Response: Therapeutic brain-responsive neurostimulation in eloquent cortex can be delivered without symptoms

To the Editors:

We would like to thank van Blooijs et al. for the opportunity to clarify our conclusion that responsive stimulation in eloquent areas does not produce involuntary motor activity or decreased motor performance when stimulation involves the primary motor cortex.

We agree that stimulation of primary motor cortex can produce involuntary movements when delivered at settings required for intracranial mapping and that this is the basis of the use of stimulation in intra- and extraoperative mapping.[1,2] We would like to clarify that the patients participating in the RNS System trials received test stimulations during in-office programming visits. If involuntary movements or other responses were elicited during testing, the stimulation parameters including the current amplitude were adjusted until the responses were no longer produced. As reported in Jobst et al.,[3] there were no adverse events related to the stimulation of eloquent cortex at the stimulation settings delivered to the patients outside of the clinic. Thus, we stand by our conclusion that therapeutic stimulation of eloquent cortex can be delivered below thresholds for producing stimulation-related adverse events.

With respect to the potential for stimulation to interfere with performance, the RNS System Pivotal trial (n = 191) included comprehensive neuropsychological assessments. These assessments were performed during a preimplant baseline, at the end of the blinded evaluation period (BEP), and at year 1 and year 2 postimplant. The neuropsychological assessments included assessments of motor performance. As reported in Morrell et al.,[4] there was no deterioration in any neuropsychological measure at the end of the BEP or at 1 or 2-years after implantation and treatment with responsive stimulation.

It is important to remember that the RNS System provides responsive or closed-loop stimulation and not continuous stimulation. As a result, patients are generally receiving <10 min of stimulation per day and the stimulation is typically delivered in brief 100-ms bursts of bipolar stimulation throughout the day. These 100-ms bursts are considerably shorter than the bipolar stimulation often used to elicit motor responses (e.g., 2–4 s) during mapping. In addition, the stimulation is only being delivered when abnormal activity is detected. Thus, we hypothesize that responsive stimulation is less likely to interfere with normal brain function and performance on tasks than if the stimulation were being delivered continuously or on a duty cycle as is the case with deep brain stimulation[5,6] and continuous focal cortical stimulation.[7–9] This is supported by the observation that poststroke patients receiving >4 h of daily motor cortex stimulation showed decreased motor performance as measured by the Fugl–Meyer Assessment, whereas those receiving <4 h of daily stimulation showed improved performance.[10]

We would like to thank van Blooijs et al. for their interest in our study and for thinking critically about our work. We hope that our clarification helps address their concerns relative to responsive stimulation of the eloquent motor cortex for the treatment of partial onset epilepsy.

Conflict of Interest

T.L.S. and M.J.M. have received support from and/or have served as paid consultants for NeuroPace, including employment and equity ownership/stock options. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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