (7–12 Hz) range, as seen in isolated idiopathic dystonia, but also in the beta range (15–30 Hz), is in alignment with our findings. Interestingly, Huebl et al. identified low frequency and beta LFP peaks in patients with either GPi or subthalamic nucleus (STN) DBS.

The observation of distinct physiological patterns in NBIA-1 is also supported by functional imaging studies: resting state positron emission tomography scans with 2-deoxy-2-[fluorine 18]fluoro-D-glucose integrated with CT, have demonstrated higher metabolic activity in the posterior putamen in NBIA-1 compared with primary dystonia (Szyszko et al., 2015).

NBIA-1 is a mixed motor disorder with elements of dystonia and Parkinsonism. We interpreted the higher GPi firing rates observed in NBIA-1 as being in keeping with the higher GPi firing rates observed in adults with Parkinson's disease compared with dystonia (McClelland et al., 2016). Huebl et al.'s study provides further evidence that the physiological patterns seen in NBIA-1 reflect the phenotypic features seen. As they point out, prominent synchronized beta activity in the basal ganglia is well recognized in Parkinson's disease and has been noted to relate to severity of bradykinesia in these patients, including during chronic STN stimulation (Neumann et al., 2017). The prominent basal ganglia beta LFP peaks observed in Huebl et al.'s study may therefore reflect the parkinsonian elements of NBIA-1. In particular, their observation that the patient with most severe bradykinesia showed the most prominent beta band activity supports this hypothesis.

In addition to differences in firing frequency, the NBIA-1 patients in our study showed a much higher proportion of regularly firing cells compared with the prominent irregular or bursting activity observed in isolated genetic/idiopathic or acquired dystonia groups (McClelland et al., 2016) or in Parkinson's disease. This observation, along with the findings of Huebl et al., provides evidence for disease-specific patterns of neuronal activity in NBIA-1.

In summary, we welcome Huebl et al.'s study and wish to raise awareness of the plight of this group of patients, who often show at least a temporary response to DBS before the inevitable decline related to the neurodegenerative process. Continued research to further delineate the pathophysiological similarities and differences between different dystonic disorders is essential if we are to optimize outcomes for the growing range of movement disorders that may potentially benefit from neuromodulation.

Acknowledgments

Verity McClelland has received support from an NIHR Academic Clinical Lectureship and an Academy of Medical Sciences Starter Grant for Clinical Lecturers and is currently supported by a Medical Research Council, United Kingdom. Post-doctoral Clinical Research Training Fellowship (MR/P006868/1).

Daniel Lumsden has received support from the Dystonia Society UK Grants 01/2011 and 07/2013 and Action Medical Research GN2097.

Jean-Pierre Lin has received grants from the Guy's and St Thomas' Charity G060708; the Dystonia Society UK Grant 01/2011 and 07/2013 and Action Medical Research GN2097.

Competing interests

Jean-Pierre Lin has received educational support and consultancy fees from Medtronic Ltd.

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https://doi.org/10.1016/j.clinph.2019.03.005

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Available online 26 March 2019