Stop Signal Reaction Time measured with a portable device validates optimum STN-DBS programming

Aborting an ongoing motor response (response inhibition) is controlled by a complex network, critically involving the hyper-direct pathway from supplementary motor area to the subthalamic nucleus (STN) [1]. Logan and Cowan first described the Stop Signal Reaction Time (SSRT), a measure of stopping efficiency [2]. Since then SSRT has been investigated in various neurological disorders. Parkinson’s disease (PD) patients have deficient response inhibition, which is independent of the severity of bradykinesia [3]. Levodopa and bilateral STN deep brain stimulation (DBS) both improve response inhibition in Parkinson’s patients [4,5].

Recently, our group has developed a portable device to measure reaction time and response inhibition, which is easy to use at the bedside or in the clinic. We have also introduced an improved measure (optimum combination SSRT; ocSSRT) which uses a Bayesian statistical approach to enhance reproducibility [5]. In this pilot study we recruited Parkinson’s patients from our movement disorders clinic, and compared ocSSRT with standard bedside clinical assessments during optimisation of bilateral STN-DBS parameters.

We included 16 patients with STN-DBS (Medtronic Activa stimulators), in whom DBS electrodes had been implanted at least six months prior to optimisation. All patients reported motor complaints with existing programming, and attended clinic to optimise simulation parameters using the N’vision 8840 physician programmer. Measurements of Movement Disorder Society- Unified Parkinson’s disease Rating Scale Part III (MDS–UPDRS III, Motor score for PD patients) and ocSSRT were made three times: with the initial DBS setting (when the patients had motor symptoms), after turning off the DBS and lastly after reprogramming, when both programmer and subject felt that the settings were optimal.

The ocSSRT box has a screen to display instructions and test results. A green and red LED act as the go and stop cues respectively (Fig. 1A). Patients started a trial by pressing and holding a button. They were told to release this quickly if the green LED illuminated (go trial), but to keep the button pressed if the red LED illuminated (stop trial). Responses to 192 trials were recorded (inter-trial interval 1–2.638s), in three blocks of 64 trials separated by a 60 s rest. Within each block, there were 48 go trials and 16 stop trials. The stop trials presented the red LED at four different delays (5–185 ms) after the green LED. The device measured the distribution of reaction times in the go trials, and the proportion of stop trials where a response was produced inappropriately. We assume that on a stop trial, two processes are initiated within the nervous system by the go and stop cues respectively, and that these race to completion. If the go process completes first, an inappropriate response is produced; if the stop process wins the race, the response is successfully inhibited. SSRT is computed from the proportion of inappropriate responses and the distribution of the reaction times in go trials. ocSSRT optimises this calculation using knowledge of the response statistics, as we have previously described [5]. Cohen’s kappa statistic was used to assess the strength of agreement between clinical assessments and reaction times.

As expected, the UPDRS III worsened after turning off DBS and improved significantly after optimising the programming. Similarly, ocSSRT also prolonged significantly after turning off DBS and shortened after optimising the programming parameters (Fig. 1BC). Interestingly, the reaction time did not show a similar trend (Fig. 1D). All 16 patients demonstrated a clinical improvement after optimising the DBS program and also showed a reduction in ocSSRT (Fig. 1E).

This pilot experiment shows that ocSSRT estimated through a portable device could be used as a tool for optimising DBS settings: there was perfect agreement between improvement on a subjective clinical rating scale widely used for evaluating the severity of the movement disorder in PD patients and ocSSRT (Cohen’s kappa = 1, p < 0.0001). This may be important for the objective documentation of the effects of treatment on motor function in PD, particularly where several different assessors are involved in optimising settings over time. It may also aid the selection of optimum settings when used in conjunction with standard clinical scales in cases where there is ambiguity. However, multi-centre studies with larger sample sizes are essential if this promising observation is to be validated. Since making these observations, we have solved some technical challenges and successfully implemented the method as a mobile phone application (app) which measures ocSSRT as effectively as our custom device. This could open the way for ocSSRT and similar measures to aid remote supervision of DBS programming or be used as a tool to support programming by the patients’ care giver.
**Author contribution**

**Akash Roy:** Study concept and design, acquisition of data, analysis and interpretation, critical revision of the manuscript for important intellectual content.

**Supriyo Choudhury:** Study concept and design, acquisition of data, interpretation, critical revision of the manuscript for important intellectual content.

**Purba Basu:** Acquisition of data, analysis and interpretation, critical revision of the manuscript for important intellectual content.

**Mark R. Baker:** Study concept and design, analysis and interpretation, critical revision of the manuscript for important intellectual content.

**Stuart N. Baker:** Study concept and design, analysis and interpretation, critical revision of the manuscript for important intellectual content.

**Hrishikesh Kumar:** Study concept and design, analysis and interpretation, critical revision of the manuscript for important intellectual content, study supervision.

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**Declaration of competing interest**

The authors declare that the research was conducted in absence of any financial and non-financial interests that could be constructed as a potential conflict of interest.

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**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2020.09.007.

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**Fig. 1. SSRT Validates Optimum STN-DBS Programming.**

A. Schematic description of SSRT task. Stop signals (illumination of red LED) occur randomly, comprising a quarter of all Go trials (illumination of green LED) at one of four interstimulus intervals (5 ms, 65 ms, 130 ms and 195 ms). Patients were instructed to release the button in response to Go trials but to keep the button depressed if the Go signal was followed by a Stop signal. **B, C, D**. UPDRS III, ocSSRT and Reaction Time respectively at the three measurement points described in the text. **E**, difference in score or reaction time between ‘optimized’ and ‘non-optimized’ measurements. Both differences have been calculated so that positive values indicate an improvement – either a decrease in UPDRS-III score (improved PD symptoms) or decreased reaction times (faster responses). For (B – E), small circles with error bars indicate mean ± SEM of the relevant group. *, significant differences (Freidman’s ANOVA followed by post-hoc test, P < 0.05). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)
References


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