

A widespread visually-sensitive functional network relates to symptoms in essential tremor

Archer, D.B., Coombes, S.A., Chu, W.T., Chung, J.W., Burciu, R.G. (University of Florida, Applied Physiology & Kinesiology), Okun, M.S. (University of Florida, Neurology), Vaillancourt, D.E. (University of Florida, Applied Physiology & Kinesiology)

Introduction

Essential tremor is a neurological syndrome of heterogeneous pathology and aetiology that is characterized by tremor primarily in the upper extremities. This tremor is commonly hypothesized to be driven by a single or multiple neural oscillator(s) within the cerebello-thalamo-cortical pathway. Several studies have found an association of blood-oxygen level-dependent (BOLD) signal in the cerebello-thalamo-cortical pathway with essential tremor, but there is behavioural evidence that also points to the possibility that the severity of tremor could be influenced by visual feedback. Here, we directly manipulated visual feedback during a functional MRI grip force task in patients with essential tremor and control participants, and hypothesized that an increase in visual feedback would exacerbate tremor in the 4–12 Hz range in essential tremor patients. Further, we hypothesized that this exacerbation of tremor would be associated with dysfunctional changes in BOLD signal and entropy within, and beyond, the cerebello-thalamo-cortical pathway.

Experimental

We directly manipulated visual feedback during a functional MRI (3 Tesla; AMRIS Facility) grip force task in patients with essential tremor and control participants. To determine if the tremor severity was associated with single or multiple brain region(s), we conducted a bidirectional stepwise multiple regression analysis

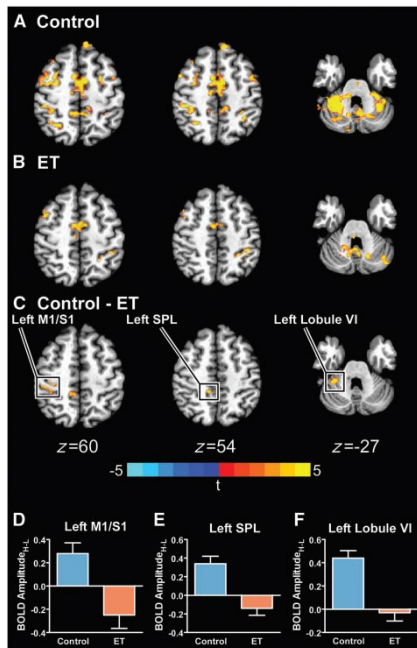


Fig.1 Between-group BOLD AmplitudeH-L differences. The significant BOLD AmplitudeH-L for controls (A), essential tremor (ET) patients (B), and the between-group difference (PFWER<0.005) (C) is shown. The boxed regions in C are plotted in D–F, in which the mean BOLD AmplitudeH-L for controls (blue) and essential tremor patients (orange) is shown. Error bars represent +/-SEM.

Results and Discussion

We found that increases in visual feedback increased tremor in the 4–12 Hz range in essential tremor patients, and this increase in tremor was associated with abnormal changes in BOLD amplitude and entropy in regions within the cerebello-thalamo-motor cortical pathway, and extended to visual and parietal areas. Birectional stepwise multiple regression analysis found that a widespread functional network extending beyond the cerebello-thalamo-motor cortical pathway was associated with changes in tremor severity measured during the imaging protocol. Further, this same network was associated with clinical tremor severity measured with the Fahn, Tolosa, Marin Tremor Rating Scale, suggesting this network is clinically relevant. Since increased visual feedback also reduced force error, this network was evaluated in relation to force error but the model was not significant, indicating it is associated with force tremor but not force error.

Conclusions

This study therefore provides new evidence that a widespread functional network is associated with the severity of tremor in patients with essential tremor measured simultaneously at the hand during functional imaging, and is also associated with the clinical severity of tremor. These findings support the idea that the severity of tremor is exacerbated by increased visual feedback, suggesting that designers of new computing technologies should consider using lower visual feedback levels to reduce tremor in essential tremor.

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