

Cerebellar Vermis Impairment in Children Treated for Brain Malignancies

A. Horska¹, A. LaClair², M. Mohamed¹, C. T. Wells³, T. McNutt¹, M. Wharam¹, E. M. Mahone⁴, and W. Kates²

¹Johns Hopkins University, Baltimore, MD, United States, ²SUNY Upstate Medical University, Syracuse, NY, United States, ³Children's National Medical Center, Rockville, MD, United States, ⁴Kennedy Krieger Institute, Baltimore, MD, United States

Introduction

Cerebellar vermis, the median segment of the cerebellum, is involved both in motor functions and non-motor behaviors.¹ In children diagnosed with brain tumors, vermal injury may result both from the presence of a tumor or from treatment, which may involve combinations of surgery, adjuvant chemotherapy, and radiation. In this prospective longitudinal study, early-delayed effects of radiation treatment in children with brain tumors or leukemia were evaluated 6 months post-radiation. The aims of this study were to assess 1) changes in anterior and posterior vermal volumes and neuropsychological performance between the two visits, 2) the effect of radiation dose on vermal volumes, and 3) association between vermal volumes and neuropsychological performance.

Methods

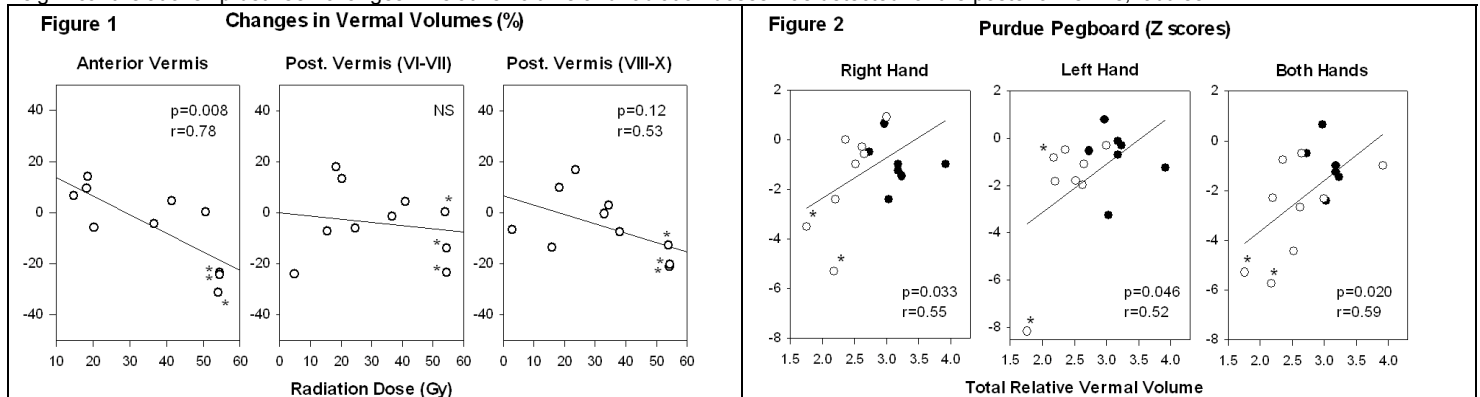
Subjects: Ten patients (7 boys, 11.6 ± 4.0 years old) treated with brain radiation were examined; the group included 3 patients with medulloblastoma who had surgery to the vermis. Ten healthy children (7 boys, 12.1 ± 3.4 years old) comprised the control group. Subjects were examined at baseline and a 6-month follow-up (in patients, after completion of radiation). **MRI:** 3-D SPGR was acquired at 1.5 Tesla with 1.5 mm slice partitions. The vermis was measured according to a modified protocol.² The midsagittal slice and one slice to the right and one to the left, were identified on each image dataset. Separate ROIs for anterior (I-V), posterior VI-VII, and posterior VIII-X lobules, drawn on all 3 slices, were used for volume calculations. In order to control for differences in brain size, volumes of the vermal subregions were divided by total cranial volume obtained at the baseline visit, resulting in relative volumes. **Neuropsychological assessment:** A battery of tests providing a broad sampling of relevant neurobehavioral domains (visual selective attention and processing speed, rapid lexical retrieval, visual-spatial working memory, visual discrimination, fine motor dexterity and speed, sustained attention, and motor persistence and inhibition) was employed. **Statistical analysis:** Two-sided T-tests were applied to compare vermal volumes and neuropsychological performance between patients and controls. For neuropsychological tests showing significant differences between patients and controls, correlation analyses were also used to evaluate the relationship between total relative vermal volumes and neuropsychological test scores at baseline and the 6-month follow-up. Linear regression analyses were used to examine the relationship between changes in relative vermal volumes (in %) and radiation doses.

Results

The following number of subjects (N=number of patients/number of controls) completed the MRI and neuropsychological (NP) evaluations: baseline (N=10/10 for both MRI and NP), first follow-up (N=10/8 for MRI, 9/8 for NP, mean time since the baseline visit 0.61/0.54 years).

There was no significant difference in the total cranial gray and white matter volume at baseline between patients (1200.9 ± 118.5 cm³) and controls (1155.3 ± 180.8 cm³) (t-test, p=0.51). However, at the baseline visit, the volume of the anterior vermis lobules I-V was 13% lower (p=0.051), volume of lobules VI-VII was 23% lower (p=0.01), and volume of lobules VIII-X was 33% lower (p=0.002) in patients compared to controls. In the patients who did not have surgery to the vermis, the volume of lobules VIII-X was 19% lower (p=0.02; N=7) compared to controls. No overall changes in relative volumes of vermal subregions between baseline and 6-month follow-up for either controls or patients with diagnoses other than medulloblastoma were detected (relative volume changes <4%). However, a significant decrease in relative volume of the anterior vermis (-26 ± 4%; p<0.001 compared to controls) and of the posterior vermis, lobules VIII-X (-18.1 ± 4.7%; p=0.03) was observed in the three medulloblastoma patients.

Linear regression analyses showed an association between changes in anterior and posterior vermal volumes between the two examinations and radiation doses (anterior vermis: r=0.78, p=0.008, posterior vermis, lobules VIII-X: r=0.53, p=0.12) (**Figure 1**; * denotes medulloblastoma patients). No significant relationship between changes in relative volume and radiation doses was detected for the posterior vermis, lobules VI-VII.



Patients had lower scores on processing speed (Visual Matching) and motor speed (Purdue Pegboard-Both Hands) (p<0.05) than controls. The Purdue Pegboard Right Hand and Left Hand scores also tended to be lower in patients (p<0.06). No significant changes in any of the neuropsychological measures between baseline and 6-months follow-up were detected in either controls or patients.

A significant relationship between total vermal volumes and Purdue Pegboard test scores was revealed, such that better (faster) performance was associated with greater total relative vermal volumes (Right Hand: r=0.55, p=0.033; Left Hand: r=0.52, p=0.046, Both Hands: r=0.59, p=0.020) (**Figure 2**; data from the 6 month follow-up scan; patients-open circles, *medulloblastoma patients; controls-filled circles).

Discussion and Conclusions

Lower relative vermal volumes in patients with brain tumors treated with combinations of surgery, chemotherapy, and brain radiation, compared to healthy children were detected prior to the completion of radiation. Impaired neuropsychological performance was observed in patients at baseline, with stable deficits remaining at 6 months post radiation. It is possible that pathological changes to the brain associated with presence of malignancy or initial clinical interventions may contribute to reductions in vermal volumes and affect neuropsychological performance. By 6 months post-radiation, further decrease in vermal volumes was detected only in patients with medulloblastoma; the decrease in vermal volumes was not associated with a corresponding decrease in neuropsychological performance. Across participants, however, there was a significant association between motor speed and vermal volumes observed at 6-month follow-up, indicating the sensitivity of measures of fine motor speed to changes in vermal anatomy.

References 1. Schmahmann JD et al. *Brain* 1998; 121:561-2. Mostofsky SH et al. *Neurology* 1998;50:121-130.

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