Structural equation modeling of resting-state temporal lobe functional connectivity

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Introduction: Functional connectivity analyses are used with increasing frequency to assess neural networks of clinical populations. These analyses allow inference as to how neural networks mediating cognitive tasks may be altered by clinical disorder. While such investigations typically focus on *task*-related (*i.e.* effective) alterations in functional connectivity patterns, resting-state (*i.e.* baseline) neural networks may likewise differ between clinical populations and healthy controls. Exploratory structural equation modeling was used to assess resting state networks in control populations for temporal lobe regions frequently associated with epilepsy.

Participants and Methods: Twenty-three adults 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 (Heberlein and Hu, 2004) 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.

Data Processing: Functional datasets underwent slice-timing correction, motion correction and linear detrending prior to automatic coregistration to the N27 brain atlas in AFNI (Cox, 1996). Functional datasets additionally underwent 0.08 Hz lowpass filtering to optimize functional connectivity analyses. Four regions of interest (right hippocampus, amygdala, insula, and dorsal thalamic nucleus) were defined as the voxel located at the ROI's N27 coordinates and its four neighboring in-plane voxels. The extracted mean timecourses of each ROI were submitted to exploratory factor analysis with structural equation modeling in LISREL (Scientific Software International). The thalamic nucleus was modeled as an exogenous variable since its correlation with other ROIs was minimal; no constraints were placed on the associations of remaining regions.

Results and Discussion: The strongest path weighting (-0.71) was observed from the amygdala to the anterior insula. The negative path weight implies an inverse relationship between these two regions. This inverse relationship may reflect the participants' fluctuating attention between external to internal stimulation, given the amygdala's function as a relevance detector for external stimuli and the insula's role in mediating interoceptive sensations (Wright and Liu, 2006; Augustine, 1996). The unexplained error variances of the amygdala and insula were strongly correlated ($r = 0.97$), suggesting a relationship between these regions that this model does not capture. The most probable explanation is that both regions are influenced by a third anatomical region not included in this model. Finally, the amygdala and hippocampus demonstrated no significant functional connectivity at rest despite their anatomical proximity. This finding supports recent evidence suggesting robust task-modulation of hippocampus-amygdala functional connectivity (Smith, 2006).

Summary: Structural equation modeling is a viable tool for assessing neural networks of resting state functional connectivity. Modeling neural networks of temporal lobe connectivity in healthy controls lays the groundwork for future analyses in clinical populations, specifically patients with temporal lobe epilepsy. Future directions include investigating the highly correlated error terms for the amygdala and insula, potentially by including additional ROIs in the model.

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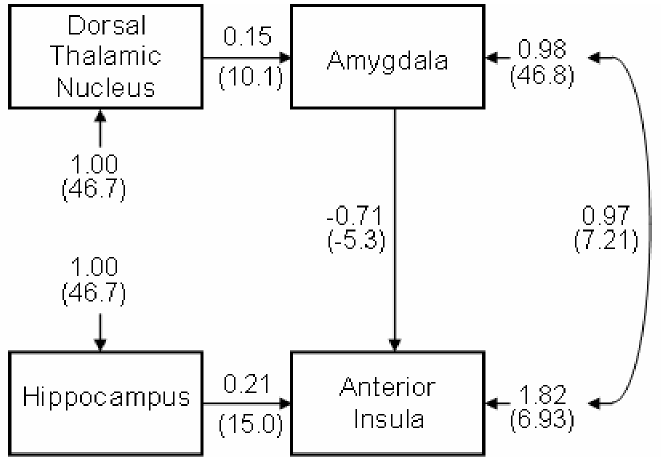

Figure 1: Structural equation model for temporal lobe resting state functional connectivity. Numerical values reflect path weights (single arrows) and correlations (double arrows), with t-scores in parentheses. GFI=0.99, AGFI=0.97, PGFI=0.20.