CORTICAL ACTIVATION INDUCED BY ELECTRICAL STIMULATION IN PATIENTS WITH MULTIPLE SCLEROSIS AND FOOT DROP

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Introduction: A common motor impairment in MS is dropped foot, characterised by weakness of the tibialis anterior. This results in an inability to dorsiflex the ankle, leading to a higher chance of stumbling and falling. Functional Electrical Stimulation (FES) is a technique used to elicit ankle dorsiflexion (ADF) movement by electrically stimulating the common peroneal nerve, and is increasingly used in gait rehabilitation to correct drop foot and improve mobility in hemiplegic gait in patients with MS [1]. Regular use of FES induces long term effects such as increased muscle strength and walking speed [1]. Although the mechanism of FES on the improvement of locomotor activity has not been established, cortical plasticity and reorganisation contributes to functional recovery after brain injury and occurs in MS [2].

Aim: To investigate the pattern of brain activation during self-initiated (Active), Passive, Electrical Stimulated (ES), and combined Active with ES-stimulated ADF movements [3-5] in multiple sclerosis (MS) patients with foot drop, comparing patients affected and non-affected legs.

Subject and methods

Subjects: Ten patients (9 female, 1 male) with relapsing remitting (RR) and early secondary progressive MS with unilateral foot drop were studied (Table 1).

Paradigm: Subjects lay supine in the scanner with one foot in a custom made footrest. Subjects performed Active, Passive, ES-induced and the ES plus Active ADF movements in a randomised order, for both the affected and non-affected leg. For each, 20s of 0.4 Hz movements was followed by 20s rest, repeated for 8 trials. The active movement was directed by visual cues, for passive movement an assistant dorsiflexed the foot. ES-induced ADF was delivered at the same rate as Active and Passive ADF [1]. During ES plus Active ADF subjects actively moved their foot during ES. Throughout, EMG was used to monitor the tibialis anterior muscle and a sensor recorded the angular displacement of the foot.

Data acquisition: fMRI data was acquired on a Philips Achieva 3T scanner using a 16-channel SENSE coil. 30 axial GE-EPI images were acquired (64x64 matrix, 192x192 mm^2 FOV, 3 mm slice thickness, TE=40ms, TR=2s). In addition, MPRAGE and T2-FLAIR images were acquired.

Data analysis: fMRI data were analyzed using SPM5. Data were realigned, normalized and 8 mm spatial smoothing applied, each ADF movement was modelled as a block in the general linear model, and a random effects group map formed. Beta values were compared in anatomically defined regions (SMA, premotor, insula cortex) for the affected and non-affected legs. EMG data was gradient artefact corrected, filtered and rectified. The mean EMG amplitude and angular displacement were assessed for each ADF, individual trials correlated with the BOLD response.

Results and Discussion:

A significant increase in angular displacement was found for the non-affected leg compared to affected leg for all conditions except for ES-induced ADF (Fig 1), and a significant correlation was found between angular displacement and EMG amplitude ($R^2 = 0.86$). For the Active task, despite a reduction in angular displacement/ EMG activity for the affected leg, an increase in BOLD response was seen in the SMA and premotor areas compared to the non-affected leg (Fig 2A and B). This may result from these secondary motor areas being used to generate motor output for the affected leg, as direct projections from primary M1 are damaged. Reduced activity in premotor and motor areas was found for the Passive condition, particularly for the affected leg. For the ES-ADF, a significant increase in activation in insula and SII was found for the non-affected leg compared to the affected one. This was also reflected in the Active+ES movement, and may result from sensory impairment in the affected leg. This study provides valuable information for future studies of plasticity and longer term plasticity/re-organisation associated with regular use of FES in people with ADF weakness due to MS.

Table 1: Patient aetiology including age, disease duration, Expanded Disability Status Scale (EDSS). Ashworth Score and FES stimulus amplitude.

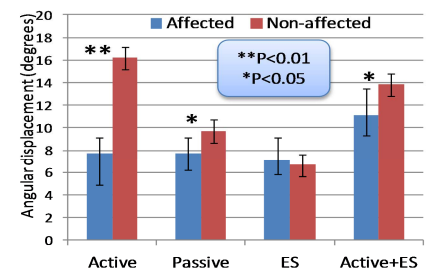| Age	Disease duration	EDSS	Ashworth		FES strength	
			Affected	Non-affected	Affected	Non-affected
(Years)	(Years)					
51.0±8.8	17.0±9.6	5.3±1.4	1.9±1.3	1.1±1.3	2.7±0.6	2.7±1.6

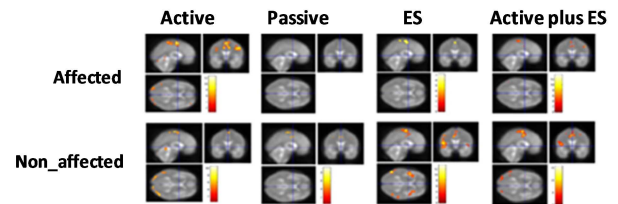Figure 1: Average angular displacement (in degree) to each of the ADF movements.

Figure 2A: Cortical response to Active, Passive, ES and Active plus ES ADF movements, data displayed at P<0.001.
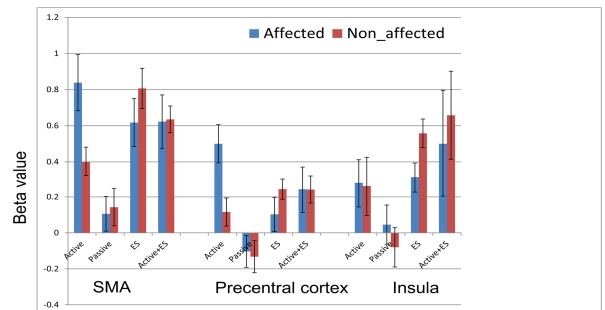

Figure 2B: Beta value in anatomically defined ROIs to each conditions.

References

1. Taylor, P. N., J. H. Burridge, et al. Arch Phys Med Rehabil 1999; **80**(12): 1577-1583. 2. Pantano, Brain 2005; **128**(9): 2146-2153. 3. Francis, S, et al. NeuroImage 2009; **44**: 469-479. 4. Dobkin, BH, et al, *NeuroImage* 2004; **23**: 370-381. 5. Ciccarelli,O, et al, *Exp Brain Res* 2005, **166**: 31-42.