Published in final edited form as:

Schizophr Res. 2016 October ; 176(2-3): 527–528. doi:10.1016/j.schres.2016.07.001.

SEVERITY OF HYPERTENSION PREDICTS THE GENERALIZED NEUROCOGNITIVE DEFICIT IN SCHIZOPHRENIA

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To the Editors

Cognitive impairment is a core feature of schizophrenia; however, no distinct pattern of neuropsychological impairments characterizing schizophrenia has emerged. Rather, impairments are observed across a broad range of cognitive domains, leading some to suggest a “generalized cognitive deficit” (Dickinson et al., 2007). Several accounts of the generalized deficit have been proposed, with the majority focusing on CNS abnormalities. However, other “general systems” abnormalities may contribute. Among the most likely factors are metabolic abnormalities (Dickinson & Harvey, 2009). In the general population, metabolic abnormalities are known to be associated with cognitive impairment (Yaffe et al., 2004). Despite increased rates of metabolic abnormalities in schizophrenia (De Hert et al., 2006) and a clear role for metabolic abnormalities in cognitive impairment in the general population, relatively few studies have examined this association in schizophrenia (Boyer et al., 2014; Dik et al., 2007; Lancon et al., 2012; Lindenmayer et al., 2012). The current study aimed to further elucidate the impact of metabolic abnormalities on cognition in schizophrenia.

Participants included 27 individuals with DSM-IV-TR diagnoses of schizophrenia or schizoaffective disorder and 33 psychiatrically and neurologically healthy controls. Patients were evaluated during periods of clinical stability as indicated by no change in medication type of dose within the past 4 weeks. Diagnosis was established via a best-estimate approach based on psychiatric history and the Structured Clinical Interview for DSM-IV (SCID). Groups did not significantly differ on age, sex, parental education, or ethnicity.

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Conflict of Interest

Ms. Morra has no conflicts to report.

Contributors

Gregory Strauss and Lindsay Morra designed the study. Statistical analyses and writing of the first draft of the manuscript were performed by Lindsay Morra. All authors contributed to and approved the final manuscript.

Participants completed the SCID and were rated on the Brief Negative Symptom Scale and the Brief Psychiatric Rating Scale. After the interview, the MATRICS Consensus Cognitive Battery (MCCB) was administered. Various metabolic factors were measured. Pulse pressure was the primary dependent measure to index hypertension. Arterial blood pressure was measured at the brachial level using an Omron series automatic blood pressure cuff. Fasting blood glucose levels were measured between 8:00 and 10:00am after an overnight fast using the One Touch Ultra 2.0 blood glucose monitor. Waist-to-hip ratio was taken using cloth measuring tape.

In patients, higher pulse pressure was associated with worse processing speed ($r = -.51$, $p < .01$), attention/vigilance ($r = -.51$, $p < .01$), working memory ($r = -.41$, $p = .04$), verbal learning ($r = -.45$, $p = .02$), visual learning ($r = -.44$, $p = .02$), and global cognition ($r = -.55$, $p < .01$). Blood glucose and waist-to-hip ratio were not significantly related to cognition in individuals with schizophrenia. Correlations were nonsignificant in controls.

Findings suggest that hypertension severity plays a role in the magnitude of cognitive impairment observed in schizophrenia. Only pulse pressure was significantly correlated with cognitive impairment in schizophrenia. Further, pulse pressure was not a significant predictor of cognition in our controls. This may in part be due to the age of our sample. The literature on metabolic dysfunction and cognition has primarily examined older samples or the longitudinal effects of midlife metabolic abnormalities on cognition. Even though groups were matched on age, the schizophrenia group may have had hypertension longer, potentially resulting in greater impact on the brain and subsequently cognition. Importantly, small sample size may also have contributed to non-significant findings in this study. Several other limitations should also be considered. First, other processes associated with metabolic abnormalities and cognition, such as oxidative stress and inflammation, were not measured in this study (Dickinson & Harvey, 2009). Second, although the MCCB is the gold standard for neuropsychological evaluations in schizophrenia, the battery is known to be imprecise in localizing circuit level function and in isolating specific cognitive domains. Future studies may want to use other approaches such as cognitive neuroscience measures, neuroimaging, and electrophysiology, which evaluate more precise domains of cognitive function.

Despite these limitations, the current findings provided support for an association between hypertension and cognitive impairment in schizophrenia. Associations were moderate across most domains, consistent with the generalized neurocognitive deficit. Findings also may have significant implications for the treatment of cognitive impairment in schizophrenia. Current treatment options include cognitive enhancing drugs and cognitive remediation programs. However, research suggests that cognitive enhancing drugs have minimal benefits in schizophrenia (Harvey, 2009), and cognitive remediation programs yield only modest improvements in most cognitive domains (Harvey & Bowie, 2012). Treatment of metabolic abnormalities through pharmacological and/or exercise interventions, in conjunction with other interventions, may represent a novel approach to the treatment of cognitive impairment in schizophrenia.

Acknowledgments

Dr. Strauss receives royalties and consultation fees from ProPhase LLC in connection with commercial use of the Brief Negative Symptom Scale and other professional activities.

Role of Funding Source.

Research supported in part by the US National Institute of Mental Health Grant K23MH092530 to Dr. Strauss and a 2014 American Psychological Association Dissertation Research Award to Ms. Morra.

The authors would like to thank the participants who completed the study, as well as staff at the Binghamton University Translational Affective Neuroscience Laboratory who contributed to data collection. We are especially thankful to members of Dr. Strauss' team who conducted subject recruitment and testing: Sara Sullivan, Kathryn Ossenfort, Kayla Whearty, and Kate Frost.

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