Identification of Three Highly Influential Measures within a Large Neurocognitive and Physiological Battery in Psychosis

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Background

Disorders on the schizo-bipolar spectrum are associated with varying levels of cognitive and visuomotor processing. Large-scale studies have examined performance across comprehensive test batteries to identify biologically similar subgroups of impairment.

Prior work has identified a three-factor structure underlying the large battery used in the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP1) study. The three factors were consistent across patient, control, and relative groups and were characterized by basic physiological measures, general cognition, and higher-order cognition.

This study was designed to identify influential measures within the B-SNIP1 test battery that may be suitable for an abbreviated battery. Participants were 345 healthy controls, 263 schizophrenia probands and 298 relatives, 180 schizoaffective probands and 197 relatives, 248 bipolar with psychosis probands and 289 relatives.

Methods

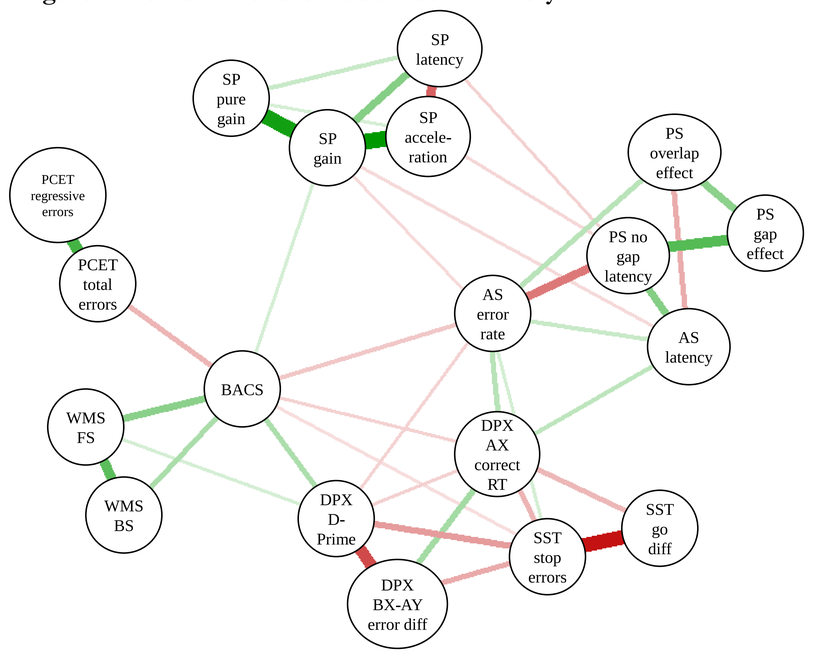
Analysis: A partial correlation network with least absolute shrinkage and selection operator (LASSO) regularization and Extended Bayesian Information Criterion (EBIC) model selection was used with lambda set at 0.5 to control for spurious connections. All analyses were conducted in R using the *qgraph* package (Epskamp et al., 2012).

Measures: The battery included neuropsychological tests, cognitive neuroscience-based paradigms, smooth pursuit eye movement, and prosaccade and antisaccade tasks.

- Brief Assessment of Cognition in Schizophrenia (BACS) Composite: The composite score from a 6-subtest measure of global cognition.
- Penn Conditional Exclusion Task (PCET): A computerized measure of executive functioning assessing learning and problem solving in response to immediate feedback, with outcomes of total errors and regressive errors.
- Wechsler Memory Scale (WMS), Third Edition, Spatial Span: A measure of spatial working memory with forward and backward span components.
- Stop Signal Task (SST): A measure of inhibitory behavioral control with outcomes of errors on Stop trials and adaptive slowing (difference in reaction time between Baseline and SST Go trials).
- Dot Pattern Expectancy Continuous Performance Test (DPX-CPT): A measure of context-processing and continuous attention, with outcomes of D-Prime (ratio of AX hits to BX false alarms), difference between BX and AY errors, and reaction time for correct AX trials.
- Smooth Pursuit (SP) eye movement: A measure of eye tracking with outcomes of latency, acceleration, and gain.
- Prosaccade (PS) task: A measure of visually guided saccade latency with outcomes of no gap (target and central fixation terminated simultaneously), gap (central fixation terminated 200 ms before), and overlap (central fixation terminated 200 ms after).
- Antisaccade (AS) task: A measure of response inhibition in which participants were asked to look at the mirror location in the opposite hemifield as the peripheral target, with outcomes of latency and error rate.

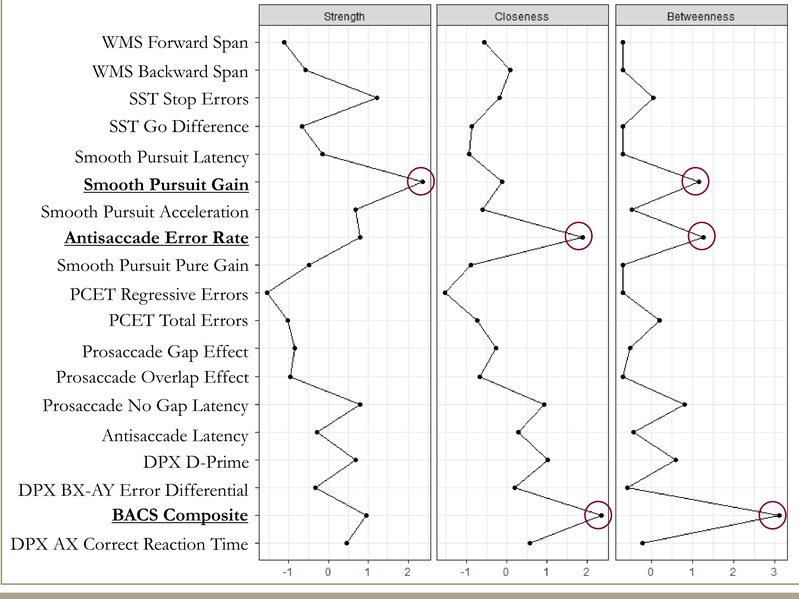
Results

Figure 1. Network model of the B-SNIP1 battery.



Note: Nodes (circles) represent individual measures in the battery and edges (lines) represent the strength and direction of correlation between two measures, controlling for all other variables in the network.

Figure 2. Centrality indices of the network identify three highly influential measures within the network.



Results

The network (Figure 1) showed strong connections within smooth pursuit and saccade tasks as well as within and between computerized paradigms of inhibitory control (SST) and attention (DPX-CPT).

Centrality indices indicated that smooth pursuit gain was the strongest node in the network, a measure of the number and strength of connections (Figure 2). The BACS composite score and antisaccade error rate had the highest betweenness, a measure of the extent the node facilitates the flow of information through the network. Smooth pursuit gain, BACS, and antisaccade error rate all had the highest closeness, a measure of the average distance between a node and the remaining nodes in the network.

In contrast, regressive errors from the PCET, SST go difference, and spatial working memory capacity had the fewest and weakest connections.

The path from more basic cognitive measures (PCET and WMS) to physiological measures occurred through general cognitive ability (BACS), while the path from higher-order cognitive measures (DPX-CPT and SST) passed through both general cognitive ability (BACS) and the antisaccade task.

Discussion

The three highly connected and central nodes identified in the network were consistent with the factor structure of key domains of general cognition (BACS), inhibitory control (antisaccade error rate), and basic visuomotor processing (smooth pursuit gain).

In network models, nodes that are highly connected and central are considered useful targets for treatment. Smooth pursuit gain, antisaccade error rate, and the BACS may be useful to include as indices of change in clinical trials in psychosis, as changes in these highly connected measures may influence broader cognitive and physiological functions.

The measures that had the fewest connections (PCET, SST, WMS) may represent cognitive processes that are independent from sensorimotor deficits that are often present in psychosis. This is consistent with differential deficits within the two dimensions of cognitive control and sensorimotor reactivity previously identified by the B-SNIP group (Clementz et al., 2016). Further, SST go difference and PCET regressive errors were not significantly associated with general cognitive ability and may be specific deficits which extend beyond generalized cognitive deficits (Ethridge et al., 2014).

References

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