Optimal temporal pattern of brain stimulation designed using computational evolution

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Supplementary Materials:

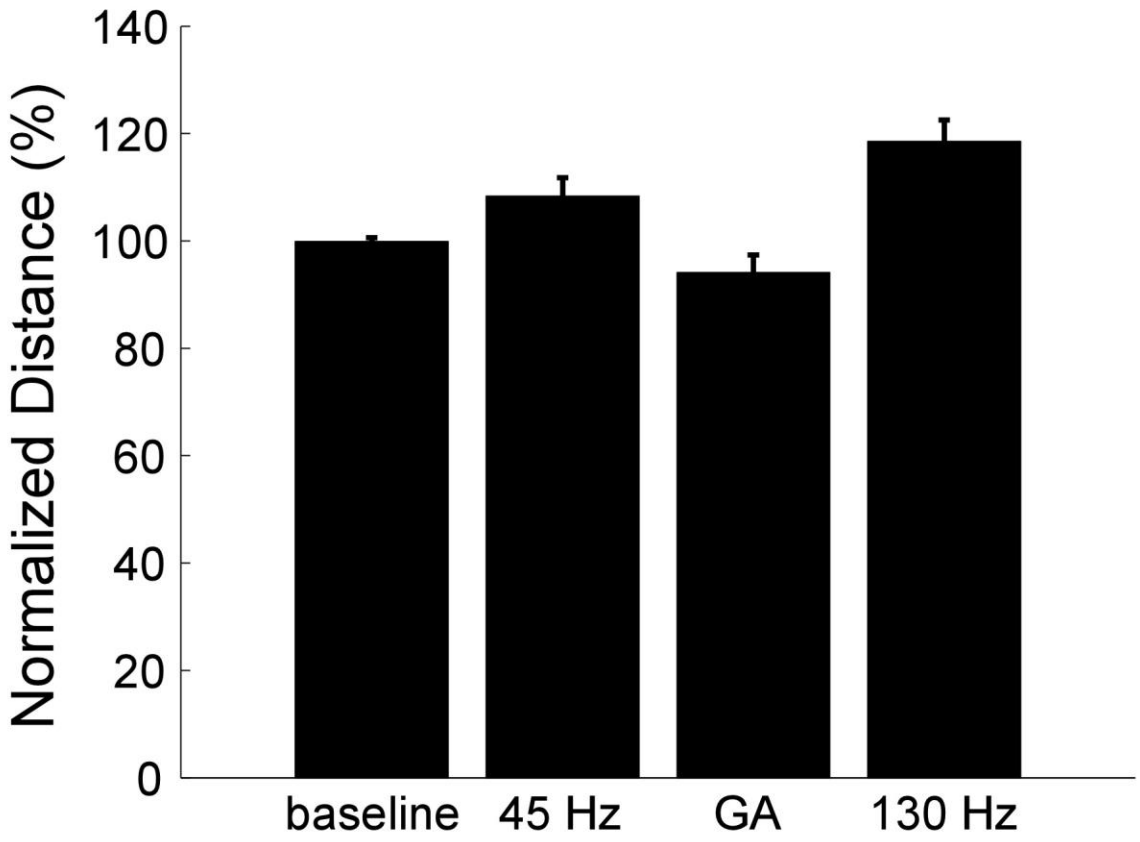

Fig S1. Effect of stimulation pattern on total distance traveled during the methamphetamine-induced circling task. Repeated measures ANOVA indicated that there was not a significant effect of stimulation condition on normalized distance traveled ($p=0.19$).

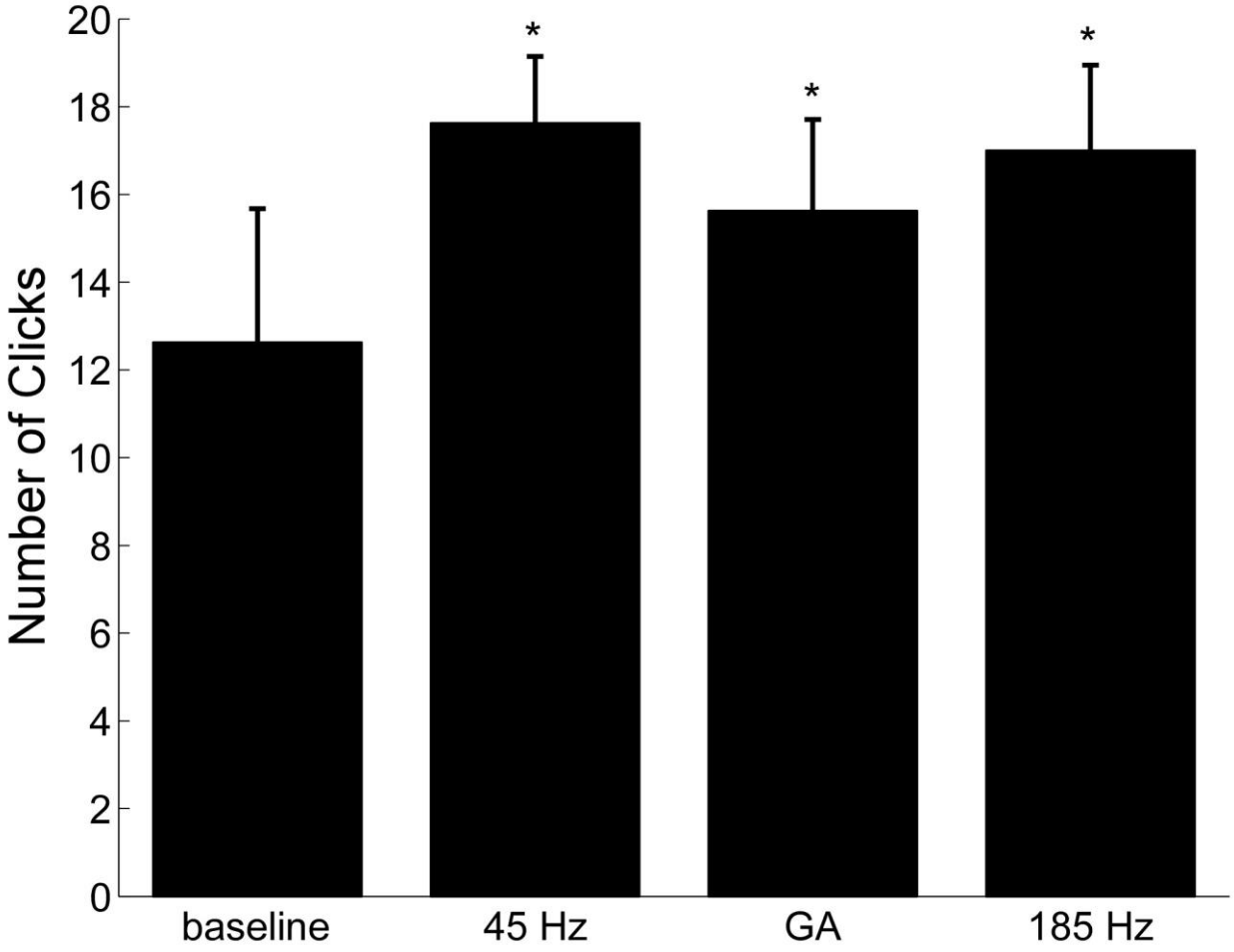

Fig. S2. Effects of stimulation patterns on finger tapping rates in persons with PD and STN DBS. RM-ANOVA indicated a significant effect of stimulation condition on rate of finger tapping ($p=0.005$), and Fisher's PLSD test indicated that all stimulation conditions significantly increased the number of clicks compared to baseline (DBS off; 45 Hz $p=0.001$, GA $p=0.02$, 185 Hz $p=0.003$, * $p<0.05$), but significant differences among DBS patterns were not observed.

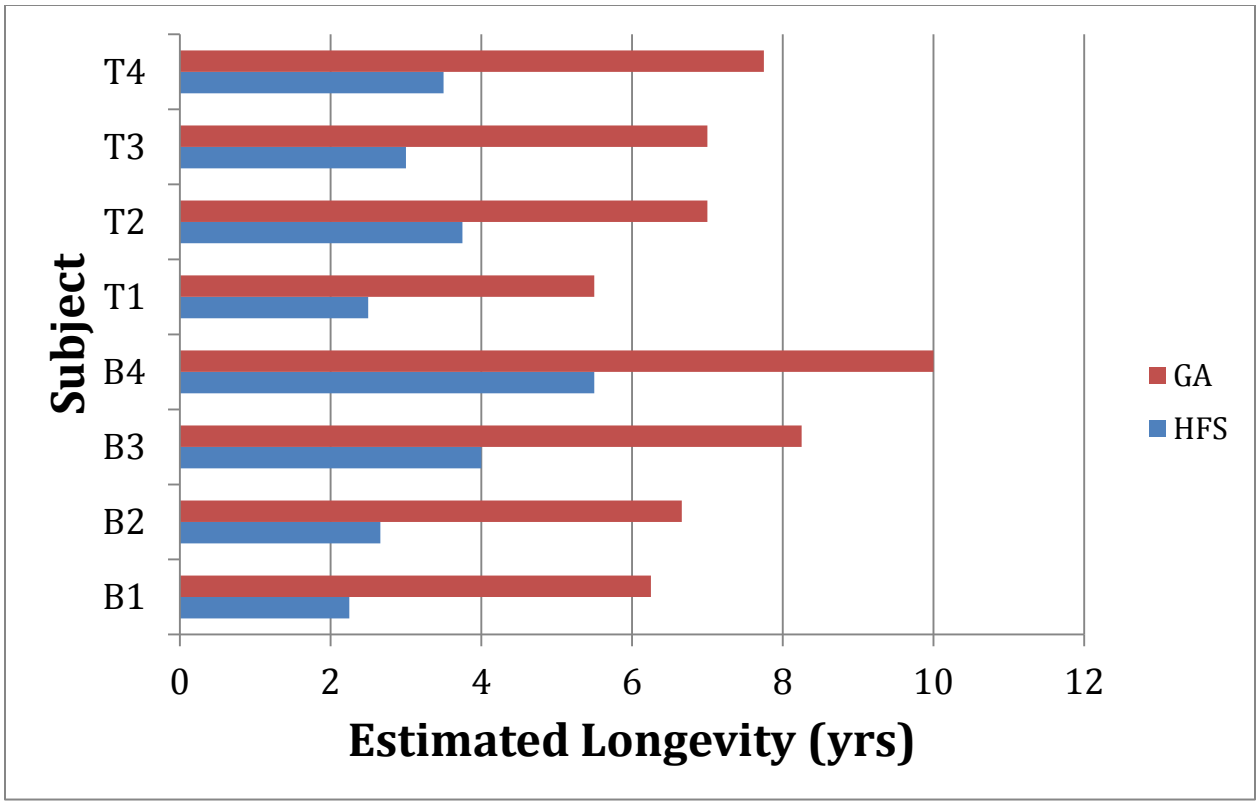

Fig. S3. Estimated battery longevity by subject with GA DBS compared to their clinical parameters. Battery longevity estimates were calculated using the Medtronic System Eligibility, Battery Longevity Reference Manual. We made several assumptions to enable estimation of battery life: that all patients had the Activa PC neurostimulator; that clinical stimulation parameters on the side contralateral to the experimental side were the same as those on the experimental side; that impedance values were 1000 Ω; and that stimulation was on continuously without cycling. Energy use values were extracted from the Medtronic Reference Manual, interpolating when necessary, and corresponding battery life estimates were found using the Longevity Estimate versus Adjusted Energy Use Figure for the Activa PC neurostimulator. Estimated battery longevities were approximately 4 years greater with the GA DBS than with the subject's actual high frequency clinical stimulation parameters.

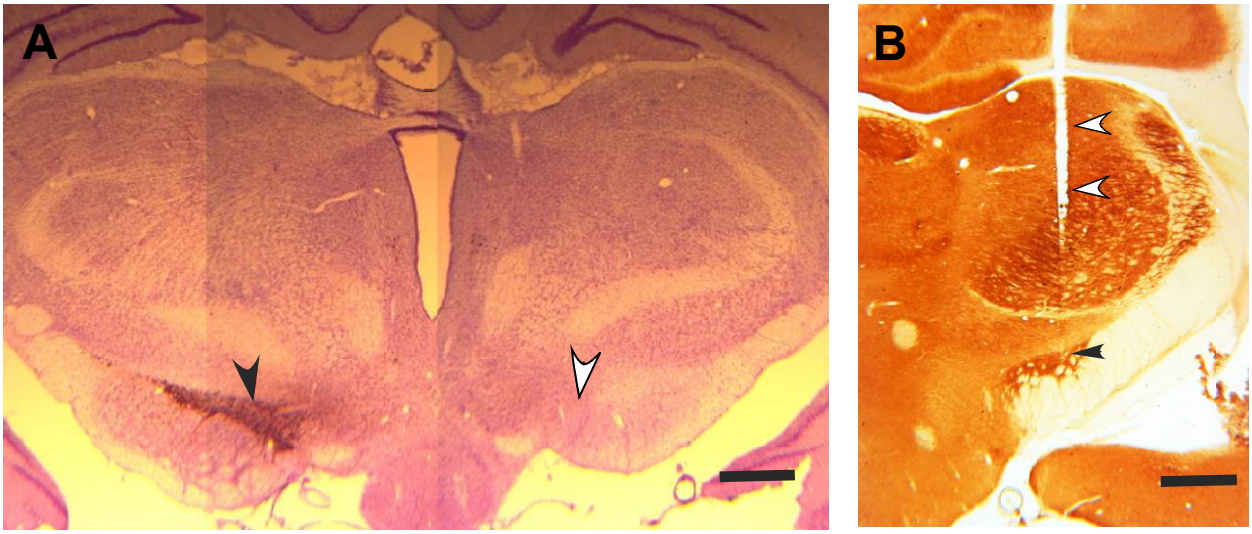

Fig. S4. Examples of post-mortem histology. (**A**) Coronal section from a 6-OHDA-lesioned rat showing loss of tyrosine hydroxylase immunoreactive neurons in the substantia nigra on the lesioned side (open arrowhead) as compared to unlesioned side (filled arrowhead). (B) Example of track from stimulating electrode (open arrowheads) with tip positioned within the STN (filled arrowhead) in section stained for cytochrome oxidase.

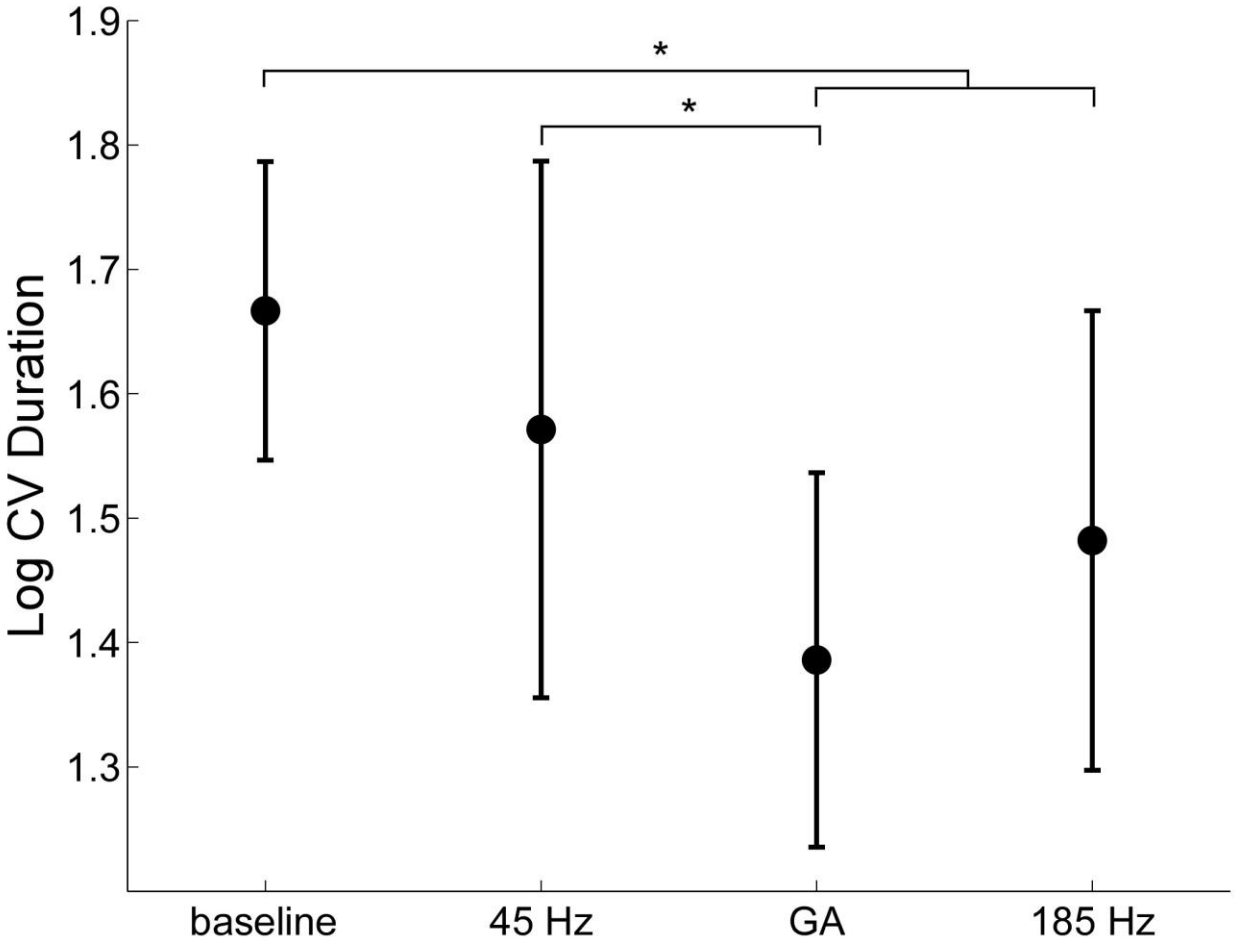

Fig. S5. Finger Tapping Log CV Duration for all three finger tapping trials in each 5 minute epoch. We decided *a priori* to include in the analysis only the second and third finger tapping trials in each 5 minute epoch. However, the results would have been very similar had all three finger tapping trials been included in the analysis. GA and 185 Hz DBS would still have reduced finger tap duration variability the most, with GA slightly outperforming 185 Hz. RM-ANOVA revealed a significant effect of stimulation condition on regularity of finger tapping ($p=0.03$), and Fisher's PLSD test was used to perform *post-hoc* comparisons between stimulation conditions. GA and 185 Hz DBS significantly improved performance in the finger tapping task relative to

baseline ($p=0.005$ and $p=0.04$, respectively), while 45 Hz did not ($p=0.25$). Tapping variability was lower for the GA DBS conditions compared to the 45 Hz DBS condition ($p=0.04$, * $p<0.05$).

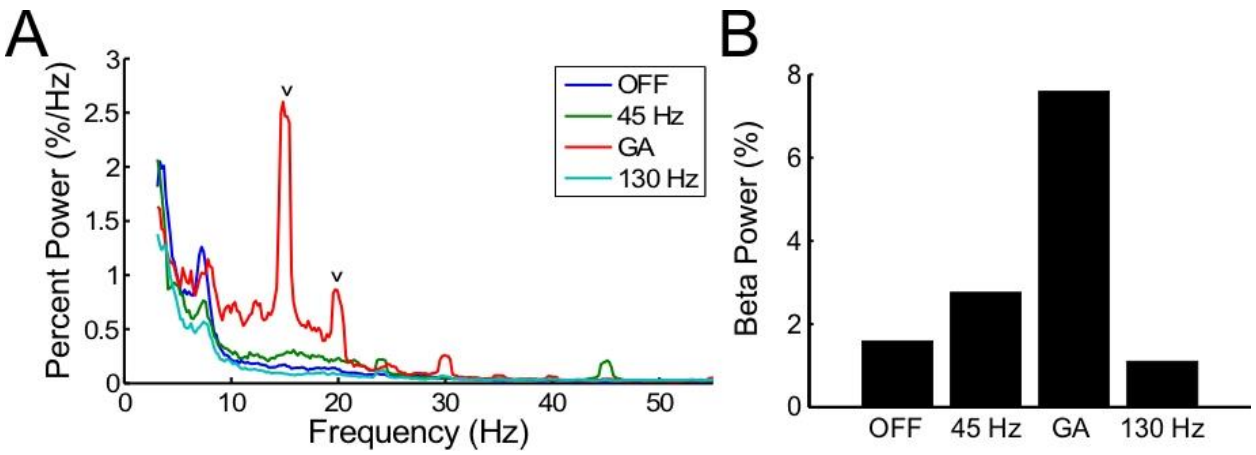

Fig. S6. Example data from a subject that did not exhibit a β peak in the spectrum of field potentials recorded in STN. The small, narrow peaks (v) in the power spectrum (**A**) are residual artifacts from amplifier blanking and signal interpolation to minimize the contribution of stimulation artifacts to the recorded signals that slightly increased the measured β power for the GA DBS condition (**B**).

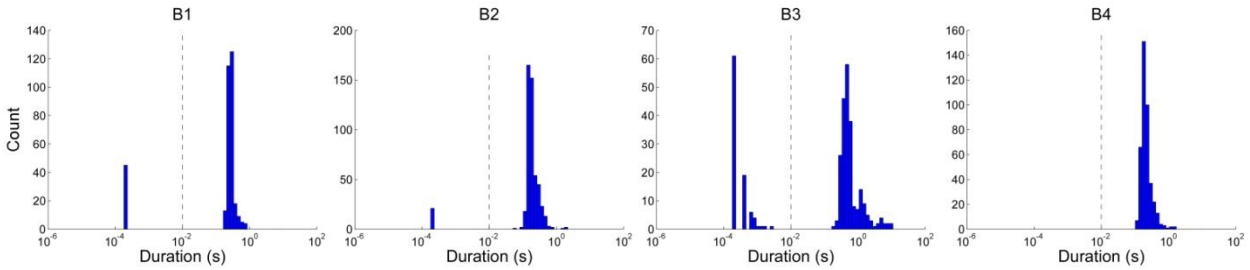

Fig. S7. Histograms of tap duration for each subject in the finger tapping task. Raw data were debounced by discarding extremely short artifacts of tapping apparatus with durations less than 0.01 s (vertical dashed line).