

## Brain Functional Connectivity in World Trade Center Responders

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**Objective:** Functional connectivity of the default mode network (DMN) during rest has been shown to be different among adults with Mild Cognitive Impairment (MCI) relative to aged-matched individuals without MCI and is predictive of transition to dementia. Post-traumatic stress disorder (PTSD) is also associated with aberrant connectivity of the DMN. Prior work from this group has demonstrated a higher rate of MCI and PTSD among World Trade Center (WTC) responders relative to the general population. The current study sought to investigate the main and interactive effects of MCI and PTSD on DMN functioning. Based on prior work, we hypothesized that MCI, but not PTSD, would predict aberrant connectivity in the DMN.

**Participants and Methods:** 99 WTC responders aged 44-65 stratified by MCI status (yes/no) and PTSD status (yes/no) and matched for age in years, sex (male vs. female), race (white, black, and other), and educational attainment (high school or less, some college / technical school, and university degree), and occupation on September 11, 2001 (law enforcement vs. other) underwent fMRI using a 3T Siemens Biograph MR scanner. A single 10-minute continuous functional MR sequence was acquired while participants were at rest with their eyes open. Group-level analyses were conducted using SPM-12, with correction for multiple comparisons using AFNI's 3dClustSim. Based on this threshold, the number of comparisons in our imaging volume, and the smoothness of our imaging data as measured by 3dFWHMx-acf, a minimum cluster size of 1134 voxels was required to have a corrected  $p \leq .05$  with 2-sided thresholding. Spherical 3 mm seeds were placed in the dorsal (4, -50, 26) and

ventral (4, -60, 46) posterior cingulate cortex (PCC).

**Results:** Individuals with PTSD demonstrated significantly less connectivity of the dorsal posterior cingulate cortex (PCC) with medial insula ( $T = 5.21$ ), subthalamic nucleus ( $T = 4.66$ ), and postcentral gyrus ( $T = 3.81$ ). There was no difference found in this study for connectivity between groups stratified by MCI status. There were no significant results for the ventral PCC seed.

**Conclusions:** Contrary to hypotheses that were driven by a study of cortical thickness in WTC responders, the impact of PTSD appears to outweigh the impact of MCI on dorsal DMN connectivity among WTC responders stratified by PTSD and MCI status. This study is limited by several issues, including low number of female and minority participants, relatively small group cell sizes ( $n = 23-27$  per cell), a brief resting state sequence (10 minutes), and lack of a non-WTC control group. Importantly, responders are a unique population so generalizability to other populations may be limited. Individuals in the current study are now being followed longitudinally to relate baseline resting state functional connectivity with cognitive changes and changes in connectivity over a four-year period.

**Categories:** Psychiatric Disorders

**Keyword 1:** post-traumatic stress disorder

**Keyword 2:** mild cognitive impairment

**Keyword 3:** neuroimaging: functional connectivity

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## 66 A Recurrent Pattern of Posterior Vermis-Predominant Cerebellar Hypoplasia (Not Dandy-Walker) Occurring with Psychosis-Schizophrenia

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**Objective:** Schizophrenia (SCZ) is a neuropsychiatric disorder with strong genetic heritability and predicted genetic heterogeneity, but limited knowledge regarding the underlying

genetic risk variants. Classification into phenotype-driven subgroups or endophenotypes is expected to facilitate genetic analysis. Here, we report a teen boy with chronic psychosis and cerebellar hypoplasia (CBLH) and analyze data on 16 reported individuals with SCZ or chronic psychosis not otherwise specified associated with cerebellar hypoplasia to look for shared features.

**Participants and Methods:** We evaluated an 18-year-old boy with neurodevelopmental deficits from early childhood and onset of hallucinations and other features of SCZ at 10 years who had mild vermis-predominant CBLH on brain imaging. This prompted us to review prior reports of chronic psychosis or SCZ with cerebellar malformations using paired search terms including (1) cerebellar hypoplasia, Dandy-Walker malformation, Dandy-Walker variant, or mega-cisterna magna with (2) psychosis or SCZ. We found reports of 16 affected individuals from 13 reports. We reviewed clinical features focusing on demographic information, prenatal-perinatal history and neuropsychiatric and neurodevelopmental phenotypes, and independently reviewed brain imaging features.

**Results:** All 17 individuals had classic psychiatric features of SCZ or chronic psychosis as well as shared neurodevelopmental features not previously highlighted including a downward shift in IQ of about 20 points, memory impairment, speech-language deficits, attention deficits and sleep disturbances. The brain imaging findings among these individuals consistently showed posterior vermis predominant CBLH with variable cerebellar hemisphere hypoplasia and enlarged posterior fossa (a.k.a. mega-cisterna magna). None had features of classic DWM.

**Conclusions:** In 17 individuals with chronic psychosis or SCZ and cerebellar malformation, we found a high frequency of neurodevelopmental disorders, a consistent brain malformation consisting of posterior vermis-predominant (and usually symmetric) CBLH, and no evidence of prenatal risk factors. The consistent phenotype and lack of prenatal risk factors for CBLH leads us to hypothesize that psychosis or schizophrenia associated with vermis predominant CBLH comprises a homogeneous subgroup of individuals with chronic psychosis/schizophrenia that is likely to have an underlying genetic basis. No comprehensive targeted gene panel for CBLH has yet been defined, leading us to recommend

trio-based exome sequencing for individuals who present with this combination of features.

**Categories:** Schizophrenia/Psychosis

**Keyword 1:** cerebellum

**Keyword 2:** brain development

**Keyword 3:** genetics

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## 67 Examination of Neuropsychological Functioning and Current Suicidal Ideation and Suicide Attempt History in Individuals with Severe Mental Illness

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**Objective:** Suicide risk among individuals with psychosis is elevated compared to the general population (e.g., higher rates of suicide attempts [SA] and completions, more severe lethality of means). Importantly, suicidal ideation (SI) seems to be more predictive of near-term and lifetime SAs in people with psychosis than in the general population. Yet, many randomized controlled trials in psychosis have excluded individuals with suicidality. Additionally, research suggests better cognitive and functional abilities are associated with greater suicide risk in psychotic disorders, which is dissimilar to the general population, but studies examining the link between cognition and suicidality are scarce. Because neuropsychological abilities can affect how individuals are able to attend to their environment, solve problems, and inhibit behaviors, further work is needed to consider how they may contribute to suicide risk in people