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Neurocognitive Performance Stability in a Multiplex Multigenerational Study of Schizophrenia

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Certain cognitive measures are heritable and differentiate individuals at risk for schizophrenia from unaffected family members and healthy comparison subjects. These deficits in neurocognitive performance in patients with schizophrenia appear stable in the short-term. However, the duration of most, but not all, longitudinal studies is modest and the majority have relied on traditional average performance measures to examine stability. Using a computerized neurocognitive battery (CNB), we assessed mean performance (accuracy and speed) and intra-individual variability (IIV) in a longitudinal study aimed to examine neurocognitive stability in European-American multiplex families with schizophrenia. Thirty-four patients with schizophrenia, 65 unaffected relatives, and 45 healthy comparison subjects completed the same computerized neurocognitive assessment over approximately 5 years. Measures of mean performance showed that patients had stable accuracy performance but were slower in many neurocognitive domains over time as compared with unaffected family members and healthy subjects. Furthermore, patients and family members showed dissociable patterns of change in IIV for speed across cognitive domains: compared with controls, patients showed higher across-task IIV in performance compared with family members, who showed lower across-task IIV. Patients showed an increase in IIV over time, whereas family members showed a decrease. These findings suggest that measures of mean performance and IIV of speed during a CNB may provide useful information about the genetic susceptibility in schizophrenia.

Key words: intra-individual variability/schizophrenia/cognition/family

Introduction

Schizophrenia is a heritable disorder with persistent neurocognitive[1–3]deficits in executive functioning, learning and memory, and processing speed.[1–4] These deficits, examined as endophenotypic markers[5] in unaffected relatives of patients with schizophrenia (eg, Cannon et al.[6]), are heritable.[3,7] Deficits in neurocognitive performance in patients with schizophrenia appear stable in the short-term.[8–10] For example, little change in variability was found over short (ie, hours) and intermediate (ie, 1 month) intervals in patients on a brief neuropsychological battery.[11] However, the duration of most, but not all,[9] longitudinal studies is modest and most have relied on traditional average performance measures to examine stability.

Mean Measures as an Index of Neurocognitive Performance

Neurocognitive deficits in schizophrenia commonly examine mean performance measures. Such comparisons indicate greater between-subject variability in patients relative to healthy individuals or family members. Greater group differences persist even when other demographic and illness-associated factors are considered.[4] Reducing group differences by classifying patients based on specific symptoms indicates differentiable neurocognitive performance patterns.[12] These group differences in neurocognitive performance are linked to genetic polymorphisms implicated in schizophrenia (eg, catechol-O-methyl transferase; COMT).[13] Moreover, unaffected relatives show substantial inter-individual variability in some neurocognitive domains and differ from