The Cg25 Resting State Network

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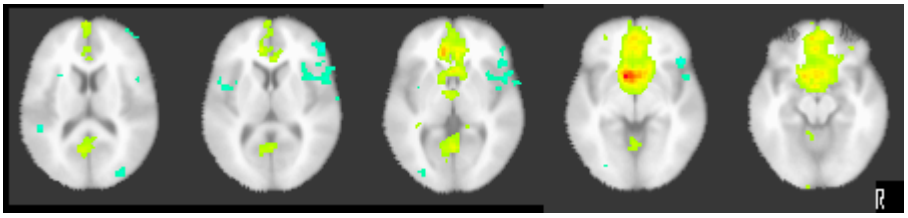
Resting state functional connectivity is a promising technique for assessing neural networks in clinical populations. Previously we have shown that resting state functional connectivity with the subgenual cingulate (Cg25) differentiates subjects with major depression from controls (1). In order to better understand the Cg25 resting state network we assessed its reproducibility in healthy subjects.

Participants & Methods: Eighteen adults (ages 22-53), with no history of psychiatry or neurological disorder participated in accordance with Institutional Review Board policy. Participants underwent functional imaging in a 3T Siemens Trio scanner (Siemens AG). A z-SAGA pulse sequence (2) was used to acquire functional images of the temporal lobe (matrix=64x64, TR=2020ms, TE=30ms, FA=90^o, FOV=220mm, 20 axial slices, slice thickness=4mm without gaps, voxel resolution 3.4 x 3.4 x 4 mm) while participants passively viewed a fixation point. Subjects also completed the Zung self-reporting depression scale (3).

Data Processing: Resting state datasets underwent slice-timing correction, motion correction, spatial smoothing with a 6.88mm (2 voxel) isotropic Gaussian filter and linear detrending prior to automatic co-registration to the N27 brain atlas in AFNI (4). The datasets additionally underwent 0.08 Hz low pass filtering to optimize functional connectivity analyses. A seed was defined as a voxel located at the N27 coordinates at the center of the subgenual cingulate. These coordinates were translated to each subject's original space using the inverse of the automatic co-registration transform. The mean time course was extracted from the seed and its four neighboring in-plane voxels. The extracted time course was used as a contrast of interest, along with the global mean time course, and six motion correction time courses as confounders, in a general linear model analysis to derive the functional connectivity maps. The overall resting state network was visualized by the mean correlation map that was constructed using a single sample t-test. Additional ROIs (subgenual cingulate (CG25), pregenual anterior cingulate (BA24), posterior cingulate (BA23), insula, medial frontal (BA10) and amygdala were selected from this map and the mean regression coefficient (beta value) was extracted for each. These values were correlated with both Zung depression index and age to better characterize the variability in the Cg25 network. Each functional connectivity map was binarized by converting beta values to z-scores and using a threshold of four standard deviations. A coincidence map was constructed by summing together these eighteen binarized connectivity maps.

Results and Discussion: The mean resting state network shows connectivity between right insula, BA10, anterior cingulate, posterior cingulate, and the subgenual cingulate (figure 1). Correlation analysis shows that strength of functional connectivity within Cg25 is positively correlated with depression scale. This is similar to the findings of (5). The strength of connectivity between Cg25 and amygdala and Cg25 with BA10 is strongly correlated with age (table 1). There is a weaker correlation between age and Cg25-Insula and Cg25-BA24. The coincidence map shows that subjects have varying amounts of connectivity with the seed in the subgenual region which includes the adjacent nucleus accumbens and hypothalamus. The anterior cingulate (BA24) is connected with the seed in about two thirds (12) of the subjects. The right insula and posterior cingulate are connected to the seed region in six of the subjects. Better understanding resting state subgenual cingulate connectivity in healthy subjects will help us better understand how this network is changed in depression. In the future we plan to further investigate this network in depressed and controls using structural equation modeling.



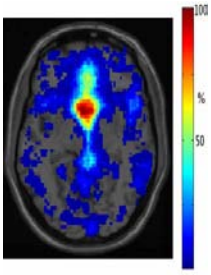


Figure 1 Cg25 Resting State Network. Figure 2 (right) Coincidence map.

	pcc	acc-ba24	cg25	insula	ba10	amygdala
R Zung	-0.21	-0.12	**0.63**	0.03	0.12	0.04
R age	-0.09	-0.37	-0.15	-0.33	**-0.52**	**0.48**

Table 1 ROI correlation with age and depression severity index, significant values in bold.

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