TITLE: ESTIMATING TREATMENT EFFECT HETEROGENEITY IN COGNITIVE TRAINING PROGRAMS

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Methodological Question Being Addressed: Since an effect modifier changes the magnitude of the intervention, different population characteristics (subgroups) may yield different results. 1) Does examining the overall group means provide an accurate understanding of treatment effects? 2) Are there groups of subjects who respond to a cognitive intervention differently, but who are obscured when group means are examined? 3) How can we use demographic and baseline psychometric data to assess subjects' behavior in order to create a model for subject assignment to cognitive interventions?

Introduction: Cognitive functioning deficits within the schizophrenia population are heterogeneous. Specifically, these deficits vary between subjects, for example in terms of disease etiology, age, sex, and level of psychopathology, concomitant medications (e.g., time medications were given prior to testing), metabolic functioning (e.g., glucose levels at the time of testing), psychiatric comorbidities, among others. These characteristics can theoretically moderate the effect of cognitive interventions on outcomes. In schizophrenia, where multiple latent sub-populations are present, the progression of the mean and the estimated overall average causal effect alone do not provide an accurate picture, while exploring heterogeneities of symptoms and clinical characteristics may better distinguish underlying phenotypes of response to cognitive interventions. Hence, using subject characteristics to model treatment interventions may be beneficial.

Methods: This study utilized data collected for 94 subjects with DSM-V schizophrenia and significant cognitive deficits who participated 12-weeks cognitive remediation. Subjects were assessed on the PANSS, PSP, MCCB MATRICS, UPSA-Brief and Emotion Perception tests. Latent Growth Mixture Modeling (LGMM) was computed to uncover discrete longitudinal mixture distributions and identify latent subpopulations, or classes. Identifying these classes can be modeled within the same framework.

Results: The largest class (56% of the sample) displayed an increase in cognitive functioning and symptom reduction as shown by a significant positive slope ($p = .030$), indicating a significant overall increase in cognition. The second largest class (26%) demonstrated cognitive improvements with no symptom reduction across time points, as indicated by a significant positive slope ($p = .041$). The smallest class (19%) demonstrated no cognitive improvements and no symptom reduction, indicated by a non-significant slope ($p = .356$). We examined the following variables: gender, age, length of hospitalization, chronicity of illness, and total level of symptomatology (PANSS), the use of concomitant mood stabilizers, metabolic values within a week of testing, time medication was given. Successive models demonstrated improved fit through three classes. Gender was not significantly different between the three identified classes and none of these covariates differentiated the classes. Compared to the largest class (56%), however, the lowest class (19%) was significantly older ($p = 0.005$), had longer length of stay ($p = 0.010$), and was significantly more likely to have higher levels of negative symptomatology ($p = 0.006$).

Conclusions: This work revealed several symptom response trajectory states in subjects with chronic schizophrenia after a cognitive intervention. The analysis emphasized a methodology for detecting methodical clustering patterns in schizophrenia within cognitive training response heterogeneities. Results would be able to assess whether individuals within a model class would benefit from specific cognitive intervention.

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