Dynamic emotional memory network in aging brain

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Introduction: Emotional memory is an important brain cognitive function and shows a positive affective bias in healthy aging [1]. However, previous studies considered the extracted time series as stationary processes [2]. Recently, studies show that dynamic coupling or functional connectivity (FC) patterns between brain regions are distinct from underlying anatomical links [3]. Emerging evidence suggests that dynamic FC may index changes in brain function or clinical biomarker. Understanding of dynamic emotion networks is important to characterize aging brain development and the related brain disorder. The aim of this study is to investigate the time-frequency features of dynamic emotional memory network FC in aging brain by using wavelet transform coherence (WTC).

Participants and methods: The right-handed participants are divided into two groups. Young group includes 28 subjects (age 19-33 years, mean 24.3±4.6 years, 17 male), Older group includes 27 subjects (age 60-85 years, mean 71.2±7.6 years, 13 male). The resting state fMRI data of two groups are obtained from Nathan Kline Institute-Rockland Sample (NKI-RS) [4]. The data preprocessing includes slice time correction, motion correction, skull stripping, coregistration, spatial smoothing (FWHM=6, sigma≈2.55), band-pass filtering (0.005-0.1Hz), linear and quadratic detrending. Then the images are normalized to Montreal Neurological Institute (MNI) template ($3\times3\times3mm^3$). All the steps are processed by AFNI and FSL.

To generate FC map, we use a 3mm-radius sphere centered at (-24, -3, -18) (MNI coordinate) in left amygdala (AMY) as seed region and voxel-based Pearson's correlation is employed. Two-sample *t*-test is then applied to calculate the significant difference between two groups ($p<0.05$, corrected by FDR). After that, we utilize the WTC to analyze the brain regions with significant difference intensively. For the sake of simplicity, four areas (FC (young>old): right precentral (60, -6, 42), right cingulate gyrus (3, 6, 45) and FC (young<old): right medial frontal gyrus (21, 66, 12), left anterior cingulate (-18, 33, 18)) are chosen to do WTC based time-frequency analysis. In each brain area, a 3mm-radius sphere centered at corresponding MNI coordinate is used as region of interest. Additionally, according to Han's work [5], we further investigate the difference in four sub-bands (Slow-6 (0.005-0.01Hz), Slow-5 (0.01-0.027Hz), Slow-4 (0.027-0.073Hz) and Slow-3 (0.073-0.1Hz)) of low-frequency BOLD fluctuations (LFBF).

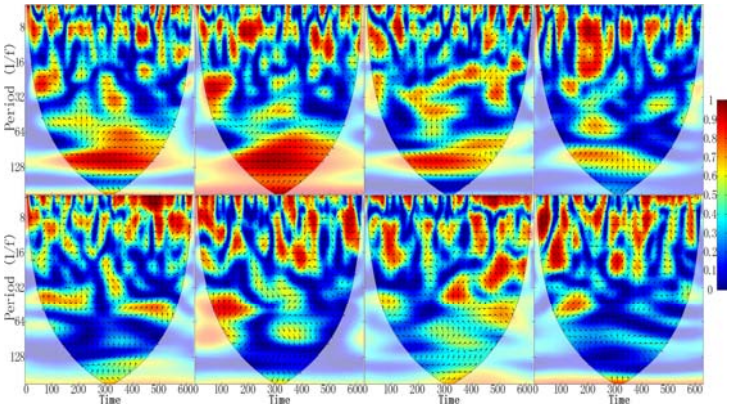

Fig. 1 WTC between left AMY and 4 selected areas. From left to right: right precentral/cingulate gyrus/medial frontal gyrus and left anterior cingulate. From top to bottom: young and old. Arrows indicate phase differences between two time series. Transparent white regions inside the cone of influence represent lower confidence of WTC (ignore these values).

Results and Discussion: Fig.1 shows the WTC of a young and an older subjects' time series between left AMY and four functional correlated areas (right precentral/cingulate gyrus/medial frontal gyrus and left anterior cingulated), respectively. As time and period (frequency) varying, the value of WTC is also changing. This demonstrates that the FC between two time series is not constant in both time and frequency scale. To investigate the difference in sub-bands of LFBF, we further define positive/negative time averaged coherence [3] based on WTC. Fig.2 shows the map of time averaged coherence between two groups. It can be seen that the differences of FC between two time series dependent on different frequency bands. More importantly, not all frequency intervals show significant difference between young and older group. Besides, more positive (negative) time averaged coherence is reflected if young group's FC is stronger (weaker) than older group. We calculate the sub-bands difference ($p<0.05$, corrected by FDR) between two groups (Fig.3). The selected areas exhibit differences in different frequency sub-bands (e.g. FC between left AMY and right precentral exhibits significant difference in frequency bands Slow-4 (positive), Slow-3 and Slow-4 (negative)). Although the causes and physiological functions of different frequency intervals in LFBF remain to be further proved, recent studies have found that the functional network at higher frequency bands (Slow-3 and Slow-4) can predict brain nodes activities at lower frequency bands [6] (Slow-4 and Slow-5) and EEG is related to the dynamic varying of LFBF to some extent [7]. Future work with both EEG and fMRI data will be helpful for exploring the in-depth mechanism of the differences in different frequency bands.

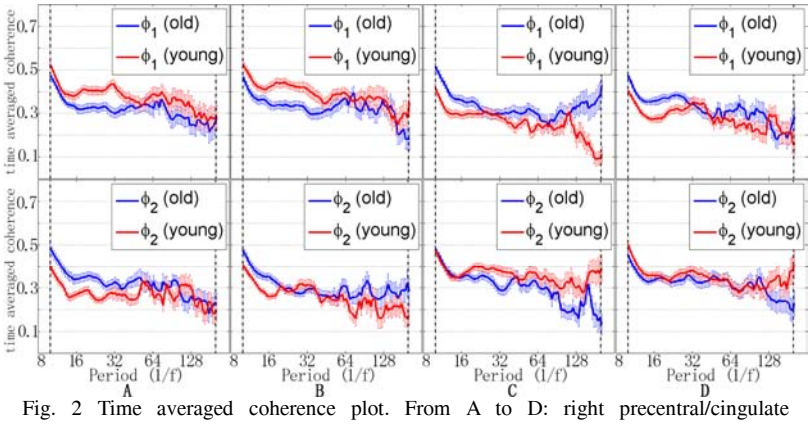

Fig. 2 Time averaged coherence plot. From A to D: right precentral/cingulate gyrus/medial frontal gyrus and left anterior cingulate. ϕ_1: positive time averaged coherence. ϕ_2: negative time averaged coherence. Black dash-dot line represents period which ranges from 10s to 200s (i.e. frequency, f ranges from 0.005Hz to 0.1Hz). Red and blue thick lines represent the mean across subjects in each group. And thin lines (error bars) represent standard error.

Conclusion: Time-frequency analysis can provide insight into the non-stationary signals. And we have confirmed that the dynamic functional connectivities of emotional memory show some differences in different sub-bands between the young and the old. The suitableness of WTC method for time-varying processes has been verified and it can offer a valid tool for the analysis of aging brain fMRI time series.

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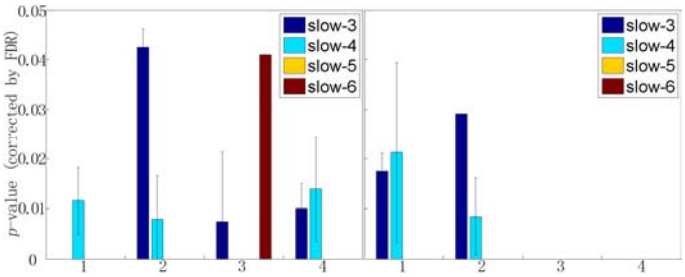

Fig. 3 The significant difference between left AMY and other brain regions in frequency sub-bands. Left: difference in positive time averaged coherence. Right: difference in negative time averaged coherence. Number 1-4 represent right precentral/cingulate gyrus/medial frontal gyrus and left anterior cingulated, respectively. Error bars represent standard error and activation bars represent the mean of *p*-value in each frequency sub-band.