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## **Children with ADHD exhibit lower fMRI spectral exponent than their typically developing counterparts**

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### **Introduction**

Complex interactions in nonlinear systems such as the human brain exhibit fractal processes which are outcomes of self-similar patterns over long time scales by a power law in the frequency domain (Schaefer et al 2014). The spectral exponent ( $\gamma$ ) of this power law can be observed as an estimator of relative health and disease especially in the case of 1/f power spectrum. It has been shown that the spectral exponent ( $\gamma$ ) of resting state fMRI time series generally lies in the range  $-1 < \gamma < 1$  (Wink et al 2006). When the spectral exponent ( $\gamma$ ) is negative, the fMRI time series exhibits greater power at low frequencies. When spectral exponent ( $\gamma$ ) is positive, the fMRI time series depicts greater power at high frequencies and when spectral exponent ( $\gamma$ ) is zero, the fMRI time series have equal power at all frequencies (Maxim et al. 2005). The aim of this pilot study is to estimate the fractal behaviour (using spectral exponent) of resting state fMRI time series of children with ADHD when compared to age-matched and gender-matched typically developing children (TDC). We expect the spectral exponent of the children with ADHD to be significantly different from that of their typically developing counterparts.

### **Methods**

Ten children with ADHD (5 female, mean age (11.05±1.67)) and ten typically developing children (5 female, mean age (10.95±1.13)) were extracted from the Kennedy Krieger Institute's resting state fMRI data repository deposited via the ADHD-200 Sample initiative. The study was approved by the local research ethics committee. Exclusion criteria included visual or hearing impairment, neurological and psychiatric disorders. Also, children with ADHD taking psychoactive medication were excluded. All children completed the Conner's Parent Rating Scale-Revised, Long version (CPRS-R) and Wechsler Intelligence Scale. Resting state fMRI data were acquired with a  $T_2^*$  weighted echo-planar imaging sequence (EPI) using SENSE 8 channel head coil in the axial plane with TR of 2500 ms, TE of 30 ms, matrix 96x96, thickness of 3 mm and 47 slices per volume (remaining 120 volumes in total after discarding the first four volumes). The fMRI data were pre-processed and the spectral

exponent characterized generating whole brain maps (using MATLAB). The statistical analyses were performed with SPSS and SPM12.

## Results

The result of the general linear model after adjusting for age shows that the mean whole brain  $\gamma$  differences between children with ADHD ( $0.559 \pm 0.019$ ) and TDC ( $0.636 \pm 0.019$ ) were significantly different ( $p=0.011$ ). When the  $\gamma$  maps were tested regionally at a corrected cluster level significance of  $p < 0.05$ , the result of the two-sample t-test (Bonferoni familiar wise error correction across the whole brain) after adjusting for age, shows significant  $\gamma$  differences between children with ADHD and TDC (Figure 1A) at the Precuneus and Cingulate Gyrus. Here, children with ADHD have lower  $\gamma$  values than the TDC. When the association between the mean whole brain  $\gamma$  values and ADHD index was tested, a significant negative correlation ( $p=0.003$ ,  $r= -0.622$ ) was found. Also, a significant negative correlation was obtained between  $\gamma$  and the ADHD index for the whole sample using the multiple regression analysis in SPM12 (Bonferoni familiar wise error correction across the whole brain) at the left Precuneus, left Cingulate Gyrus and right middle occipital gyrus (see Figure 1B). No differences in full-scale intelligence were found.

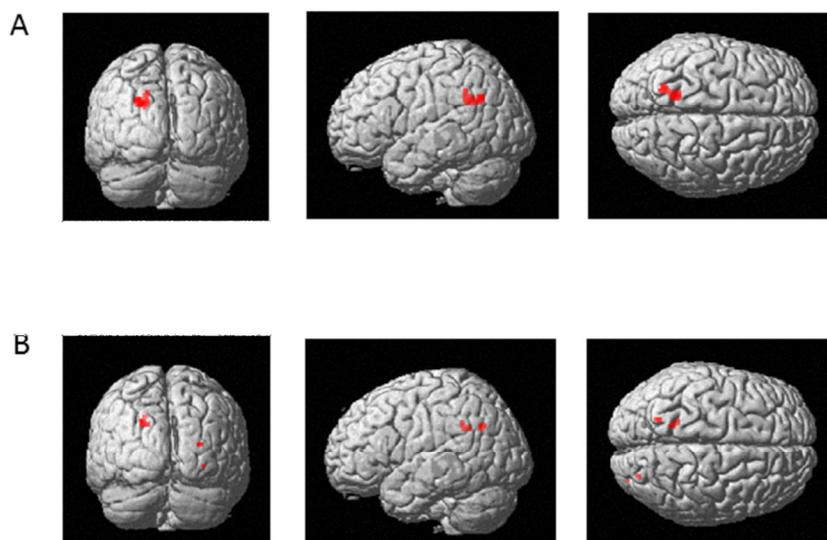


Figure 1: (A) Differences in spectral exponent between children with ADHD and typically developing children. (B) Correlation between the spectral exponent of the whole sample and their ADHD index.

## Conclusions

Our analysis shows that both the children with ADHD and TDC exhibited positive spectral exponent ( $\gamma$ ) which implies that their fMRI time series depicts greater power at high frequencies. However, the children with ADHD exhibited significantly ( $p < 0.05$ ) lower spectral exponent ( $\gamma$ ) than their typically developing counterparts in brain regions consistent

with abnormalities in ADHD brain dynamics. Our results have shown that spectral exponent ( $\gamma$ ) may be a useful tool in revealing abnormalities in ADHD brain dynamics.

### **Acknowledgments**

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### **References**

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