Patterns of activation and connectivity in fronto-temporal language networks during sentence processing in patients with schizophrenia: A multimodal imaging investigation

Kirsten Weber¹,²,³, Ellen Lau⁴, Ben Stillerman¹,³, Arim Choi Perrachione³, Nate Delaney-Busch³, Gina Kuperberg¹,²,³

¹Massachusetts General Hospital, ²Harvard Medical School, ³Tufts University, ⁴University of Maryland

During sentence comprehension, we bind words together to form a coherent message-level representation. To this end, areas of the language network, such as the inferior frontal and temporal gyri, need to communicate with each other. There is evidence that in patients with schizophrenia fronto-temporal connectivity is abnormal (Friston and Frith, 1995; Li et al., 2010), and that this may contribute to patients’ impairments in building and using context (Kuperberg, 2010). We conducted an MEG and fMRI experiment in which 17 patients with schizophrenia and 18 demographically matched controls read sentences and random lists of words (presented in pseudorandom order). Using both MEG and fMRI techniques, we looked at differences between patients and controls across the language network in contrasting sentences and word lists. With MEG, we examined sources of power modulation in the beta frequency band using beamformer source localization techniques. With fMRI, we examined BOLD activity. Both MEG and fMRI revealed differences between patients with schizophrenia and healthy controls in the modulation of inferior frontal and temporal regions. The control group showed the expected pattern of more activity within both regions to sentences versus random word lists. Patients, however, showed the opposite pattern of modulation, with more activity to the word lists than to the sentences. In the fMRI experiment, this abnormal increase in activity to the word lists was seen in both left temporal and left inferior frontal cortices, whereas in the MEG experiment, it was primarily seen in the bilateral inferior frontal cortices. Using fMRI, we also examined task-related functional connectivity patterns (McLaren et al., 2012). We defined a seed in the left posterior temporal gyrus and looked for brain-wide connectivity changes. Relative to controls, patients showed significantly reduced connectivity to the left inferior frontal gyrus when reading the sentences. Interestingly, relative to controls, patients also showed significantly increased connectivity to more anterior temporal regions when comparing word lists to sentences. These abnormal activation and connectivity patterns across frontal and temporal areas within the language network in patients with schizophrenia might contribute to their impairments in building and using context. Specifically, we suggest that the increased activity in temporal and/or frontal cortices to the word lists might reflect an inappropriate tendency to make sense of unrelated lists of words, contributing to the language and thought disorganization that can characterize schizophrenia.