# Investigating Cognitive Practice Effects in Schizophrenia Using Repeated Assessment at Short Retest Intervals Prior to Randomization in a Clinical Trial

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**Methodological Issue Being Addressed** Aim is to investigate the extent and predictors of practice-related improvement in cognition in a clinical trial in schizophrenia as measured by a digital battery of tests.

**Introduction** In clinical trials of schizophrenia, improvement in cognition in both placebo and treatment arms is common. Such improvement may impact the ability of clinical trials to identify any cognitive benefits of new pharmacotherapies (Keefe et al., 2011). Depending on the design, improvement in performance on cognitive tests may reflect a practice effect, the consequences of an expectation of benefit (i.e. a placebo effect), or an indirect consequence of improvement in psychiatric symptoms that occurs with trial participation. Investigating improvement in performance on cognitive tests conducted repeatedly after randomization makes it difficult to disentangle the effects of practice, expectation, or symptomatic change on performance. We therefore measured the effects on performance of multiple repeated and brief cognitive assessments, given at short retest intervals, in a single session, in people with schizophrenia who had satisfied inclusion criteria for a clinical trial of negative symptoms, but who had not been randomized to a treatment condition (i.e. prior to baseline). This design allows determination of the effects of practice absent any effects of expectancy or trial-related symptomatic change.

**Methods** Patients with stable schizophrenia (n=235), who had been receiving an approved antipsychotic drug for greater than six months, aged between 18 and 65 years, with a score > 20 for the 7 negative symptom items of the Positive and Negative Symptoms Scale (PANSS), and a Calgary Depression Schizophrenia Scale (CDSS) score < 6, a Simpson Angus Scale (SAS) score < 12 were recruited for a large clinical trial [NCT01488929]. Prior to the baseline assessment for this trial, all participants completed four consecutive assessments of cognition, using a brief computerized test battery (~12-minutes) consisting of four tests (Cogstate Brief Battery) measuring in turn, psychomotor speed, attention, working memory and visual learning. After completing each test battery, participants were allowed 10 minutes rest. Performance scores were compared across assessments using linear mixed models (LMM) that include age, sex, age at onset and education (yrs) as covariates. Relationships between symptomatic status and improvement across assessments were determined with multiple regression.

**Results** The LMMs showed no main effect or interaction effect that reflected practice for any

component of the computerized test battery: mean change from baseline across four assessments were uniformly small, non-systematic in direction (d's -0.05 & 0.02) and did not reach significance. There was no change in estimates of group variance across assessments for each subtest. For each subtest, age significantly predicted performance while the visual memory test in the battery, education also predicted performance. Coefficients of variation for repeated administration of each test ranged between 3% and 8%. While total positive and negative symptom scores were associated significantly with performance on each cognitive subtest, the magnitudes of these correlations ranged only between r= 0.2-0.3).

**Conclusion** In individuals with schizophrenia characterized by high levels of negative, symptoms, assessed prior to randomization in clinical trial, repeated administration of cognitive tests gave rise to no improvement in performance on cognitive tests, despite reassessment being conducted four times at short retest intervals. Furthermore, there was no increase in variance in performance for any test. This stability of performance characteristics suggests that practice effects observed in placebo conditions in clinical trials reflect processes other than test familiarity or experience. Such factors could include expectancy or placebo effects, indirect effects of a reduction in clinical disease symptoms. It is possible that the use of the repeated assessment at short re-test intervals gave rise to decreased motivation or increased fatigue and these factors acted to suppress practice effects in this experiment. We think this unlikely because even with the repeated assessment the time for testing was less than that required in the clinical trial itself, the test battery was brief and participants allowed rest times. There was also no increase in group estimates of variability in performance either within sessions or between sessions.

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## Keywords


| Keywords |
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| Cognition |
| Schizophrenia |
| Practice effects |


**Guidelines** I have read and understand the Poster Guidelines

**Disclosures** This research involved collaboration of employees at Cogstate and Cognition Metrics.

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