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Somatotopic organization of STN and DBS implications in Parkinson's disease - A case report of a woman "halved" by DBS stimulation

The anatomy and functional connections of basal ganglia have been extensively studied in humans and primates [1]. In particular, it is known that the subthalamus nucleus (STN) has neurons inserted in parallel and segregated circuits wiring connections among limbic, associative, and motor systems both in the cortex and the basal ganglia [2]. In the STN, neurons involved in motor control are placed in its dorsolateral region and present a somatotopic distribution, which is maintained in the afferences from the cortex and in the projections towards other structures of the basal ganglia [3].

The use of Deep Brain Stimulation (DBS) for the treatment of movement disorders is now a common practice, and the STN is notably targeted for motor modulation in Parkinson's Disease (PD) [4].

Here we report about the case of a female patient affected by idiopathic PD since the age of 56 with right-side rigid-akinetic motor symptoms. After 11 years of disease progression, due to shortening of the therapeutic window and difficult tolerance to dopaminergic treatments, we decided to candidate her for bilateral STN-DBS. In accordance with our practice, the STN was targeted by merging MRI with frame-CT brain scans. Moreover, we used microelectrode recording (MER) with three tracks to better map out the target nucleus and identify ideal lead placement during surgery. Intraoperative electrophysiological recording confirmed that both the electrodes were properly sited in the STN; the post-surgery brain images (both CT and MRI scans) also documented that the tip of both leads were correctly positioned in the subthalamic region bilaterally. After the DBS intervention, the best contacts activated resulted at the second most dorsal area of the STN in both hemispheres. Within few days after the Internal Pulse Generator (IPG) activation, the motor response in the upper limbs was optimal, while tremors and slight hypertonia were observed in the lower limbs, predominant in the right side; moreover, dyskinetic movements appeared in the neck and lower face. Decreasing dopaminergic drugs, while increasing intensity of stimulation was detrimental on this pattern of symptoms; activation of the most dorsal contacts resulted in worsening of dyskinesias in the upper parts of the body. We then changed stimulation strategy by activating the second most ventral contact bilaterally obtaining a better result in motor control of the lower limbs, but not of the upper limbs and face; the same occurred by activating the most ventral contacts in both hemispheres. We finally configured a bipolar and asymmetric modality of stimulation: between the two most cranial contacts in the left hemisphere, and between the two most ventral contacts in the right hemisphere. This scheme resulted as the less harmful for the patient, even though the discordance between the upper and lower part of the body continued and a clear difference in motor control between the lower limbs and the upper limbs and face persisted.

In our clinical practice, we regularly treat PD patients who undergo brain surgery for DBS stimulation; when we regulate the parameters of stimulation soon after DBS implant, our choice as to which contact to activate and which parameters to regulate are usually guided not only by the findings of intraoperative MER, but also by the knowledge of the anatomo-functional distribution of STN cells and their somatotopic organization. Nevertheless, the ineffectual results of DBS modulation in this patient seemed not to respect the physiological somatotopic organization of the STN, in which limbs representation is located along the dorsolateral two-thirds of the nucleus, where descending fibers from the primary motor cortex enter the STN [5]: the leg-related neurons being located ventromedially, the arm-related neurons more laterally, and the oromandibular musculature in the middle of the sensorimotor region, more ventrally respect to the limbs representation [6,7] [Fig. 1a]. Based on the clinical responses to the STN-DBS stimulation we observed and considering the different contacts activated at different depths and with different patterns of stimulation, we speculate that this patient may carry an anatomical variation of neuron distribution within the STN; in particular as if the somatotopic representation of her "homunculus" were doubled-over, with legs representation well deeper than the arms [Fig. 1c].

To our knowledge, this is the first and unique report of such a "side effect" of STN-DBS. If our hypothesis is true, we wonder if the common routine utilized in the majority of DBS-centers – i.e. targeting and most importantly measuring the functional distribution of the cells within the STN by MER - is the best practice to be followed or whether we should consider a more accurate examination, by testing both proximal and distal joints of all four limbs while stimulating at different depths during lead positioning. In fact, considering that limbs are physiologically represented on the same layer on the STN [6,7], we usually test the motor response

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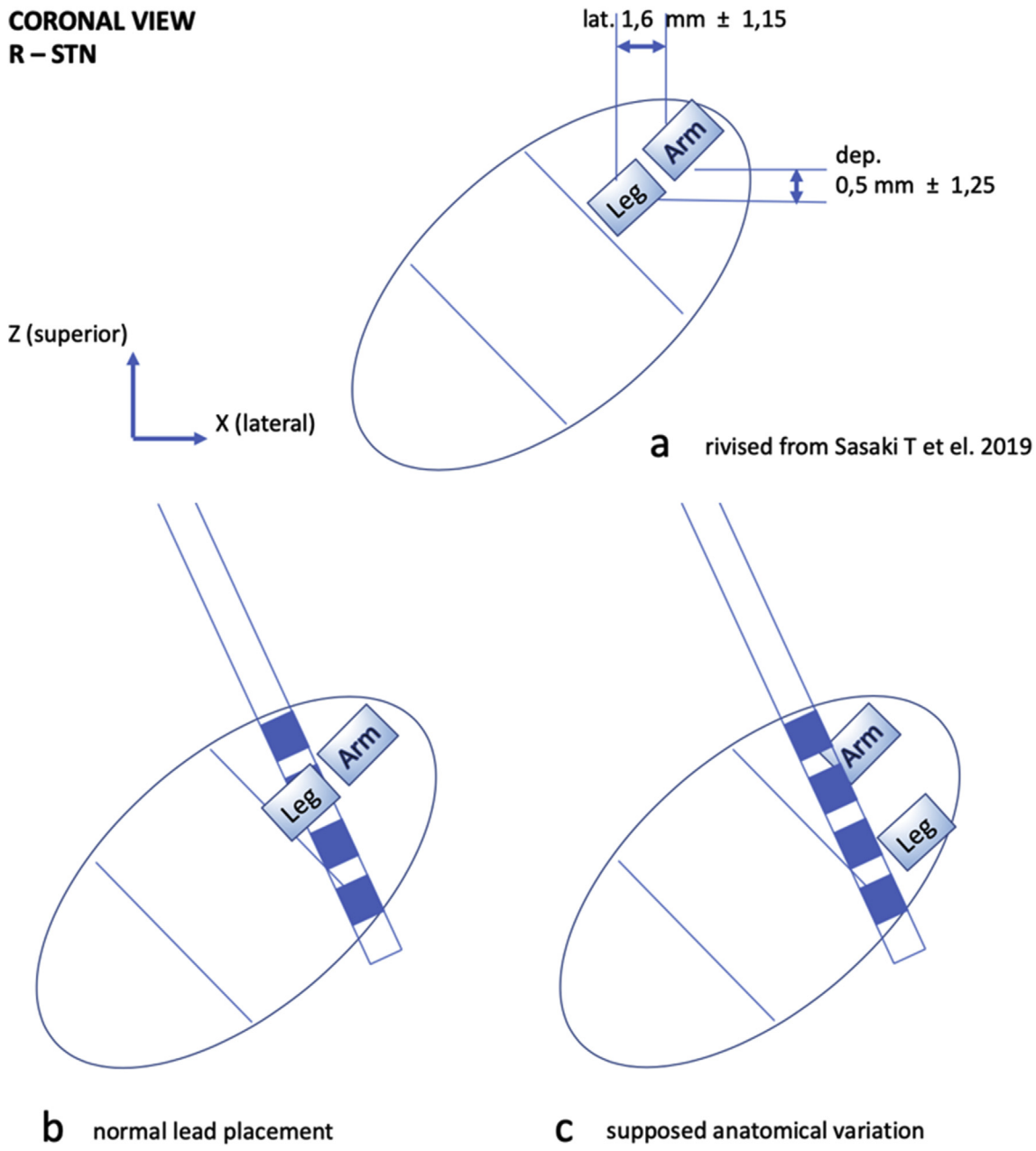

Fig. 1. Graphical representation of the coronal view of the right STN.
a) Revised from Sasaki T et al. 2019 – the average distances between upper and lower limbs in depth (dep) and in laterality (lat) are reported.
b) Usual placement of electrode-catheter in the dorsolateral STN.
c) Supposed "doubled-over" anatomical variation.

only in the upper limbs, assuming that the response would be the same in the lower limbs as well. On the other hand this more detailed examination would lengthen surgical time. Even if it may not be worth to carry out such a detailed examination routinely, we hope that the description of our case will be useful for other DBS professionals facing similar unusual response in their clinical practice.

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