Effects of gender and music on global functional connectivity density at 4T MRI

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INTRODUCTION: The local functional connectivity density (*l*FCD)[1] of the brain hubs has been shown to increase when subjects listen to music compared to when they don't, while resting with their eyes open in the MRI scanner[2]. However whether such significant variations could be detectable by standard graph theory measures of degree centrality (i.e. global functional density, *g*FCD) has not been tested yet. Here we used magnetic resonance imaging (MRI) and *g*FCD whole brain mapping to determine the number of functional connections at each voxel location in 113 healthy subjects (age = 18-56; 74 males and 39 females). Our working hypothesis was that music would increase the *g*FCD in the brain. We further hypothesized that these increases would be correlated with music "liking" scores across subjects and be affected by gender.

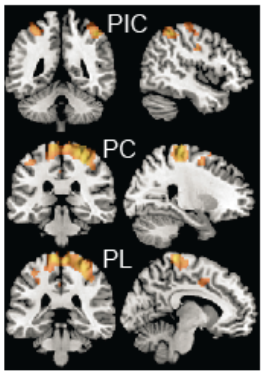

Fig. 1 *g*FCD enhancement in parietal inferior cortex (PIC), precentral cortex (PC) & paracentral lobule (PL) under conditions with vs. without music (P*corr* < 0.001; Within-subjects ANOVA)

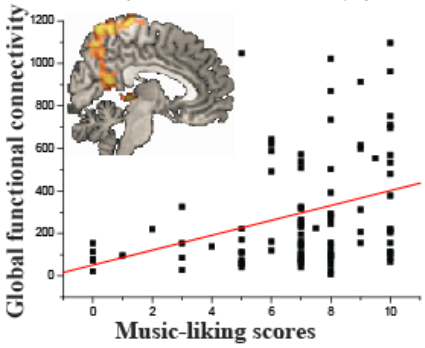

Fig. 2 Correlation between *g*FCD and music-liking scores for 91 subjects in L paracentral lobule; BA 6 (Simple regression; R = 0.34146; SD = 255.27615; N = 91; P*corr* = 9.24837E-4)

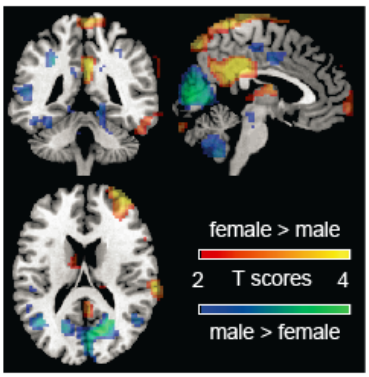

Fig. 3 *g*FCD distribution with and without music compared between male and female subjects (P*corr* < 0.001; Within-subjects ANOVA with a gender covariate)

METHODS: Two conditions were tested when subjects rested with their eyes open in the MRI scanner: 1) resting state without stimulation other than the minimal acoustic noise of the MRI acquisition (baseline condition), and 2) resting state while in addition subjects listened to classical music through MRI compatible headphones [music condition: the Death of Aase (Peer Gynt; Suite No.1, Op.46 – 2; Berliner Philharmoniker; 1988) by Edvard Grieg].Functional MRI datasets (N = 226; 113 pairs) with blood oxygenation level dependent (BOLD) contrast were acquired in a 4-Tesla Varian/Siemens scanner using a T2*-weighted single-shot gradient-echo planar imaging sequence (TE/TR = 20/1600 ms, 3.1 mm resolution, time points = 195). Earplugs (28 dB attenuation of sound pressure level) and headphones (30 dB attenuation of sound pressure level) were used to further minimize the interference effect of scanner noise during MRI acquisition. Immediately after the music condition scan, subjects rated how much they liked the music (from 0 to10). The fMRI time series were realigned and spatially normalized to the MNI stereotactic space using SPM2. Signal fluctuations associated with subject's motion (multi regressions with the six realignment parameter) and physiologic noise (0.01-0.10 Hz band-pass filtering) were removed[1,2]. *g*FCD maps with 3-mm isotropic resolution were computed for each condition and subject using Pearson correlation (R > 0.6) and data parallelism. A workstation with 24 processing threads was used to speed up the calculation of the *g*FCD (CPU time: 5-min/ per subject at 3-mm isotropic resolution)[4]. The *g*FCD maps were spatially smoothed (8-mm). Within-subjects ANOVA with a gender covariate and simple regression analyses were used to evaluate music and gender related changes on *g*FCD using SPM2.

RESULTS: Figure 1 shows that the *g*FCD in motor and somatosensory cortices was significantly increased while subjects listened to music compared to when they did not ($P_{corr} < 0.001$). In addition, regression analyses across 91 subjects showed that the music "liking" scores had a positive correlation with the strength of the gFCD in precuneus and the motor cortex (Fig. 2; $P_{corr} < 0.0001$). Significant gender effects on the *g*FCD were observed (Fig 3). Females had higher *g*FCD than males in default mode network regions (precuneus/posterior cingulate, the main short-range hub in the human brain[1], and motor cortex), while males exhibited higher *g*FCD than females in the visual cortex (the main long-range hub in the human brain[3]) ($P_{corr} < 0.0001$).

DISCUSSION: The enhancement of the *g*FCD by classical music (relative to baseline) and the significant correlation between the music-liking scores with *g*FCD in the precuneus and motor cortex support the hypothesis that music perception involves both cognitive and sensory-motor functions[5] where auditory-motor interactions and the motor cortex have important roles in music processing [5]. The gender effects on *g*FCD at 4 Tesla corroborate similar effects previously reported in a large sample[4], suggesting a gender dimorphism in the brain functional connectivity than supports music perception.

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