Brain glucose consumption abnormalities in neuro-Behçet's disease: a preliminary 18F-FDG PET/CT study

Sirs,

Neurological involvement (namely neuro-Behçet's disease, NBD) is a relatively uncommon but life-threatening complication of Behçet's disease (BD) (1). Parenchymal involvement primarily affects the cerebral hemispheres, brainstem, optic nerve, spinal cord while non-parenchymal involvement is a consequence of intracranial vascular disease and includes cerebral venous thrombosis, arterial dissection, acute meningeal syndrome and intracranial hypertension (2-4). To date, brain magnetic resonance imaging (MRI) represents the gold-standard in demonstrating structural abnormalities in patients with NBD (5). More recently, 2-deoxy-2-(18F) fluoro-D-glucose (18F–FDG) Positron Emission Tomography/Computed Tomography (PET/CT) is emerging as a powerful tool for the evaluation of cortical and subcortical brain disorders (6); however, the role of 18F–FDG PET in NBD has been evaluated only in isolated case reports (7, 8). In this preliminary study, we aimed at investigating brain glucose consumption in patients with NBD. To this purpose, three groups of subjects were recruited: A) Subjects with NBD (NBD group, n=6) diagnosed by a consultant neurologist according to recently proposed International Consensus Recommendation (ICR) criteria (1); B) BD patients classified according to the International Criteria for Behçet's Disease (ICBD) (9) in which neurological involvement was excluded following neurological examination (BDwN, n=7); C) Healthy subjects (CG group, n=17).

Within NBD patients, only two patients displayed a MRI picture partially correlated with neurological clinical manifestations: one patient suffered from a mesial temporal lobe epilepsy secondary to parenchymal lesion in the right temporal pole, whereas another patient suffered from headache due to bilateral transverse sinus stenosis, as MRI venography showed. Three patients showed parenchymal lesions without any relationship with accompanying neurological syndromes. Finally, MRI was normal in another patient, despite the presence of severe neurological symptoms.

All patients underwent 18F–FDG (185-210 MBq *i.v.*) PET/CT combined with a low-amperage CT scan of the head for attenuation correction (Discovery VCT, GE Medical Systems). Images acquisition, data processing and statistical analysis were performed as previously described (10).

As compared to CG, NBD showed a significant reduction of brain glucose consumption in left and right cingulate gyrus [Brodmann Area (BA) 24, BA 23 and BA36], left precuneus (BA7) and in left temporal lobe (BA 38) (Fig. 1, Table I). At a sub-cortical level, we found a significant reduction of brain glucose consumption in right brainstem. We did not find any area of increased glucose consumption in NBD as compared to CG. As compared to BDwN patients, NBD showed a significant reduction of brain glucose consumption in right and left parahippocampal gyrus (BA 30 and 19) and in right posterior cingulate cortex (BA23). We did not find any area of increased glucose consumption in NBD as compared to BDwN. We did not find significant differences in brain glucose consumption when comparing BDwN with CG.

On the basis of our preliminary results,

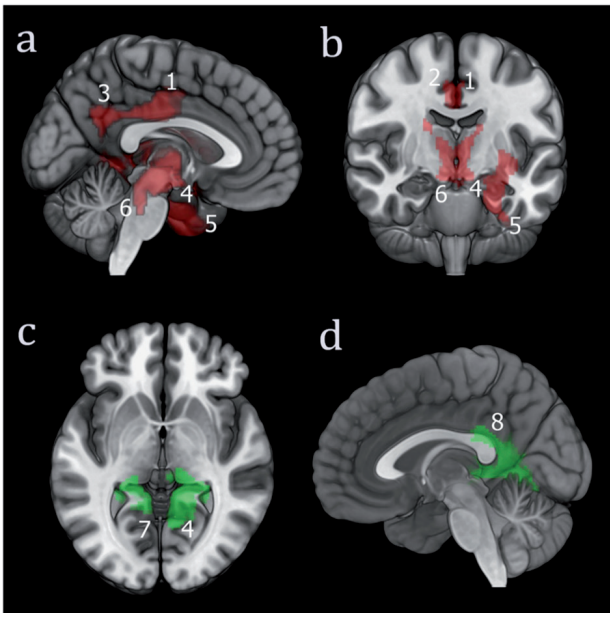

Fig. 1. Graphical representation of brain glucose metabolism in control group (CG) *vs.* neuro-Behçet's disease (NBD) (a, b) and in Behçet's disease without neurological involvement (BDwN) *vs.* NBD (c, d). Areas of reduced 18F–FDG uptake in NBD are highlighted in red (CG *vs.* NBD) and in green (BDwN *vs.* NBD), respectively. Areas legend: 1) left cingulate gyrus; 2) right cingulate gyrus; 3) left precuneus; 4) left parahippocampal gyrus; 5) left superior temporal gyrus; 6) right midbrain; 7) right parahippocampal gyrus; 8) right posterior cingulate gyrus.

Table I. Statistical parametric mapping (SPM) comparisons between 18F-FDG uptake in NBD (n=6) and CG (n=17) and in in BDwN (n=7) and NBD (n=6).

Comparison	Cluster level			Voxel level			
	Cluster Extent	Cluster p (FDR corr.)	Cluster p (FWE corr.)	Z score of maximum	Talairach Coordinates	Cortical region	BA
CG - NBD	1444	0.006	0.012	5.04	0, -18, 36	Left cingulate gyrus	24
				4.58	6, -26, 32	Right cingulate gyrus	23
				3.90	-6, -56, 32	Left precuneus	7
	6212	0.000	0.000	4.43	-24, -10, -36	Left precuneus	36
				4.24	-24, -40, -6	Left parahippocampal gyrus	36
				3.99	-28, 4, -44	Left superior temporal gyrus	38
	907	0.032	0.041	4.01	8, -16, -10	Right midbrain	-
BDwN - NBD	3156	0.000	0.000	4.29	18, -40, 2	Right parahippocampal gyrys	30
				3.78	-26, -42, -4	Left parahippocampal gyrus	19
				3.77	8, -54, 18	Right posterior cingulate	23

Analysis performed using statistical parametric mapping (SPM8, Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab R2015b (Mathworks, Natick, MA, USA). Threshold of $p<0.001$, uncorrected for multiple comparisons at voxel level. A value of $p\leq0.05$, corrected for multiple comparison at cluster level, was accepted as statistically significant. In the 'cluster level' section on left, the number of voxels, the corrected p value and the cortical region where the voxel is found, are all reported for each significant cluster. In the 'voxel level' section, all of the coordinates of the correlation sites (with the Z-score of the maximum correlation point), the corresponding cortical region and BA are reported for each significant cluster. In the case that the maximum correlation is achieved outside the grey matter, the nearest grey matter (within a range of 7mm) is indicated with the corresponding BA.

BA:Brodmann's area; FDR: false discovery rate; FEW: family-wise error; CG: control group; NBD: neuro-Behçet's disease; BDwN: Behçet's disease without neurological involvement.

NBD patients show reduced glucose consumption in prefrontal and temporo-parietal lobes and midbrain independently of lesional areas. A possible explanation may lie in the vasculitic process affecting small vessels, that, being below the sensitivity threshold for detection of vascular wall inflammation, may be indirectly reflected by reduced perfusion of downstream cortical areas. In conclusion our data, although limited by the explorative nature, suggest that cerebral glucose metabolism abnormalities may represent a distinctive feature of NBD patients independently of the cortical lesion sites. If further confirmed, our results may represent a hypothesis-generating basis for future studies aimed at investigating the potential role of 18F-FDG PET in predicting the future onset of NBD and defining the potential usefulness of 18F-FDG PET in classifying those patients presenting with neurological symptoms but no (or equivocal) evidence of disease on MRI.

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