

Functional MRI in Pediatric Cancer Survivors during Cognitive Remediation

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Introduction

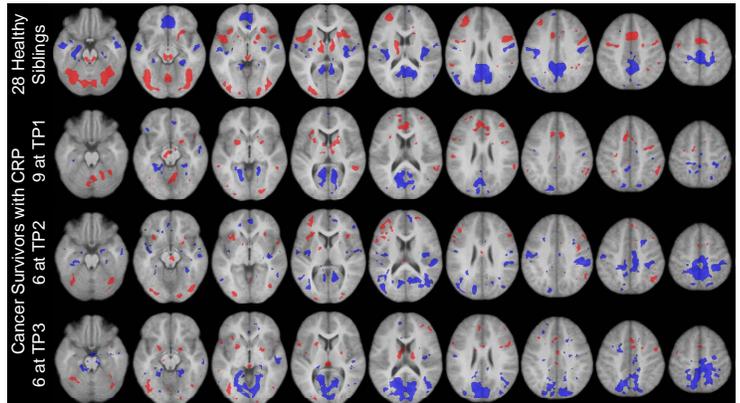
While cure rates for childhood lymphoblastic leukemia (ALL) and brain tumors (BT) have increased dramatically in recent decades, survivors of ALL and BT have a high incidence of cognitive deficits, which are associated with brain injury caused by central nervous system (CNS) disease and/or treatments directed at the CNS. As the most ambitious test of cognitive remediation for brain injury with either children or adults, a randomized clinical trial of the Cognitive Remediation Program (CRP) was conducted on pediatric cancer survivors at seven sites in the United States¹. Optional imaging examinations were offered to the participants at one site for a pilot study to investigate the utility of functional MRI (fMRI) to identify neural correlates of cognitive deficits and response to remediation. Here we report the fMRI responses to a continuous performance test (CPT)² from pediatric cancer survivors during the CRP trial.

Methods

Subjects: The fMRI study was approved by the IRB, and informed consent was obtained from each participant. At our site, 20 BT and ALL survivors (12 on CRP and 8 wait-list controls) were eligible for the CRP phase III clinical trial¹ and all were offered optional fMRI exams at three time points: baseline at screening (TP1), six months after TP1 when the CRP sessions were completed (TP2), and six months after the end of CRP (TP3). Survivors in the control group were also offered CRP after TP2. As a result, fMRI data were acquired 14 survivors (6 controls and 8 on CRP, age 12.2±0.9 years) at TP1; 10 survivors (4 controls and 6 on CRP) at TP2; and 6 survivors (all on CRP) at TP3. Finally, fMRI data were obtained in 28 age-matched healthy siblings (age 12.7±0.6 years) of the survivors at one time point. **The CRP:** a tripartite model that combined interventions derived from brain injury rehabilitation, educational psychology, and child clinical psychology. Participants in the CRP were trained on 20 two-hour weekly sessions over 4-5 months¹. **fMRI:** A modified Conners' CPT was used in the fMRI exams². The task was to push a button for every serially presented letter except 'X' during task blocks and to look at a fixation cross during rest blocks. fMRI data were analyzed with SPM software (<http://www.fil.ion.ucl.ac.uk/spm/>). Images were normalized to the standard MNI space and survivors with brain lesions that interfered the normalization were excluded from 2nd level random effect analyses. **MRI:** 1.5T Siemens Symphony scanner. Single shot T2*-weighted EPI (TR = 2.06 sec, TE = 50 msec, FOV = 192 mm, matrix = 64x64, slice thickness = 5 mm, 23 slices, and bandwidth = 1954 Hz/pixel) was used for fMRI data acquisition.

Results and Discussion

Group activation maps for the CPT are shown in the figure. Sites with greater activation during task blocks are shown in red; sites with greater activation during rest blocks are shown in blue. The healthy sibling's brain activation was consistent with existing models of motor control, visual object processing and attention control and was almost the same as the adult's brain activation with the same fMRI paradigm². The survivor's brain activation was remarkably less than the sibling's in the frontal, temporal, and occipital cortices during task periods and in the orbital frontal region during rest periods. After the CRP, more left occipital/temporal activation at TP2 and TP3 than at TP1 and more left frontal activation at TP2 than at TP1 were noticed. These changes may indicate more efficient letter recognition to support task performance after remediation. However, due to the small number of participating survivors, these changes were not detected in the more rigorous 2nd level comparison analyses among the different time points and between the control and the CRP groups of the survivors.



Conclusions

The multicenter clinical trial of the CRP demonstrated gains for the participants while long-term clinical significance remains unknown¹. This pilot fMRI study showed that fMRI is feasible in the childhood cancer survivors during remediation, and the differences in activation between survivors and healthy children suggests that fMRI will be useful to investigate the neural correlates of the cognitive deficits that these patients suffer. Furthermore, changes in patterns of activation in survivors following remediation may yield insights into the neural basis of response to remediation and help to understand why some survivors respond better than others.

References

1. Butler RW, et al., J.Consult Clin.Psychol. 2008;76:367-378.
2. Ogg RJ, et al., Magn Reson.Imaging 2008;26:504-512.