Attention Deficits in Survivors of Childhood Cancer

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Introduction

Children surviving cancer or cancer therapy that affects the central nervous system are at risk for neuropsychological and cognitive impairments impacting academic performance and quality of life. Evidence from behavioral studies suggests cancer and therapy-induced deficits in attention underlie these impairments. We report fMRI measurements in childhood cancer survivors that show altered patterns of brain neural activity during a continuous performance task, as compared to healthy siblings, and that altered brain activity is associated with differences in behavioral performance between the groups.

Methods

Subjects. This study was approved by the SJCRH Institutional Review Board and written informed consent to participate was obtained for all subjects. The sample included 24 survivors of childhood cancer (median age 14 years (6-17), 13 acute lymphoblastic leukemia (ALL), 11 brain tumor (BT)) and 11 age-similar healthy sibling controls (median age 14.5 (7-16)). All patients were more than one year off therapy, which included chemotherapy and/or radiation directed at the central nervous system. *MRI*. 1.5T Siemens Symphony scanner. Single shot T2* weighted EPI (TR = 2.06sec, TE = 50 msec, FOV =192 mm, matrix =64x64, slice thickness = 5mm) was used for fMRI data acquisition. *fMRI paradigm:* blocked design continuous performance test (CPT)(1) with 20 sec of task alternated with 20 sec of rest for 6 blocks. 2) *Data Analysis:* SPM99 software was used, processing included realignment, smoothing and normalization. The thresholds for activation were $p = 0.001$ (uncorrected) and 5 voxels ($p < 0.01$ corrected). Activation was evaluated in nine regions of interest were defined based on a preliminary study of healthy adults, (right, left inferior frontal cortices; right, left dorsal frontal cortices; right, left inferior medial occipital cortices; cingulate cortex; inferior parietal lobule; cerebellum)(2)

Results and Discussion

There were no significant differences in reaction time or commission error rates between the groups, but omission error rates were significantly higher in patients (3.1%) than in siblings (1.0%) ($p < 0.01$). There were no significant differences in the peak bold signal detected in any of the regions of interest. However, the total volume of activation was lower ($p = 0.05$) in survivors (694 voxels) than in siblings (1480). The decrease in activation was not uniform in all regions, with no difference in volume of activation in the right inferior frontal ROI. Large differences in cingulate ($p = 0.01$) and left occipital (extrastriate visual) ($p = 0.02$) activation were associated with differences in omission error rates (Fig. 1). In addition to differences in degree of activation, the average distance of peak activation in individual subjects from the target regions of interest was larger ($p < .01$) for survivors (10.43 mm) than healthy siblings (5.98 mm). These preliminary results indicate less and more diffuse cortical activation in survivors compared to healthy siblings. Overall, the altered pattern of activation in patients suggests that deficits in CPT performance are associated with decreased top-down control of visual attention.

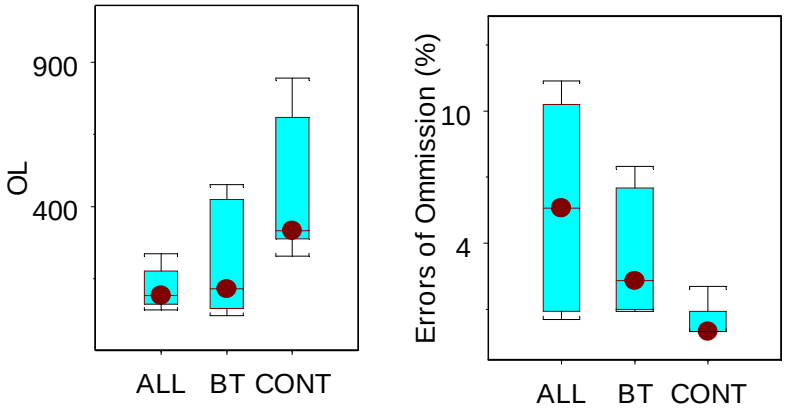

Fig. 1 Activation in the left extrastriate visual areas in the occipital lobe (OL) and rate of omission errors for patients (ALL and BT) and siblings (CONT).

References

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