CAMCI: Advancing the Use of Computerized Screening in Healthcare

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Analysis Plan

Validation of CAMCI Algorithm and MoCA with Neuropsychological Adjudication

CAMCI will group participants into three classifications: impaired, non-impaired, and intermediate. Likewise, the neuropsychological adjudication will provide a consensus classification for participants into impaired, non-impaired, and intermediate and thus, CAMCI classifications will be compared to clinical adjudication. Similarly, MoCA classification will be evaluated against the neuropsychological adjudication. MoCA scores are classified as non-impaired (MoCA ≥ 26) or impaired (MoCA <17), with intermediate scores occurring between 18-25. To validate the CAMCI and MoCA against the neuropsychological adjudication, we will evaluate positive and negative predictive agreement, accuracy and error bias. Accuracy is defined as the correct identification using CAMCI: ACC=[TP+TN]/total; error bias will be a contrast ratio of false positives and false negatives: FP-FN/FP+FN.

Agreement analysis

Two methods will be used to evaluate the agreement of CAMCI to non-reference (Montreal Cognitive Assessment, MoCA) and reference (clinical adjudication) standards. First, using linear regression, agreement analysis will be done to compare the subject device, CAMCI score (expected to range from 0-50), and the MoCA score (ranging from 0-30). Agreement will be evaluated using the scatterplot, linear regression equation and confidence intervals, and Pearson correlation. It will be expected that each of these evaluation methods will show that those patients who score high on the CAMCI will also score high on the MoCA, indicating agreement between the range of scores that are non-impaired. Likewise, we will expect to see low scores on the CAMCI to be found in those who also show low MoCA scores, indicating agreement in the ranges of impaired scores on both assessments.

Next, agreement will be assessed using the clinical adjudication categories and the CAMCI classifications. The following table will be used to display the frequencies showing the distribution of patients into the CAMCI classifications (impaired, non-impaired, intermediate/indeterminate) by clinical adjudication (normal, impaired, indeterminate). From this summary, percent agreement (positive and negative), confidence interval estimates, and quadratic weighted kappa will be used to assess the agreement between CAMCI and the reference standard. Finally, this analysis will be repeated with the omission of the intermediate group to show the performance of CAMCI for those who are clearly impaired and clearly non-impaired.

Example, Agreement analysis (general case in 3x3):

		Classification		
		Impaired	Intermediate	Non-impaired
TEST	Impaired	TP*	FP	FP
	Intermediate	FN	TP	FP
	Non-impaired	FN	FN	TN

* TP=True Positive, TN=True Negative, FP=False Positive, FN=False Negative

Example, Agreement analysis (for current study)*:*

Classification by Clinical Adjudication				
		Impaired	Intermediate	Non-impaired
CAMCI	Impaired	a	b	c
	Intermediate	d	e	f
	Non-impaired	g	h	i

Classification by Clinical Adjudication				
		Impaired	Intermediate	Non-impaired
MoCA	Impaired	a	b	c
	Intermediate	d	e	f
	Non-impaired	g	h	i

Positive percent agreement (PPA, %) = 100 X (a + e) / (a + b + c + e + f)
Negative percent agreement (NPA, %) = 100 X (i) / (d + g + h + i)
Accuracy (ACC) = [(a + e) + (i)] / total n
Error Symmetry ([(b + c + f) – (d + g + h)] / total n

Change Metric

Test-retest descriptive statistics (mean, standard deviation) will be calculated and compared for the clinical groups (impaired, intermediate, non-impaired). Difference scores will be calculated and analyzed for retest effect and to identify any patterns (improvement/decline) that might differ between the groups on retest. Finally, repeated measures analyses will be used to assess group X retest differences. This information will be used to determine whether adjustments will be made to the reliable change calculations.

Change in test scores will be modelled using a Reliable Change Index (RCI) method to determine whether the change in test scores is due to the reliability of the measure (rather than due to chance alone). This method is beneficial because it is well-documented and is one that accounts for measurement error and practice effect (Chelune et al., 1993; Hensel, 2007). It has also been shown (Hsu et al., 1999) to account for regression to the mean. Reliable change will be evaluated at the 6-month, one-year, and two-year intervals.

Using normative data from a prior sample, and data gathered from the non-impaired clinical group, an appropriate strategy will be identified for the identification of cut-off scores for clinically significant change (Jacobson and Truax, 1991). Data will then be used to derive standard error of the mean (SEm), test-retest reliability coefficients, and standard error of the difference (SEdiff) statistics. The latter, SEdiff, will identify the variability in the distribution of the change scores that would be expected if there were no change between test and retest. Finally, 90% and 95% confidence intervals will be calculated to identify the amount of difference that would have to be observed in either direction to assume that the difference occurred beyond chance (at significance levels of 5% and 2.5%, respectively).

Reliable change will be calculated using the following formula for all data regardless of clinical group:

$$RC = \frac{x_2 - x_1}{SE_{diff}}$$

Using established methods (Chelune et al. 1993), index scores will classify patterns of change as “gain”, “no change”, and “loss”. Likewise, the same individuals will be grouped based on change in clinical adjudication between those identified as impaired, intermediate, and non-impaired at each assessment, categorizing status change as “improved”, “no change”, and “declined”. These groups will be analyzed based on the confidence intervals, accuracy, and reliable change index. Analysis will include the assessment of practice effect.

References

Chelune GJ, Naugle RI, Luders H, Sedlak J, Awad IA. Individual change after epilepsy surgery; Practice effects and base-rate information. Neuropsychology, 1993; 7: 41-52.

Hensel A, Angermeyer MC, Riedel-Heller SG. Measuring cognitive change in older adults: reliable change indicies for the Mimi-Mental State Examination. J Neuro Neurosurg Psychiatry 2007; 78: 1298-1303.

Hsu LM. Caveats concerning comparisons of change rates obtained with five methods of identifying significant client changes: comment on Speer and Greenbaum (1995). J Consult Clin Psychol 1999; 67: 594-98.

Jacobson, N.S., & Truax, P. Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. Journal of Consulting and Clinical Psychology, 1991; 59, 12-19.