ESTIMATING TREATMENT EFFECT HETEROGENEITY IN COGNITIVE TRAINING PROGRAMS

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Background

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.

Methodological Question:
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 a precise 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?**

Methods

Population:
This study utilized data collected for 94 subjects with DSM-V schizophrenia and significant cognitive deficits who participated 12-weeks cognitive remediation.

Analysis:
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.

Assessments:
Positive and Negative Syndrome Scale: PANSS
Personal and Social Performance Scale: PSP
MATRICS Consensus Cognitive Battery: MCCB MATRICS,
UCSD Performance-Based Skills Assessment: UPSA-Brief and Emotion Perception tests

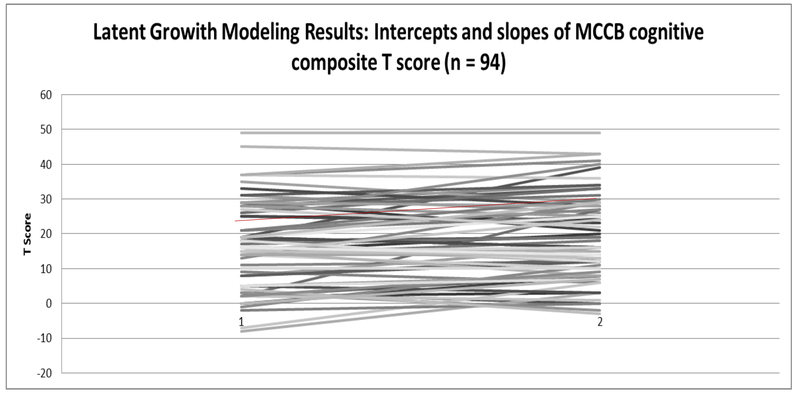
Results

Study Data

Data were taken from a randomized controlled trial assessing a 12 week treatment with computerized cognitive remediation intervention combined with a social cognitive treatment. Our analysis examined the response to treatment.

Latent Growth Models

We used latent growth modelling (LGM) to examine response to treatment, from baseline to 12 weeks of treatment, across MCCB cognitive composite. With LGM, we calculated two latent variables for each patient: (1) an intercept (first time point of the curve), (2) a slope (changes in the scores over time).



The intercepts and slopes for 94 subjects were different from the mean intercept and slope for the group (indicated by the red line). These results suggested that it would be beneficial to conduct growth mixture modelling (GMM) because the assumption of common intercepts and slopes is not accurate.

Growth Mixture Models

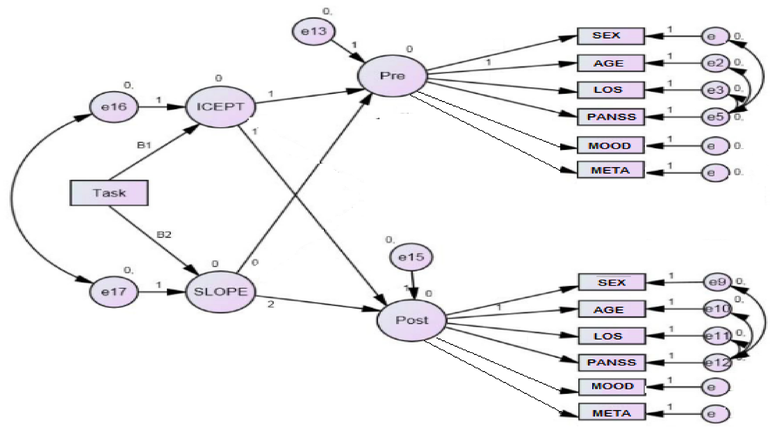
Three subgroups were identified with different response patterns

56% sample
Showed an increase in cognitive functioning and symptom reduction (p = .030), indicating a significant overall increase in cognition.

26% sample
Showed cognitive improvements with no symptom reduction across time points

19% sample
Showed no cognitive improvements and no symptom reduction, indicated by a non-significant slope

Post-Hoc Comparison



- 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. Compared to the largest class (56%), the lowest class (19%) was older (p = 0.005), had longer length of stay (p = 0.010), and more likely to have higher levels of negative symptomatology (p = 0.006).

Conclusions

The analysis emphasized a methodology for detecting methodical clustering patterns within cognition response heterogeneities. Results would be able to assess whether individuals within a model class would benefit from specific cognitive intervention.

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