

# P.843: An exploration of practice effects on cognitive test performance in a clinical trial of cognitive impairment associated with schizophrenia

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## Background

In clinical trials of Cognitive Impairment Associated with Schizophrenia (CIAS) an important methodological issue has been improvement with placebo treatment. Improvement in performance on cognitive tests in the absence of intervention is often interpreted as a practice effect. Such effects may be of concern in clinical trials, since they might impact the detection and interpretation of treatment effects. Data from repeated assessments in individuals with schizophrenia at brief retest intervals, and with a large sample would allow for exploration of the presence and nature of a practice effect and potential relationships to demographic and clinical characteristics.

## Demographic and Clinical Characteristics

There were 230 participants (Table 1). The inclusion criteria for the study were: diagnosis of schizophrenia; stable dose of approved atypical antipsychotic for at least two months prior to Screening; age 18 – 65; lack of psychiatric hospitalization for two months prior to Screening; clinical history of stable psychotic symptoms for 1 month prior to Screening; stable positive symptoms of schizophrenia for 4 weeks prior to Day 1; score >20 PANSS negative; no current major depressive disorder or history of major depressive disorder for 6 months prior to screening; SAS score <12; stable housing; and an informant who is not a group home resident.

Table 1: Demographic and Clinical Characteristics

Demographic	Level	N (%)	Mean (SD)
Age			38.6 (10.71)
Sex	Female	94 (40.3)	
	Male	139 (59.7)	
Race	Asian or Indian	1 (0.4)	
	Black	31 (13.3)	
	Other	3 (1.3)	
	Pacific Islander	2 (0.9)	
Smoker	White	196 (84.1)	
	UNK	1 (0.4)	
	Current	136 (58.6)	
Education	Never	78 (33.6)	
	Past	18 (7.8)	
	UNK	1 (0.4)	
BMI	Completed High School	115 (49.6)	
	Completed Post-Graduate	28 (12.1)	
	Completed Undergraduate	62 (26.7)	
	Did not complete High School	27 (11.6)	
UPSA_B			26.4 (4.90)
PANSS_Positive			69.7 (18.59)
PANSS_Negative			13.9 (3.72)
PANSS_General			25.8 (3.47)
SANS_Total			36.9 (5.93)
			69.3 (13.72)

## Statistical Methods

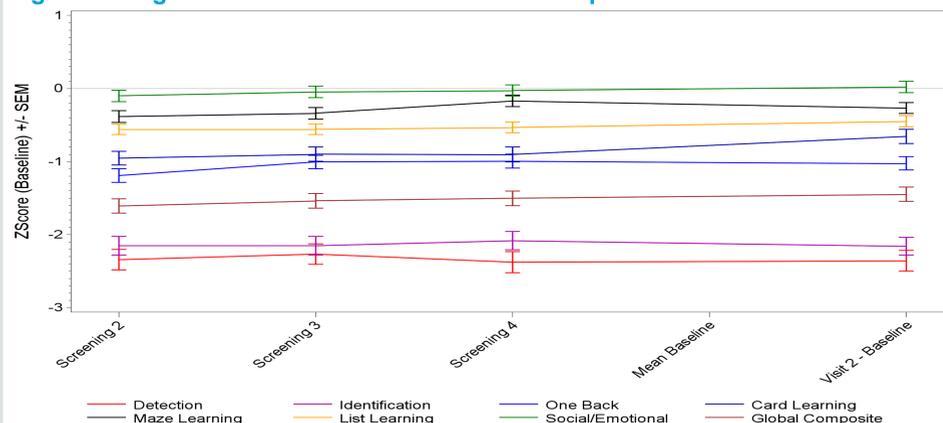
- Data for 230 participants from the placebo arm of a clinical trial were analyzed
- Cognition was assessed using the Cogstate Schizophrenia Battery (CSB) comprising Detection, Identification, One Card Learning, One Back, International Shopping List, Social-Emotional Cognition, and Groton Maze Learning tests (Table 2)
  - A standardized composite score was also calculated, where at least 5/7 complete tests were available
- Participants completed a familiarization session to orient them to assessment requirements, which was excluded from all subsequent analyses
- The CSB was administered on a further four occasions, Screening 2, 3 and 4 (within 2 days) and Baseline (within 30 days after Screening 4)
- Presence of changes with repeated assessment were evaluated via simple regression, and mixed linear models using demographic and clinical covariates

Table 2: Cogstate Schizophrenia Battery (CSB)

Test name/ component	Test paradigm	Cognitive domain	Outcome measure	Avg. time required
Groton Maze Learning	Hidden-pathway maze learning	Executive function	Number of errors made over five learning trials (Lower score = better performance)	7 minutes
International Shopping List – Learning Trials	Verbal list learning	Verbal learning	Number of words recalled successfully across the three learning trials (Higher score = better performance)	5 minutes
Detection	Simple reaction time	Psychomotor function	Speed of performance; mean of the log <sub>10</sub> transformed reaction times for correct responses (Lower score = better performance)	3 minutes
Identification	Choice reaction time	Attention	Speed of performance; mean of the log <sub>10</sub> transformed reaction times for correct responses (Lower score = better performance)	3 minutes
One Back	N-back working memory	Working memory	Speed of performance; mean of the log <sub>10</sub> transformed reaction times for correct responses (Lower score = better performance)	4 minutes
One Card Learning	Pattern separation	Visual learning	Accuracy; Arcsine transformation (Higher score = better performance)	6 minutes
Social Emotional Cognition	Emotional face recognition	Social cognition	Accuracy; Arcsine transformation (Higher score = better performance)	6 minutes

A single familiarization assessment prior to baseline ensures stable repeat performance for many cognitive tests and test paradigms in people with CIAS

Figure 1: Cognitive Test Performance Over the Repeated Assessments



## Results

### Simple Regression of Score Over Time at Group Level

Simple regression showed a small but statistically significant effect on performance with repeated assessment for the One Back test (Cohen's d = 0.2, p = 0.0257) and negligible effects for all other tests/outcome measures (Cohen's d ≤ 0.11, p ≥ 0.2273) (Figure 1).

Table 3: Best Predictors of Variance Across all Tasks and Composites determined by Stepwise Backwards Regression

Backward regression showed the most common predictor of test performance was the PANSS Negative Scale (8/8 outcomes), followed by age (7/8 outcomes). After covarying out each of the biggest predictors (age, sex, PANSS Negative, PANSS Positive, smoking status), there was a small increase in the amount of variance explained by repeat assessment for all tests/outcome measures apart from Groton Maze Learning. However, repeated assessment never explained a statistically significant proportion of the variance (Table 4).

Variable	Detection		Identification		Card Learning		One Back		Maze Learning		List Learning		Social/Emotional		Global 5+	
	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p
Age	0.2560	0.0000	0.2391	0.0000	0.2432	0.0000	-0.1459	0.0000	0.1793	0.0000	-0.1933	0.0000	-0.1837	0.0000		
Gender	0.1113	0.0003	0.0879	0.0048							0.1463	0.0000				
PANSS_Negative	0.2466	0.0000	0.2459	0.0000	0.1886	0.0000	-0.1532	0.0065	0.1266	0.0003	-0.1262	0.0051	-0.1848	0.0000	-0.2917	0.0000
PANSS_Positive							-0.0971				-0.0895	0.0042				
Smoker											0.0934					

## Conclusions

- Following a familiarization assessment on the cognition battery, negligible practice effects were seen
- A single initial familiarization assessment prior to baseline ensures stable performance for many tests and test paradigms
- Thus, challenges with respect to data interpretation related to learning and practice could be reduced or negated
- Notably, clinical and demographic factors including negative symptoms and age may be more important predictors of cognitive test performance and remain key considerations in the selection, stratification and evaluation of CIAS clinical trial participants

