A Comparison of the CANTAB Schizophrenia Battery and the MCCB in Two Phase 2 Clinical Trials of Subjects with Stable Schizophrenia

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INTRODUCTION

The MATRICS consensus cognitive battery (MCCB) was developed as a consensus approach to testing cognition in clinical trials of cognitive impairments associated with schizophrenia (CIAS). The selected tests were chosen to meet psychometric criteria, including adequate test-retest reliability, minimal practice effects, and evidence of sensitivity to drugs. The battery, presented in a mostly pencil-and-paper format, contains ten tests covering seven cognitive domains known to be affected by schizophrenia. The CANTAB schizophrenia battery includes eight computerized neuropsychological tests presented on a touchscreen computer and selected to assess the same seven domains covered by the MCCB. This study evaluated the relationship between the MATRICS and CANTAB schizophrenia batteries in the baseline evaluations of two phase 2 clinical trials.

METHODS

Two multicenter trials in stable subjects with schizophrenia were conducted at approximately 45 sites in the United States. Both investigated the procognitive effects of novel investigational compounds as add-on therapy to antipsychotics. The same design was used in both trials, with one placebo and two active dose groups (planned N=70/group; total N=420 for both trials). Eligibility criteria were consistent with MATRICS guidelines. Subjects were currently taking one or two atypical antipsychotics at the time of study entry. The CANTAB battery (excluding Verbal Recognition Memory) and the MCCB were administered for practice on the initial screening visit. Baseline assessments for the two batteries were staggered in order to reduce subject burden such that the MCCB was administered on Day -1 and the CANTAB Battery administered approximately 1-2 weeks prior at Screening Visit 2. The baseline UPSA-2 was administered with the MCCB on Day -1, with no practice assessment during screening. CANTAB outcomes for the Principal Components analysis were selected based on their clinical meaningfulness based on prior experience of drug effects on these tests and effect size differences between clinical populations and healthy controls. The principal components analysis was conducted in SPSS version 21.0 using the Dimension Reduction procedure with no rotation. Components were selected based on an eigenvalue greater than one. All reported correlations are Pearson R.

RESULTS

Demographic information for the combined trials is given in **Table 1**. Baseline score for each battery are presented in **Table 2**. The correlations between MCCB and CANTAB for the seven MATRICS cognition domain scores varied from r = 0.28 to r = 0.60 (**Table 3**). The relationship of MCCB with the UPSA-2 agreed with previous published results with r = 0.62.

Table 1. Demographics

Demographic	Result
Age	42.6 years (mean)
Race	Black = 47.4%
	White = 33.4%
Sex	Male = 54.4%
	Female = 45.6%

Table 2. Baseline MCCB and CANTAB Scores

	Mean	SD
MCCB		
Composite	27.4	12.3
Speed of Processing	32.9	11.9
Verbal Learning	36.4	7.89
Working Memory	35.0	11.6
Reasoning/Problem Solving	40.5	9.49
Visual Learning	37.2	12.2
Attention	36.5	12.3
Social Cognition	36.6	13.3
CANTAB		
SWM (Between Errors)	21.6	10.6
RVP A'	.868	.058
ERT (Total Correct)	42.9	9.04
5CRT	440	116
PAL (Total Errors)	34.7	36.0
OTS (Problems Solved 1st Attempt)	7.64	3.00
DMS (% Correct 12 second delay)	72.5	23.8

CANTAB Abbreviations: SWM=Spatial Working Memory; RVP=Rapid Visual Processing; ERT=Emotion Recognition Task; 5CRT=5-Choice Reaction Time; PAL=Paired Associates Learning; OTS=One Touch Stockings of Cambridge; DMS=Delayed Match to Sample.

Table 3. Correlations Between CANTAB Tests and MCCB Tests in the Seven MATRICS Domains

MATRICS Domain [test(s)]	CANTAB Test	Correlation of CANTAB Measure with MATRICS Domain Score
Working Memory (WMS-III Spatial Span; Letter-Number Span)	SWM Between Errors	-.43
Processing Speed (BACS Symbol Coding; Category Fluency; Trails A)	RTI 5-Choice RT	-.28
Attention/Vigilance (CPT-IP)	RVP A'	.60
Visual Memory (Brief Visuospatial Memory Test-R)	PAL TEA	-.40
Reasoning/Problem Solving (NAB Mazes)	OTS Correct First Choice	.29
Social Cognition (MSCEIT)	ERT Total Correct	.36

We completed a principal components analysis on *a priori* defined outcomes from each of the seven CANTAB tests:

1. Spatial Working Memory between errors - The number of times the subject revisits a box in which a token has previously been found in the same problem
2. Rapid Visual Processing A-prime - A signal detection measure of sensitivity to the target, regardless of tendency to respond
3. Emotion Recognition total correct responses squared
4. 5-Choice Reaction Time
5. Paired Associates Learning total errors
6. One Touch Stockings of Cambridge problems solved on first choice
7. Delayed Match to Sample percent correct (12000 ms delay)

The relationship of the first principal component of the CANTAB schizophrenia battery also correlated with the UPSA-2 at r = 0.55 (see **Figure 1**). The MCCB composite correlated with the principal component of the CANTAB battery at r = 0.69. Correlations for composite scores are given in **Table 4** and presented as scatterplot in **Figure 2**.

Table 4. Composite Measure Correlations

	MCCB Composite	CANTAB Principal Component	UPSA-2 Total Score
MCCB Composite	–	0.69	0.63
CANTAB Principal Component	–	–	0.56

Figure 1. Scatterplots of MMCB Composite and CANTAB Principal Component with UPSA-2
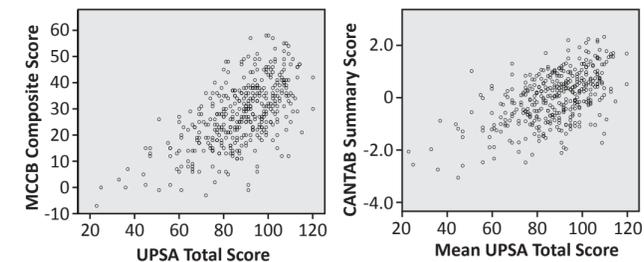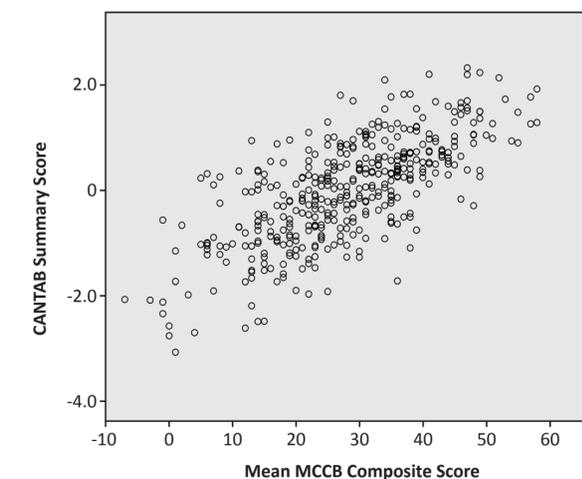

Figure 2. Scatterplot of MCCB Composite and CANTAB Principal Component

CONCLUSIONS

Using data from two large, US-based phase 2 trials of schizophrenia, we compared the cognitive scores obtained at baseline on several hundred patients on the MCCB and CANTAB cognitive batteries. We found that, while correlation of the domain scores from the two batteries varied considerably across the different domains, the summary scores were well correlated. This finding suggests that the batteries may assess different aspects of some domains, but summary scores nevertheless can provide similar appraisals of overall cognitive performance. Both batteries were moderately correlated with functional capacity as measured by the UPSA-2.

DISCLOSURES