The Utility of the NIDA Phenotyping Assessment Battery in a Combined Enrichment Strategy for Determining Eligibility in Addiction Clinical Trials

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Introduction

- The success of a clinical trial is dependent upon ensuring that the effects of the intervention will not be diluted by inclusion of subjects who are inappropriate for a given study, such as if their clinical presentation is very atypical.

- While a DSM diagnosis is typically used to determine substance use disorder (SUD) "type" (e.g., Opioid) and addiction severity, it is not a sufficient method to classify individual subtypes of SUD, based on clusters of dominant symptoms.

- Recently, much attention has focused on assessment methods to minimize participant heterogeneity in order to enhance signal detection by classifying or subtyping individuals with SUD along distinct neurofunctional domains (e.g., the NIDA Phenotyping Assessment Battery (PhAB) for SUD) [1,2]

- Other sample enrichment strategies include identification and exclusion of anomalous subjects in clinical trials.

Aims

The present study sought to utilize behavioral phenotyping data to both "cluster" individuals by neurobehavioral response patterns (based on NIDA PhAB performance/responses), and identify anomalous subjects who would not be appropriate for inclusion in a clinical trial.

Methods

- Secondary data collected as part of a feasibility study of the NIDA PhAB were used for the present analyses (N=187).

- Assessment data were normalized and hierarchical clustering dendrograms were created using R statistical software. A dendrogram built upon Euclidean distance measure was chosen, as the variables of interest were continuous.

- Boxplots were used to examine cluster performance on each of the individual PhAB domains of interest (for this example, negative emotionality was the target).

- "Outlier" performance within the target cluster was evaluated for eligibility.

Sample Characteristics

Age	Mean (SD)	43.3 (12.9) years	Range 18-69
Sex		N (%)	
Female		76 (40.6%)	
Male		111 (59.4%)	
Race			
Caucasian/White		36 (19.3%)	
African American/Black		146 (78.0%)	
Other		5 (2.7%)	
Primary SUD Diagnosis (DSM5)			
Opioid		83 (44.4%)	
Cocaine		48 (25.7%)	
Opioid & Cocaine		9 (4.8%)	
Cannabis		47 (25.1%)	

Results
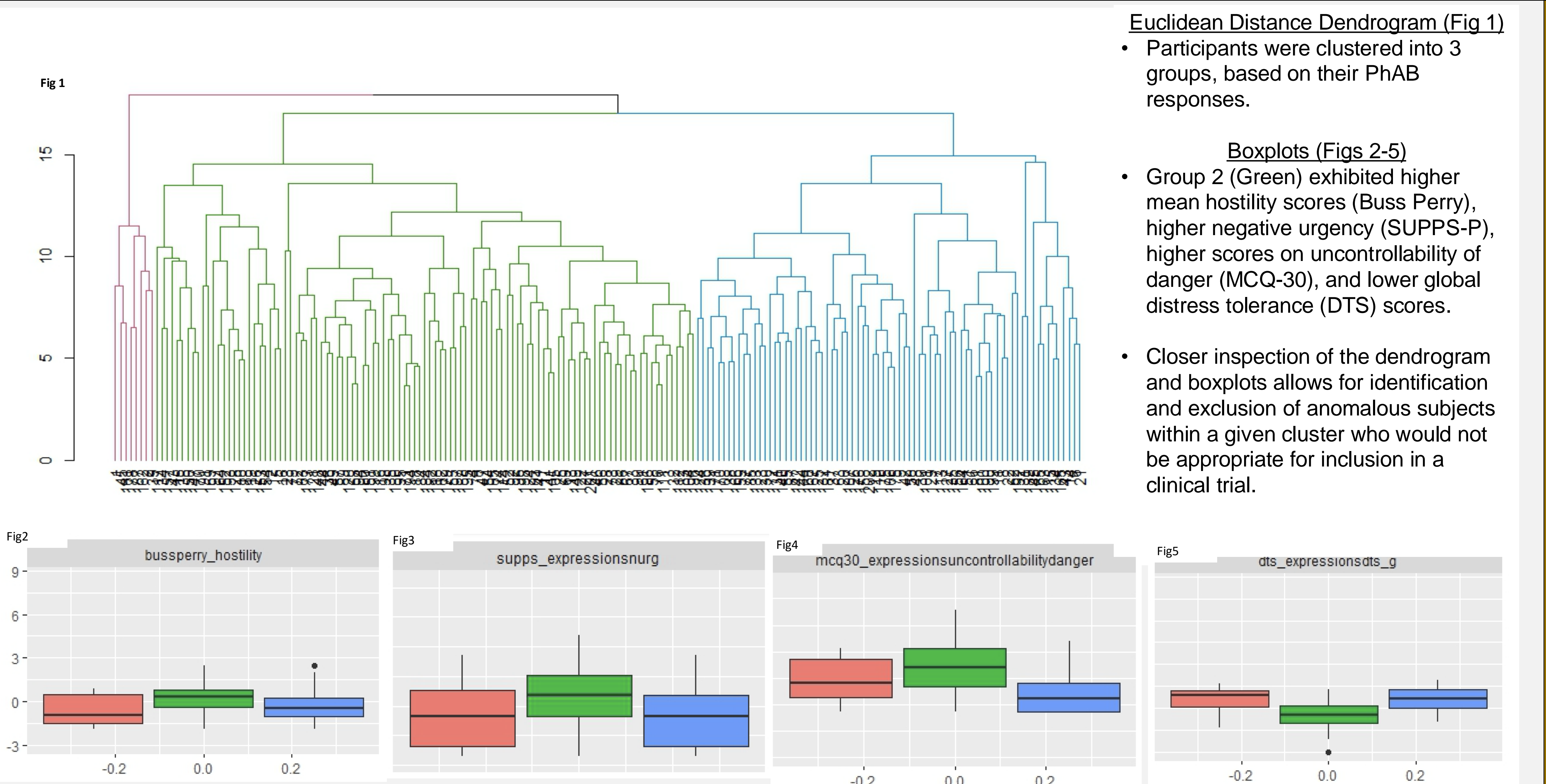
Fig 1

Euclidean Distance Dendrogram (Fig 1)
- Participants were clustered into 3 groups, based on their PhAB responses.

Boxplots (Figs 2-5)
- Group 2 (Green) exhibited higher mean hostility scores (Buss Perry), higher negative urgency (SUPPS-P), higher scores on uncontrollability of danger (MCQ-30), and lower global distress tolerance (DTS) scores.

- Closer inspection of the dendrogram and boxplots allows for identification and exclusion of anomalous subjects within a given cluster who would not be appropriate for inclusion in a clinical trial.

Fig2 — bussperry_hostility

Fig3 — supps_expressionsnurg

Fig4 — mcq30_expressionsuncontrollabilitydanger

Fig5 — dts_expressionsdts_g

Conclusions

- Given the considerable cost, participant burden, and resources necessary to conduct a clinical trial, novel methods to eliminate anomalous subjects and increase statistical power have garnered interest among clinical trials researchers.
- The NIDA Phenotyping battery has been identified as a potentially useful tool to aid in selection of appropriate subjects for a given clinical trial (e.g., "treatment matching"), based on neurobehavioral performance.
- When paired with analytical enrichment techniques, anomalous participants may also be identified and eliminated within a given PhAB subgroup.
- The PhAB appears to be ideally suited for use as an enrichment strategy in addiction clinical trials.

References

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