Functional connectivity changes as detected by resting-state functional MRI: three cases of patients with focal cerebellar lesions

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TARGET AUDIENCE: Neuroscientists with an interest in the cerebellum and its connections to the cortex.

PURPOSE

The cerebellum plays a role in a wide variety of complex non-motor behaviours due to the extensive connections to many cerebral associative areas (1;2).The cerebellar output channels have been demonstrated to be spatially segregated and to focus on functionally distinct cortical systems (3). This anatomical connectivity pattern suggests a functional segregation of cerebro-cerebellar connections that may support the role of the cerebellum in cognition. Resting state (RS) functional magnetic resonance imaging (fMRI) has proven useful to investigate functional brain networks at rest and it should be particularly suitable in the case of the cerebellum because the function of each subregion is defined by its connectivity with the rest of the brain. In order to clarify the functional topography within the cerebellum, in this study we used RS functional connectivity analyses in a cohort of healthy subjects and patients with unilateral lesions of the cerebellum.

MATERIAL AND METHODS

29 healthy subjects (HS) [mean(SD) age=54.17(6.59)] and 3 patients with left cerebellar lesions (Cb-1,Cb-2,Cb-3; mean/SD:49/11.5) were enrolled for the study. Lesion characterization was assessed using the spatially unbiased atlas template of the cerebellum and brainstem (SUIT) (4) (Fig 1). All subjects underwent an MRI examination at 3.0T, including a 3D modified driven equilibrium Fourier transform (MDEFT) and 220 fMRI volumes collected with T2* weighted echo planar image (EPI) scans. Three single cases were studied separately. ***Rs-fMRI data processing:*** Data were pre-processed using Statistical Parametric Mapping (Wellcome Department of Imaging Neuroscience; SPM8; http://www.fil.ion.ucl.ac.uk/spm/), and in-house software. Pre-processing included correction for head motion, compensation for slice-dependent time shifts, normalization to the EPI template in MNI coordinates provided with SPM8, and smoothing with a 3D Gaussian Kernel with 8mm^3 full-width at half maximum. For each patient, a spherical mask (radius= 8mm) was obtained by using Marsbar (Poldrack, 2007). The spheres (seed regions) were centered within the cerebellar grey matter (GM) affected each patient's lesion. The average RS-fMRI time series over the sphere was extracted for the patient presenting the corresponding lesion and for all the HS. The time series was then used as a regressor in a 1st level SPM analysis, thus extracting the voxels in the brain significantly correlated with it. In order to assess whether the presence of the lesions affects the connectivity in each patient, a 2nd level analysis compared the contrast images for positive correlation obtained at the first level between each patient and the HS group , using a two-sample T-Test model. Results were considered significant at $p < 0.05$ FWE correction.

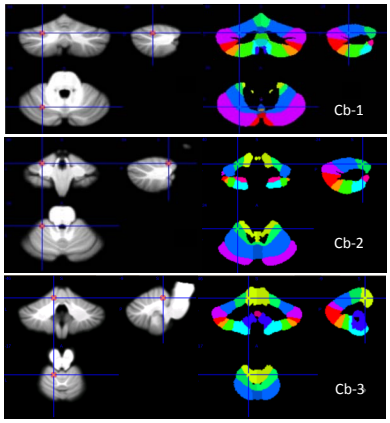

Figure 1. Seed regions used for SBA. Each seed was defined as a 8mm-radius sphere centered within the cerebellar lesion for each patient. Cb-1: *x -26, y -64,z-29*; Cb-2 : *x-24, y-40,z-24*;Cb-3:*x-9,y-46,z-17*.

RESULTS

Lesion mapping revealed minimal overlap between patients (Fig 2). The RS fMRI data showed significant patterns of functional connectivity (FC) between the seeds and cortical and subcortical areas. Significant functional correlation was also detectable between homologous regions of the two cerebellar hemispheres. The second level analyses showed patterns of altered FC involving both contralateral and ipsilateral cortical areas. Areas of altered FC was found at level of left and right caudate nucleus in Cb-1, right lateral occipital cortex in Cb-2, and left parietal cortex in Cb-3 (Fig 3).

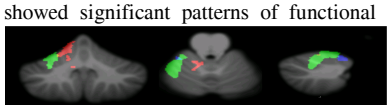

Figure2. Patients' lesions are labeled in different color for Cb-1 (green), Cb-2 (blue) and Cb-3 (red). Minimal overlap between lesions occurred as shown.

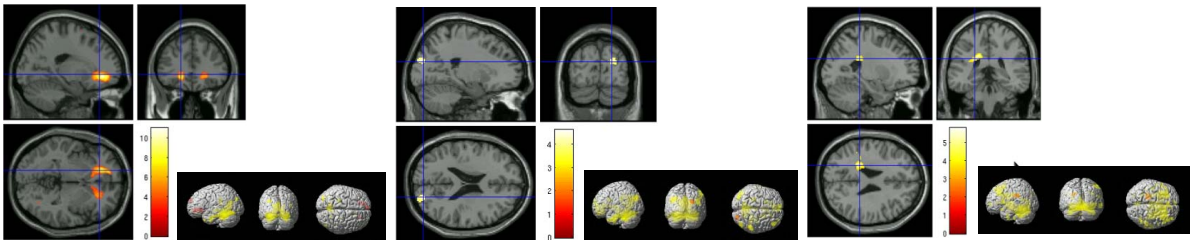

Figure3. For each of the patients (from left to right, Cb-1, Cb-2, and Cb-3), the sections show the regions of altered FC, while the render shows the pattern of connections with the seed (in yellow) in the whole population, and the areas of altered connectivity in each patients (in red).

DISCUSSION Our results are in accordance with human neuroimaging data of cerebellar functional topography (5). Using RS, we were able to define the pattern of connectivity between cerebral cortex and specific cerebellar lobuli. Although a contralateral mapping between cerebral areas and strength of correlation in the cerebellar regions has been previously showed (6), we provide the first evidence that unilateral cerebellar lesions may induce ipsilateral cortical FC changes. Furthermore, the pattern of FC alteration observed in the present study suggests that additional sub-regions within the same cerebellar lobules contributes to distinct functional networks. These data demonstrate the usefulness of rs-fMRI approach in characterizing individual networks as well as functional alteration in single case studies.

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