Individualized prediction of ADHD based on patterns of altered tract integrity over the whole brain: a performance test on adult females with ADHD using diffusion spectrum imaging

Yu-Jen Chen[1], Yun-Chin Hsu[1], Yu-Chun Lo[1], Shur-Fen Susan Gau[2], and Wen-Yih Isaac Tseng[1,3]

[1]*Center for Optoelectronic Medicine, National Taiwan University College of Medicine, Taipei, Taipei, Taiwan,* [2]*Department of Psychiatry, National Taiwan University Hospital, Taipei, Taipei, Taiwan,* [3]*Molecular Imaging Center, National Taiwan University, Taipei, Taipei, Taiwan*

Objectives: Diffusion magnetic resonance imaging has been widely used to investigate structural differences between patients with mental disorders and healthy participants. However, there is no study showing the capability of individualized prediction of the mental disorder based on the differences in tract integrity over the whole brain. In this study, we used the tract-based automatic analysis (TBAA) method [1] and performed a test of the method to predict adult females with attention deficit/hyperactivity disorder (ADHD). TBAA, a software tool developed in-house, provided the estimation of generalized fractional anisotropy (GFA) along predefined 74 major tracts over the whole brain. Subjects were separated into an investigating group (A) and a predicting group (B). Whole-brain difference (WD) was defined from group A. A series of masks were determined at different effect sizes (ES) and cluster sizes (CS) from WD; the cluster size was defined as continuous steps with the same level of ES. Individual subjects of group B were compared step by step with WD and different indices derived from different masks were assigned to each subject to predict disease . The performance of prediction was evaluated using receiver operating characteristic (ROC) curve analysis. In this study, we selected a subgroup of ADHD, i.e. adult females with ADHD, to examine the performance of the method.

Methods: Figure 1 shows the flow chart of our method. Twenty ADHD females (blue) and 20 matched healthy females (red) (ADHD: 31.3 ± 8.4, range: 18-47 years old; controls: 30.6 ± 8.1, range: 18-45 years old) were recruited in the analysis of group A. Images were acquired on a 3T MRI system with a 32-channel head coil (Tim Trio, Siemens, Erlangen, Germany). Diffusion spectrum imaging (DSI) was acquired for 102 diffusion encoding gradients with the maximum diffusion sensitivity b_{max} = 4000 s/mm^2 using a twice-refocused balanced echo diffusion echo planar imaging sequence (TR/TE = 9600/130 ms, image matrix size = 80 x 80, spatial resolution = 2.5 x 2.5 mm^2, and slice thickness = 2.5 mm). TBAA method [1] was applied to subjects to assess the whole-brain white matter properties. A total of 7400 GFA values, named connectogram, were estimated at 7400 localized steps along 74 tracts as standardized information for each subject. WD was determined by comparing the mean GFA values at each of 7400 steps between two groups. Series of masks were determined to represent the locations containing different ES and CS in WD (ES: 0, 0.05, 0.1,..., 1; CS: 1, 2, 3,..., 15). For group B (15 ADHD: 32.1 ± 7.8, range: 19-43 years old; 17 controls: 30.1 ± 8.2, range: 18-43 years old), the whole-brain tract information of each subject was assessed by performing TBAA first. An ADHD-like index (ALI) was then estimated for each subject by using following steps. 1) ADHD-or-control maps (AOC) were estimated for all 7400 steps by comparing the connectogram with WD. Steps with GFA values closer to ADHD than to control were noted as ADHD-liked, otherwise as control-liked. 2) Masked AOC (mAOC) was derived by applying a mask to AOC. Steps passing the criteria of the mask were reserved for mAOC. 3) ALI was defined as the number of steps which were ADHD-liked in the mAOC. The performance of prediction was evaluated with ROC curve analysis by comparing the ALI scores and clinical diagnostic results. Masks with different criteria of ES and CS were applied to evaluate what kind of difference between ADHD patients and healthy participants over the whole brain has the best capability in distinguishing the two groups.

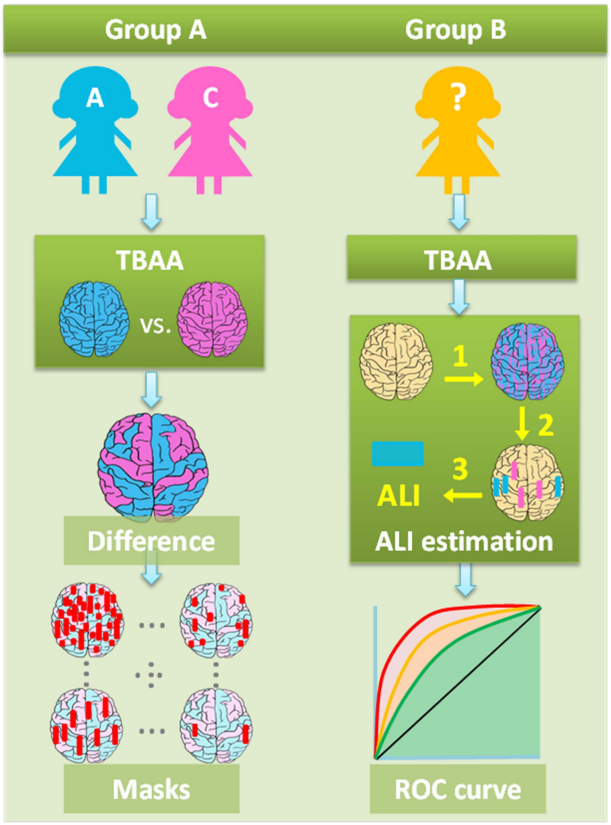

Figure 1. The schematic diagram of the method

Results: Figure 2 shows the maps of area under ROC curves (AUC) (red with AUC > 0.8, yellow with AUC ≥ 0.7, and green with AUC < 0.7). The lower left corner of the map indicated the AUC without applying any mask. The highest AUC of 0.84 was found when the mask with ES > 0.75 and CS > 4 steps (about 4 mm of tract length) was applied.

Conclusions: In this study, we examined the performance of predicting adult females with ADHD based on the patterns of altered tract integrity over the whole brain. The whole-brain tract information was compared with predefined differences between ADHD and healthy participants to calculate an index of ALI indicating the similarity with ADHD. Our results showed that the prediction performance was high (AUC > 0.8) when we compared the steps with high ES (ES > 0.65) and more continuous neighbors along tracts (CS > 4). In conclusion, the information of the whole-brain tracts estimated by TBAA method is potentially useful for predicting adult female with ADHD. Our study warrants a prospective study to validate the diagnostic accuracy of the method.

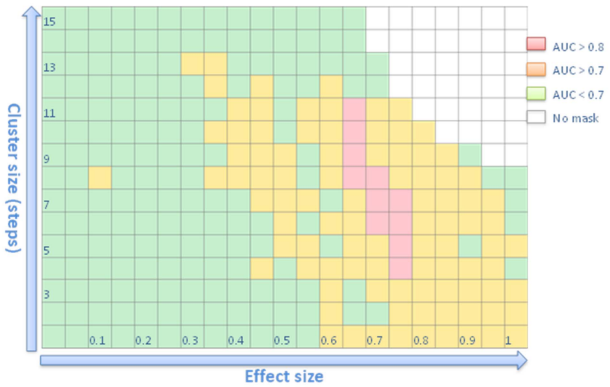

Figure 2. Maps of area under curves.

Reference: [1] Chen, Y. J. et al. (2014).