Voxel-based lesion symptom mapping to explain the cognitive-postural interference phenomenon in multiple sclerosis

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INTRODUCTION

- Cognitive-postural interference (CPI) refers to deterioration of balance while performing a concurrent cognitive task.
- This phenomenon can be estimated as dual-task cost (DTC), i.e. the change in postural sway from single-task (ST) to dual-task (DT) performance.
- There is emerging evidence that people with multiple sclerosis (MS) may present pathological CPI level compared to general population, with detrimental effects on their quality of life and increased risk of falls[1,2].

OBJECTIVE

- To investigate the disease-altered structure-function relationship that underlies the CPI phenomenon in people with MS.

METHODS

- We collected behavioural and magnetic resonance imaging (MRI) data of 96 patients with MS .
- Fourty-eight sex and age-matched healthy individuals were also recruited in a 1:2 ratio among the University personnel as controls.
- **Dual-task experiment:** patients and controls were tested by means of static posturography under ST and DT conditions (i.e. while performing the Stroop test), using a standard force platform (Prokin PK-254P).[3]
- **Image Analysis:** lesion volume (LV) measurement, co-registration of lesion masks to standard space template and calculation of voxel-based lesion symptom maps (VLSM) were performed on brain images by Jim 7.0 (www.xinapse.com) and MRIcron (www.nitrc.org/projects/mricron).
- We analyzed only brain images of patients who were scanned in the same outpatient centre using a superconducting 1.5 Tesla magnet (GE Signa Excite) in a span of one month from dual-task experiment.

RESULTS

- Demographic, behavioural and clinical data of patients and controls are shown in **TABLE 1 (below)**; patients had larger postural sway than controls in both ST and DT condition.

TABLE 1	Patients (n=96)	Controls (n=48)	p
Sex, male:female	32:64	16:32	1.00
Age, years	41.8 (10.6)	40.7 (8.6)	0.42
Body mass index, kg/mq	23.2 (4.0)	23.5 (3.7)	0.38
Educational level - median [range]	13 [8 to 18]	13 [8 to 18]	0.33
Time since first symptom, years	13.6 (8.6)	N/A	-
EDSS score - median [range]	3.0 [1.0 to 6.0]	N/A	-
Postural swayST, mm	311 (134)	198 (63)	**<0.001**
Postural sway^{DT}, mm	428 (182)	245 (72)	**<0.001**
Dual-task cost, % - median [range]	-38 [-6 to -96]	-24 [-2 to -47]	**<0.001**
T2-LV, cm^3 - median [range]	11.17 [0.37-96.72]	N/A	-
T1-LV, cm^3 - median [range]	0.85 [0.03-10.20]	N/A	-
T1:T2 ratio - median [range]	0.10 [0.01-0.40]	N/A	-

All values are mean (standard deviation) unless indicated otherwise

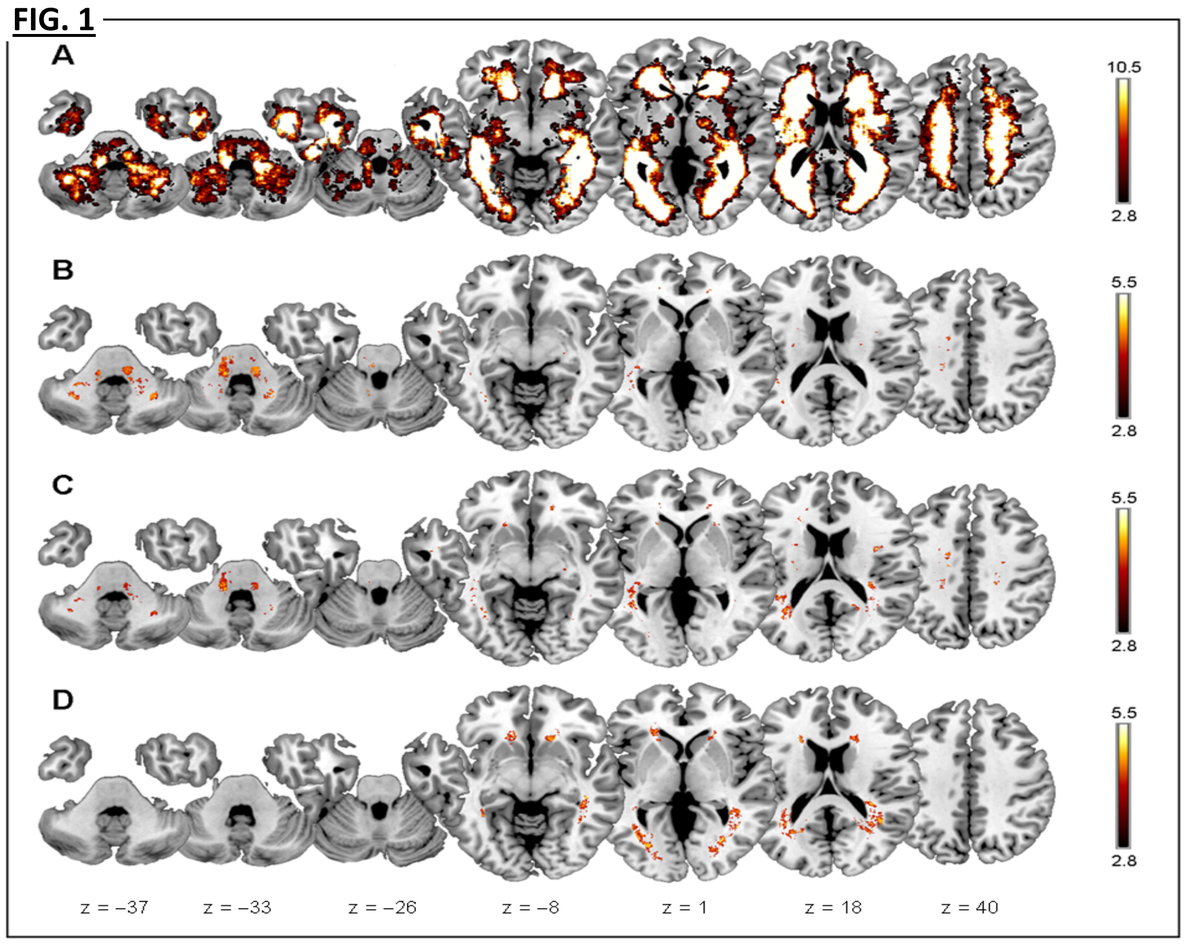
- Spearman rank-order correlations between findings from DT experiment (postural sway in ST and DT conditions and DTC) and demographic, clinical and MRI variables in patient group are shown in **TABLE 2** (below).

TABLE 2	PosturalswayST	Posturalsway^{DT}	Dual-task cost
Age	0.18	0.22	-0.18
Body Mass Index	-0.07	-0.08	0.05
Educational level	-0.20	-0.18	0.01
Time since first symptom	**0.34***	**0.36***	-0.10
EDSS score	**0.50#**	**0.51#**	-0.05
T2 lesion volume	**0.25***	**0.35***	-0.22
T1 lesion volume	**0.31***	**0.41#**	**-0.27***
T1:T2 ratio	0.17	0.21	-0.12

*** $p \leq 0.01$; # $p < 0.001$**

- Probabilistic spatial distribution of T2 lesions showed the highest occurrence of clusters in the bilateral periventricular white matter of both hemispheres, followed by infratentorial clusters in brainstem and middle cerebellar peduncles (**FIG. 1/A**).
- The postural swayST correlated with lesion probability in several infratentorial areas, ($p<0.01$ after FDR correction; **FIG. 1/B**).
- The postural sway^{DT} correlated with lesion probability in middle cerebellar peduncles, but to a less extent ($p<0.01$ after FDR correction; **FIG. 1/C**).
- We found clusters of T2 lesions in distinct anatomical regions (anterior corona radiata, sagittal stratum and posterior thalamic radiations, bilaterally) to be correlated with DTC of balance ($p<0.01$ after FDR correction; **FIG. 1/D**).
- Probabilistic spatial distribution of T1 lesions showed the highest occurrence of clusters in the bilateral periventricular white matter of both hemispheres, but the VLSM did not reveal any significant association with behavioural data using T1-lesion masks (not shown).

FIG. 1



Voxel-based lesion symptom mapping of T2-hyperintense lesions superimposed on axial standard template: overlay of all lesions (A), Brunner-Munzel rank-order correlations with postural sway in single-task condition (B), dual-task condition (C) and dual-task cost of balance (D). Only voxels that survived a 1%-false discovery rate cut-off threshold are displayed. Montreal Neurological Institute (MNI) coordinates are reported at the bottom of figure.

CONCLUSION

- Our findings suggest that the CPI phenomenon in MS has multifactorial causes, including neurodegenerative processes driven by chronic axonal loss and disconnection along specific areas implicated in visuo-spatial attention and task-switching abilities.
- Our findings suggest three distinct (not mutually exclusive) strategies for improving performance of MS people in DT situations:

  (i) executive function and visuo-spatial attention should be rehabilitated over the other cognitive domains;[3]

  (ii) pre-frontal areas could represent a putative target for brain modulation by non-invasive stimulation techniques;[4]

  (iii) dopamine agonist therapy could represent a suitable treatment as most disconnected areas are innervated by dopaminergic neurons (striatum and pre-frontal cortex).[5]

REFERENCES

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