Functional MRI revealed the decrease of working-memory capacity and the impaired function of working-memory circuits in 22q11.2 deletion syndrome

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Target audience: Pediatric neurologist, neuro-radiologist, fMRI researcher

Purpose:

22q11.2 deletion syndrome, also known as velocardiofacial syndrome (VCFS), is the second most common autosomal chromosomal abnormality after Down syndrome. Deletion of chromosome 22 at band q11.2 results in a constellation of somatic phenotypes as well as significant neurocognitive deficits. Childhood impairment of cognitive functions such as sustained attention, working memory (WM) and verbal learning[1] are universal in VCFS patients and regarded parallel those seen in schizophrenia[2]. Structure MRI studies found the cerebral volume decrease and multiple localized brain parenchyma abnormalities, some affect the brain WM circuits [3]. Relatively few functional MRI studies of VCFS have been reported [4]. Kate et al explored the 2back WM function changes and showed reduced inferior parietal activation in VCFS children. No complete hierarchical WM loads were explored so far to provide the comprehensive brain activation deviation patterns in VCFS patients. In the present study we used consecutive n-back task based fMRI to probe the overall characterization of the functional imaging phenotypes of the disorder, which may add further understanding of the neural correlates of VCFS.

Methods:

17 children (9 patients, 8 normal controls) aged 13–15 years were included in the study. Informed written consent was obtained in all patients as approved by the Institutional Review Committee. Patients and normal controls were age and sex matched. Psychological assessment and n-back (n=0.1.2) task-based fMRI were conducted in all subjects. MRI scanning was completed on a 3.0T GE HD scanner (Waukesha, WI). High-resolution structural images were acquired using a 3D fSPGR pulse sequence (166 contiguousl axial slices, TR/TE:7.49/2.98 msec, ti=450ms; FOV=25.6cm2,Flip angle: 12 degree, voxel size=1x1x2mm). Functional images were acquired using an inward spiral pulse sequence (TR=1.5s;TE=30ms; FOV=25.6cm2;flip angle=600;voxel size=4 mm3, 30 contiguous axial slices). Individual and group fMRI analyses were performed using the FSL software (FMRIB Software Library, University of Oxford, Oxford, United Kingdom)[5].

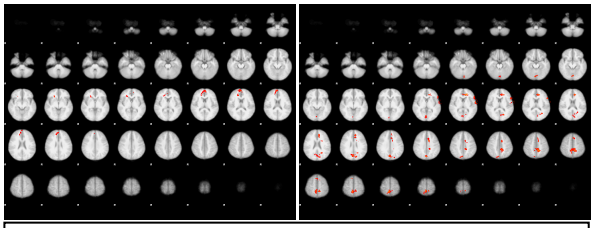

Fig 1. Increased prefrontal activation in 0 back WM load (left panel) and increased frontal-parietal network activations in 1 back WM load (right panel) showed after subtracting activations of controls from those of patients.

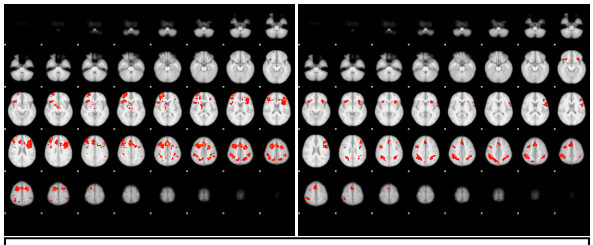

Fig 2. Reduced brain activations under 2 back WM load was observed in patients (right panel) compared with controls (left panel).

Results:

When compared with normal controls, VCFS patients demonstrated more and broader activations in lower levels of WM load(0,1 back conditions. Fig 1). In patient group, early involvement of prefrontal activity showed in 0 back and increased frontal-parietal network activations showed in 1 back, which included precuneus, cuneal, lingual gyrus and cingulated, paracingulate gyrus. In highest WM load condition (2 back), both group exhibited increased brain activations, but less increment was observed in patient group (Fig. 2). Patients also showed less hierarchical increasing activation in response to each phase of WM load increase (1-0 and 2-1 back conditions); hierarchical activation differences between patients and controls were mainly located in prefrontal area (Fig. 3). All the statistical activation maps were thresholded at Z>2.3 and a cluster significance of P=0.05.

Discussion:

Our study provided preliminary evidence on the disturbances of WM functional patterns in brain of VCFS patients by using hierarchically incremental WM tasks. For tasks of low to moderate difficulty (0.1 backs), patients showed increased cerebral activity and broader involvement of typical fronto-parietal WM circuits, which appeared to be less required in normal controls given the relative ease of the tasks. These increased brain activities in lower WM load suggests a limited or deficient WM capacity and less efficiency of WM network in patients. In high-demand task condition (2 back),patient group actually exhibited reduced brain activities, suggesting their reduced ability to cope with the increased task difficulties (as supported by our behavioral results). Due to the disproportionate usage of WM capacity, patients failed to have normal hierarchically increment in 1-0back and 2-1back conditions, most severely involved areas are left prefrontal and cingulate gyrus, both are main components of WM circuits. Our preliminary findings here thus represent an early report on the overall impairment of WM function in VCFS patients, and are in accord with a newly formalized cognitive reserve hypothesis [6], which is thought to be the basis to maintain adequate cognitive performance through complex yet optimized patterns of increased and decreased cerebral activities.

Conclusion:

Hierarchical impairment patterns of WM deficits in VCFS patients were investigated and are reported here in this abstract. It is anticipated that these findings can potentially serve as functional imaging biomarkers of the disorder and contribute to the evaluation of cognitive ability and cognitive remediation in patients.

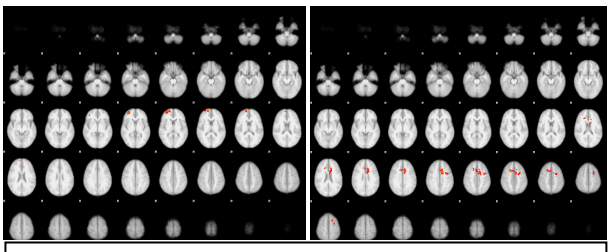

Fig 3. Less activation increment of patients in prefrontal area under 1-0 (left panel) and 2-1back condition (right panel).

Reference:

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