Savva Pronin Elective Report for RMS

Local field potentials in the thalamus and zona incerta during urinary functions

Background: Control of the lower urinary tract is complex and involves the integrated activity of distributed brain and spinal regions. However, the contribution of individual brain regions to bladder control is poorly understood**.** Implanted deep brain stimulation (DBS) electrodes enable the measurement of local field potential (LFP) signals from localised regions in the brain. Such recordings can provide insight into neurophysiological control of organ systems and pathophysiology of disease, and thus is relevant for the study of bladder control and dysfunction. Previous work has demonstrated measurable effects of DBS at the ventral intermediate nucleus of the thalamus (VIM) on urodynamic recordings during bladder filling[1] and that beta-frequencies in the globus pallidus interna but not the subthalamic nucleus are both implicated in urinary voiding and correlate with urinary tract symptoms in a cohort of patients with Parkinson's disease[2]. However, LFP analysis of VIM signals with regard to lower urinary tract behaviour has not been performed.

Aims: To investigate neuronal oscillations in the VIM during imagined voiding, pelvic floor contraction and urinary voiding as well as their association with lower urinary tract symptoms. Signals from the zona incerta (ZI) were also recorded in patients with electrodes that spanned VIM/ZI, as a comparison nucleus.

Methods: 5 patients with VIM DBS were recruited; in 3 of these the electrodes also entered the ZI. 3 had essential tremor, 1 dystonic tremor and 1 Parkinson's disease. LFPs were recorded during three experiments: imagined voiding, pelvic floor contraction/relaxation and urinary voiding.

Bipolar channels were created by subtracting adjacent contacts for both the VIM and ZI. The signal was down-sampled to 1000 Hz in Spike2 and exported to MATLAB. The signal was low-pass filtered at 100 Hz, high-pass filtered at 2 Hz, and band-stop filtered at 50 Hz with a Butterworth filter. Power spectral density (PSD) analysis was performed on individual trials. These were then averaged per patient and then across patients. PSDs were also created for averages normalised by total power. Frequency bands were defined as: 2-4 Hz delta, 4-8 Hz theta, 8-12 Hz alpha,12-30 Hz beta, 30-90 gamma. Statistical comparison was done using Wilcoxon rank-sum test in individual patients and signed-rank test across patients.

Linear regression in SPSS was used to assess the correlation between beta oscillatory power during voiding normalised to rest, and urinary symptoms assessed by the International Consultation on Incontinence Lower Urinary Tract Symptoms questionnaire was explored.

Results: Significant frequency and frequency band changes were observed in the VIM and ZI during pelvic floor contraction/relaxation and imagined void at a single subject level, however, there was no significant change in LFP power during any experimental condition when signals were averaged across participants (Figure 1).

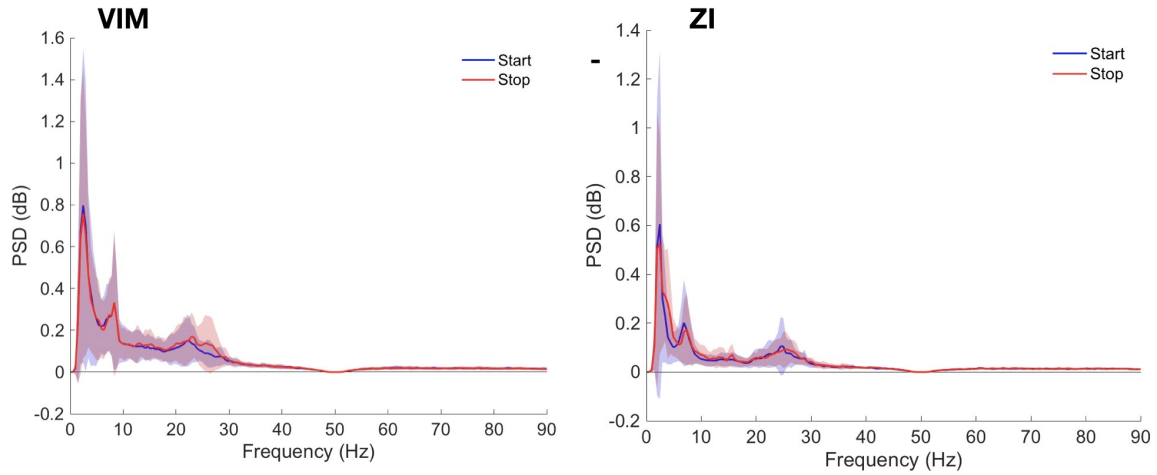

Figure 1. Power spectral density analysis of 'start/stop imagining [voiding]' in the ventral intermediate nucleus of the thalamus and the zona incerta averaged across all subjects.

Beta power during voiding normalised by resting beta power in the VIM, but not the ZI, significantly correlated with ICIQ scores for voiding (p=0.014), frequency (p=0.036) and incontinence (p=0.015) (Figure 2).

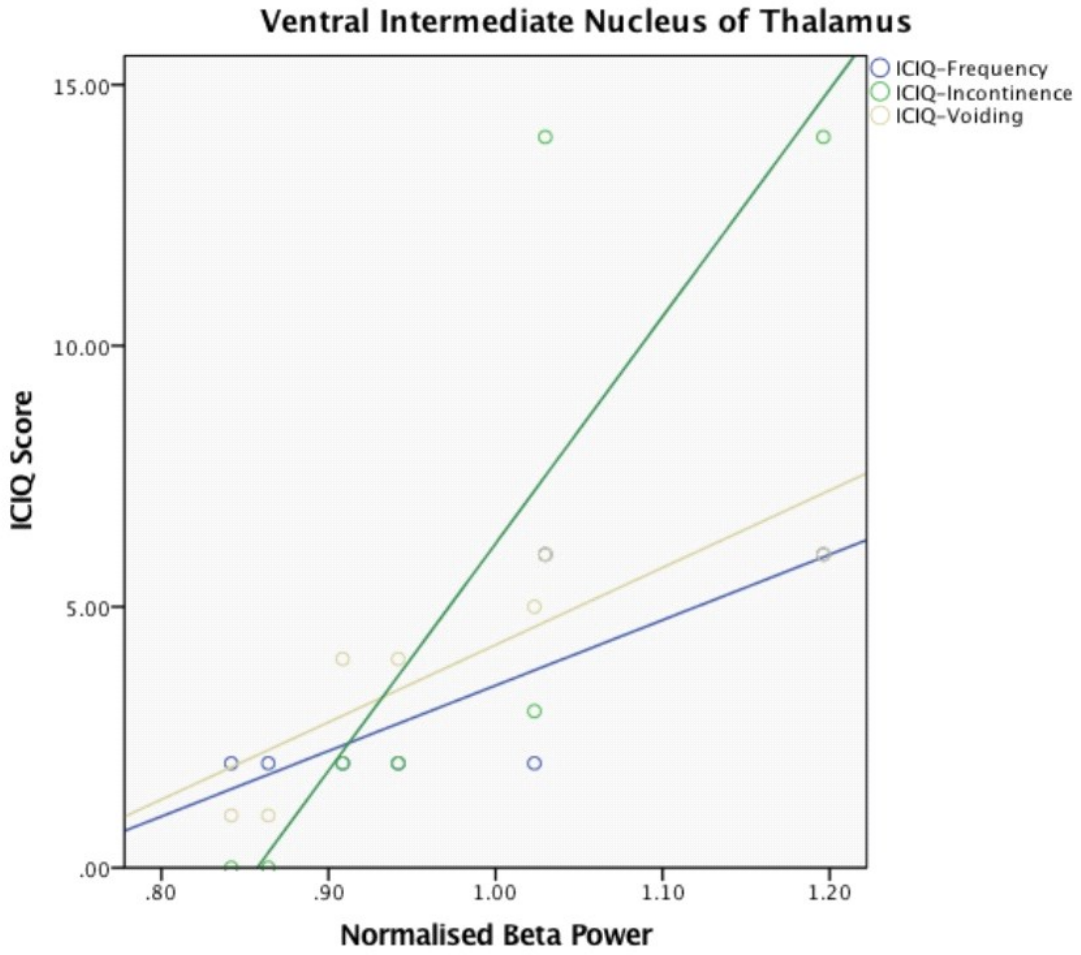

Figure 2. Correlation between International Consultation on Incontinence Lower Urinary Tract Symptoms questionnaire and normalised beta power in the ventral intermediate nucleus of thalamus.

Conclusions: There was no significant change in oscillatory power in the VIM or ZI during imagined void, pelvic floor contraction/relaxation or voiding. This implies that the VIM/ZI are not involved in normal voiding, however, our small sample size and heterogeneous population may have prevented us from detecting an effect. Significant bands in individual patients suggest hidden variables. Significant correlation between VIM beta power and lower urinary tract symptom severity in this patient group suggests that the beta signal may be of pathophysiological relevance for lower urinary tract symptoms.

This project has been accepted for a oral presentation at the XXIII congress of the European Society for Stereotactic and Functional Neurosurgery (ESSFN) in Edinburgh on September 26-29, 2018, at The Royal College of Surgeons.

References

1. Kessler TM, Burkhard FC, Z'Brun S, et al. Effect of thalamic deep brain stimulation on lower urinary tract function. Eur Urol. 2008;53:607–612.
2. Roy HA, Aziz TZ, Fitzgerald JJ, Green AL. Beta oscillations and urinary voiding in Parkinson disease. Neurology 2018; published online March 23, 2018