

# Development of a Symbol Cancellation Test (SCT) for use in pediatric clinical trials in Sub-Saharan countries

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## Introduction

In African Sub-Saharan developing countries, the progress in diagnosing and monitoring of therapeutic intervention for cognitive health has been critically slowed down by the paucity of tools for pediatric cognitive assessment. Current clinical trial psychometric practices rely on a limited number of instruments developed in other countries (i.e., USA). There is a compelling need for culturally appropriate assessment tools which are sensitive to the local context of use. **Symbol Cancellation Test** is a diagnostic method to detect impairment of selective attention in a school-aged pediatric population in a context of a severely under-resourced healthcare system. A pencil and paper cancellation task was designed based on consensus reached by a panel of experts, including Zambian pediatricians, a pediatric neurologists, and clinical psychologists.

## Methods

SCT psychometric properties were assessed in a field trial, sponsored by Leoben Research and approved by Zambian Regulatory Authorities. Participants (children, aged 5-17 years-old, 50% male) were recruited at multiple clinical facilities and schools in Zambia, and 450 completed the SCT assessment. SCT provides a summary measure of selective attention: a Visuo-Motor Processing Speed Index (VMPSI) is calculated as ratio of sum of correct hits/test execution time (expressed in seconds). Hits value ranges between 0 and 108. Maximum execution time is 180 seconds. Higher values indicate higher ability. SCT reliability was estimated as stability after test-retest (24-48 hours) using intra-class correlations, two-way random-effects model, absolute agreement. Clinical utility was evaluated on a sub-sample of study participants by comparing three clinical groups - neurological and behavioural disorders (NEU), medical non-neurological (MED), chronic psychosocial stress and deprivation (CPSD) – to healthy controls (HC). Effect of age on SCT outcomes was assessed using a simple regression model.

## Results

Reliability estimate was acceptable ( $n = 95$ , ICC CI 95% = 0.68-0.86). As expected, visuo-motor processing speed increased over age. A one-way ANOVA showed a significant effect of the type of chronic health condition on visuo-motor processing speed at the  $p < .05$  level,  $F(3, 182) = 23.99$ ,  $p = 0.000$ . *Post-hoc* pairwise comparisons (Bonferroni's post-criterion test) indicated that HC mean score ( $n = 85$ ,  $M = 0.96$ ,  $SD = 0.3$ ) was significantly different from the other three disease conditions: NEU ( $n = 29$ ,  $M = 0.54$ ,  $SD = 0.3$ ,  $p = .000$ ), CPSD ( $n = 46$ ,  $M = 0.59$ ,  $SD = 0.23$ ,  $p = .000$ ), and MED ( $n = 26$ ,  $M = 0.71$ ,  $SD = 0.29$ ,  $p = .003$ ); there was no significant difference between NEU, MED, and CPSD groups.

## Conclusions

The results support the validity of SCT use to evaluate the effect of different disease conditions on pediatric cognitive functioning. We found that the presence of a neurological condition or prolonged exposure to psychosocial stress and deprivation are associated to lower visuo-motor processing ability. The encouraging results of our study highlight the potential of SCT as a viable, reliable, and cost-effective solution for child's cognitive health assessment in Zambia. Future research should characterise SCT clinical utility and diagnostic accuracy (i.e., sensitivity and specificity) in relation to specific disease conditions. These results also warrant further validation of SCT use to monitor treatment response in clinical trial settings.

## SCT Test Structure

*Symbol cancellation involves searching, scanning and detection for a pre-defined target against a background of distractors that are arranged in a matrix organised in rows and columns. The Data Capture Sheet is placed in front of the subject showing the organised array (dimension: 25x17cm) containing 324 familiar shapes (\*, <, +), 108 targets and 236 distractors, equally distributed across four quadrants, with 27 targets and 54 distractors each. The subject is not allowed to change the position of the sheet and is asked to mark every target symbol by a single slanted line. The subject is asked to strike corresponding targets as fast as he/she can. The task is interrupted at 180 seconds from start. A brief training session is conducted before the test session.*