Therapeutic Effect of Intensive Sensory Motor Integration Training in Children with ADHD: a multimodal approach using fMRI and VBM

C. Lai[1], T-C. Yeh[1,2], C-M. Cheng[3], M-H. Yen[4], and S-S. Jung[5]

[1]Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan, Taiwan, [2]Department of Medical Education and Research, Taipei Veterans General Hospital, Taipei, Taiwan, Taiwan, [3]Department of Medical Research and Education, Taipei Veterans General Hospital, Taipei, Taiwan, Taiwan, [4]BioInno Health Technology, Taipei, Taiwan, Taiwan, [5]Taiwan Research Institute of Learning Disability, Taipei, Taiwan, Taiwan

Background

Attention Deficit Hyperactive Disorder (ADHD) in children can be effectively treated with Sensory Motor Integration (SMI) training (Jung 1998 and 2003). However, the correlation of brain activity levels with the resulting improvements was not well delineated. This study utilized BOLD-based fMRI using attention Go/No-Go task, voxel-based morphometry (VBM) and behavior ratings to investigate the efficacy and brain locations responsive to SMI training.

Materials and Methods

(1) Normal/ADHD subjects and behavioral study

The study subjects included 10 normal male students, 10 male students with ADHD/C (combined type ADHD as defined by DSM-IV) post-SMI training, and 10 male students with ADHD/C pre-SMI training with the approval of institutional ethic and radiation safety committees of Taipei Veterans General Hospital. The age of the subjects ranged from 9 -12 years old (11.2 +/- 1.4, mean +/- one standard deviation), none were taking medications, and all had an IQ above 90. Behavioral data were collected from three groups for (1) parents' SMI checklist, (2) parents' ADHD checklist, and (3) behavior rating by the child's elementary school teacher before and after SMI training.

(2) FMRI and VBM

All three groups underwent BOLD- based fMRI study using the attention paradigms of Go/No-Go task with response-controlled and stimuli-controlled sessions as previously described in pharmacological approach (Vaidya et al, 1998). Block-designed paradigms were implemented using Presentation software (Neurobehavioral Systems, CA, USA) with graphic materials delivered by a mirror system in MR scanner. Each task lasted approximately 9 minutes and consisted of eight alternating go, no-go and fixation blocks, each 22 seconds. For go blocks without target picture, subjects were instructed to press a button for every picture. For no-go blocks, subjects were instructed to press the button for every picture except the target picture, which appeared 50% of the trials. In the response-controlled session, go and no-go blocks had equal numbers of key presses. In the stimulus-controlled task, go and no-go blocks had an equal rate of presentation differed in the number of button presses.

Images were acquired using a 1.5T MRI system (Sonata, Siemens, Germany) equipped with an actively shielded gradient and a quadrature head coil. Subjects' heads were immobilized with a vacuum bean-pad in the scanner. Functional data were acquired with a T2*-weighted gradient-echo EPI (TR/TE/θ= 2000 ms/40 ms/90°, slice thickness = 5 mm, inter-slice interval = 1 mm, FOV = 230 mm, 64 × 64 × 20 matrix, whole brain covered). For each slice, 269 images (NR, repetition number) were acquired. The first five dummy images were discarded from the analysis to eliminate non-equilibrium effects of magnetization. Anatomical images were acquired using a high-resolution 3D T1-weighted, MP-RAGE sequence (Magnetization Preparation Rapid Gradient Echo; TR/TE/TI/θ= 1810 ms/4 ms/1100ms/15°, 256 × 256 × 128 matrix, FOV = 230 x 230 x 192 mm). VBM study of the anatomical images was conducted using data of ADHD/C pre-SMI training and normal groups.

(3) Data Analyses

Data were analyzed with statistical parametric mapping (SPM2, the Wellcome Department of Cognitive Neurology, London, UK). Scans were time corrected, realigned, normalized, and spatially smoothed with a 8-mm FWHM Gaussian kernel. Hierarchical subtractions between the tasks were done to examine differential engagements of attention processing. Regions of interest were evaluated using a significance level threshold set at $P < 0.001$ (uncorrected) with spatial extent larger than 20 voxels. Fixed-model group analyses were obtained for each group. *Z* maxima were localized on the normalized T1 structural image and labeled using the nomenclature of Talairach and Tournoux. VBM was performed using optimized VBM procedures adapted to SPM2 with deformation modulation and self-template of ADHD/C pre-SMI training and normal groups.

Results

MANOVA analysis of all behavior ratings showed a significant difference ($P < 0.05$) in the post-SMI training group. In response-controlled sessions, No-Go vs Go results revealed a significant difference ($P < 0.05$) between the pre- and post-SMI training groups in the pre-frontal area, medial frontal area, cingulate gyrus, and caudate nucleus (**Figure 1**). The pre-SMI training group showed limited activation in fronto-striatal regions. As compared to normal controls, the post-SMI training group showed improvement of activation in corresponding regions. BOLD-based fMRI results in the post-SMI training group were correlated with clinical improvements based on teachers' and parents' observations and check-list findings of improved full concentration, skillful fine movement and execution ability. VBM showed reduction of gray matter in left prefrontal, left parietal and right temporal regions in ADHD/C pre-SMI group.

Conclusions

Functional and morphological correlates of ADHD were illustrated by optimized VBM and BOLD-based fMRI using Go/No-Go attention paradigm. Intensive SMI training is an effective and lasting therapeutic intervention for children with ADHD.

Acknowledgement

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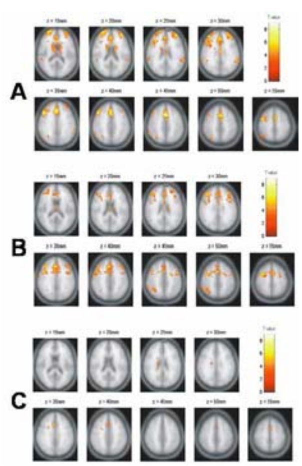

Figure 1 : Improved BOLD activation in fronto-striatal regions in No-Go vs. Go results; A: normal subject; B: ADHD/C post-SMI training; C: ADHD/C pre-SMI training

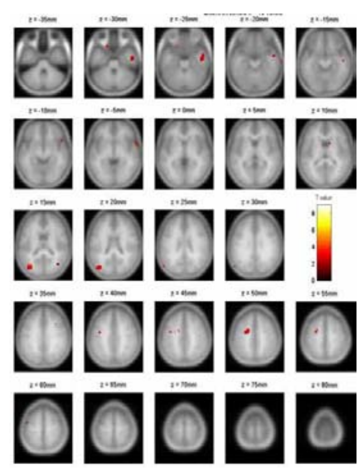

Figure 2 : VBM showed gray-matter volume reduction in left prefrontal, left parietal and right temporal regions in naive ADHD group.

References

Jung 1998, Special Education Quarterly 66, 4-8; Jung et al 2003, Manual of The International Conference of The Special Education 271-290; Vaidya et al, 1998, PNAS USA, 95, 14494-9.