Targeting human PPN: few patients, numerous disputes

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Sir, Dr Yelnik highlights an important issue, already extensively addressed (consider Mazzone et al., 2007a,b in response to Zrinzo and co-authors). Briefly, there is no doubt that some figures were misleading (Stefani et al., 2007). In describing our original approach to the first six Parkinson’s disease (PD) patients double-implanted in the subthalamic nucleus (STN) plus the pedunculopontine nucleus (PPN), we have emphasized the trajectory through the nucleus peripeduncularis (Ppd) instead of the final target area. Nevertheless, as clarified by sagittal CT-scan projections (Stefani et al., 2007; Mazzone et al., 2007a), the distal leads are positioned well below the ponto-mesencephalic line and the catheter tip lies into the nucleus tegmenti peduncolo-pontinus (Tg.pd.po) (Shaltenbrand and Wahren, 1977), hence stimulating a functional sub-region attributable to PPN. The surgical trajectory (from lateral to medial) was chosen via Ppd in order to minimize surgical risks, otherwise difficult to estimate if a more medial trajectory through the sub-rubral portion of the substantia nigra (and in close proximity to the IV cranial nerve) had been performed. The utilized coordinates (for instance $z \geq 13$) support further the notion that the lemniscus medialis was crossed and the Tg.pd.po reached (Mazzone et al., 2007b).

Several evidence should compose public health concerns. At first, intra-operatory Local Field Potentials are recorded to assess the catheter advancement to PPN (Mazzone et al., 2007b); second, post-surgery investigations show that low-frequency PPN stimulation modulates the Hoffmann reflex threshold; third, best clinical response are observed when 25 Hz stimulation is delivered, mostly in bipolar modality (0–1/4–5), through the distal contacts embedded inside the pons of Varolio (Stefani et al., 2007). Thus, the a-specific involvement of griseum other than PPN is unlikely, although the size of the present devices impedes to exclude aprioristically some degree of current spread to adjacent structures.

In conclusion, we would like to stress that, despite the abundant literature on mammalian PPN, nobody knows the best target, yet, in humans. Our pioneering studies should encourage, and not halt, further investigations in non-human primates and in larger cohorts of PD patients.

References