ORIGINAL ARTICLE

Discrimination of the Cognitive Profiles of MCI and Depression using the KBNA

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ABSTRACT: ***Objective:*** The current study sought to determine if the Kaplan-Baycrest Neurocognitive Assessment (KBNA) was capable of discriminating individuals with subjective memory complaints associated with depression from individuals with mild cognitive impairment (MCI). ***Methods:*** Scores on 12 subtests of the KBNA were compared for 27 participants with MCI and 28 participants being treated for depression using Bonferroni correct between-group comparisons for each subtest. KBNA subtest scores were corrected for age and education. ***Results:*** Significant between-group differences were obtained on six subtests with large effect sizes (Cohen's d) ranging from 1.19 – 1.58. The six subtests involved encoding and delayed episodic memory for verbal and visual information. Using logistic regression analysis, five subtests of the KBNA were able to correctly classify 96.4% of study participants. ***Conclusion:*** The results from this preliminary investigation indicate that the KBNA has the potential to serve as a brief and reliable assessment tool capable of distinguishing individuals with subjective memory complaints associated with depression from individuals with MCI in a clinical setting. Limitations of the current study and future research are discussed.

RÉSUMÉ: Discrimination des profils cognitifs du déficit cognitif léger et de la dépression au moyen du KBNA. ***Objectif :*** Le but de cette étude était de déterminer si le Kaplan-Baycrest Neurocognitive Assessment (KBNA) pouvait distinguer les individus qui ont des pertes de mémoire subjectives associées à une dépression de ceux qui ont un déficit cognitif léger (DCL). ***Méthode :*** Les scores obtenus lors de 12 sous-tests du KBNA chez 27 sujets atteints de DCL et 28 sujets traités pour dépression ont été comparés en utilisant la correction de Bonferroni pour les comparaisons entre groupes pour chaque sous-test. Les scores aux sous-tests KBNA ont été corrigés pour l'âge et le niveau de scolarité. ***Résultats :*** Des différences significatives entre les groupes ont été observées pour 6 sous-tests avec de grandes tailles d'effets (d de Cohen) allant de 1,19 à 1,58. Les 6 sous-tests comportaient l'encodage et le rappel de la mémoire épisodique pour l'information verbale et visuelle. À l'analyse de régression logistique, 5 sous-tests du KBNA étaient capable de classifier correctement 96,4% des sujets. ***Conclusion :*** Les résultats de cette étude préliminaire indiquent que le KBNA pourrait être utilisé comme outil d'évaluation bref et fiable, capable de faire la distinction en clinique entre les individus qui ont des pertes de mémoire subjectives associées à la dépression et ceux qui ont un DCL. Nous discutons des limites de notre étude et des recherches à effectuer à l'avenir.

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Individuals with Mild Cognitive Impairment (MCI) or depression often present with subjective memory complaints (SMC). A persistence of SMC after treatment for depression may lead to a presumption of MCI; therefore being able to accurately distinguish between these two disorders becomes crucial. A neuropsychological battery that best discriminates between these two disorders is needed[1,2] as early diagnosis of MCI as well as dementia is becoming increasingly important due to the availability of pharmacological and nonpharmacological treatments for both disorders.[3] The correct diagnosis of first episode or recurrent depression in older adults is equally important as cognitive impairments in this disorder may be reversible when effective treatments are administered, however these can only be accessed when a diagnosis is given.[4]

Depression and MCI often co-occur[2,5] and, for a subset of elderly individuals, late-life depression, MCI, and dementia might form a continuum.[6] Depression and MCI are also often mistaken for each other, as there is a significant amount of overlap in the cognitive complaints present in these two disorders.[7] Zihl and colleagues[8] reported no significant differences in the neuropsychological profiles of individuals with depression and cognitive impairment and individuals with MCI when both groups were compared to healthy controls.

The presence of cognitive dysfunction in depression is now clearly established[2,9], but cognitive deficits in older populations with depression are more heterogeneous than those in younger populations.[10,11] Cognitive deficits in depression are more likely to be present in those with long histories of recurrent depression and in those with first episode late-life depression,[9] and are less likely to remit fully after treatment in older versus younger populations.[11] This treatment resistance results from an interaction with age, depression severity, and also possible co-morbidity with MCI.[10-12] The combination of depression with MCI has a worse outcome and a higher rate of conversion to dementia than MCI alone.[13]

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Depressed individuals have a high number of SMC[4]. However, the high number of SMC in depression is a confound when distinguishing depression from MCI as SMC are also diagnostic criteria for MCI.[14] In fact, Mitchell[15] proposed that subjective cognitive complaints should no longer be used to diagnose MCI given their ubiquity in many other disorders of older adults, including depression.

The cognitive domains most often found deficient in late-life depression involve episodic memory, processing speed, executive functions, and visuospatial ability.[9,10] On the other hand cognitive deficits are not always found in depression. Fischer and colleagues[4] reported that although depressed individuals had significantly higher numbers of cognitive complaints, no significant differences were obtained on a battery of neuropsychological tests, when they were compared to individuals without depression.

Although MCI was first described as an impairment in episodic verbal memory,[16] subsequent studies have revealed that MCI is a heterogeneous condition[17,18] and a comprehensive neuropsychological assessment is necessary for accurate diagnosis.[19] Therefore, the classification of MCI as primarily an impairment of memory,[20] with the distinction between depression and MCI based on impairments in executive functions being unique to depression,[11] is no longer adequate. MCI is classified under three subtypes: pure amnestic MCI, multi-domain MCI, and non-amnestic MCI.[17,20,21] Due to the heterogeneity of MCI, any cognitive domain and almost any task has the potential to be impaired in one of the three subtypes of the disorder.[8]

There is currently no screening measure for cognitive impairment that can reliably distinguish depression from MCI. Sikkes and colleagues[22] reported that the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) could distinguish between Alzheimer's disease (AD) and MCI, and AD and SMC, but the IQCODE could not distinguish between MCI and SMC. The most reliable distinctions and correct diagnoses come from thorough, and often time consuming, neuropsychological assessments.[2]

The ideal would be to have a relatively brief, but thorough test battery that could reliably distinguish depression from MCI.[23] The Kaplan-Baycrest Neurocognitive Assessment (KBNA) is a good candidate for this task as it consists of 12 core subtests evaluating episodic memory (verbal and visual), attention control, working memory, language production, reasoning, and cognitive flexibility. It takes 50 - 65 minutes to complete. Scores on the various KBNA subtests and indices have been shown to be correlated with other neuropsychological tests including the Dementia Rating Scale, Wechsler Adult Intelligence Scale-R, Wechsler Abbreviated Scale of Intelligence, Wechsler Memory Scale-III Logical Memory and Mental Control, California Verbal Learning Test-II, Rey-Osterrieth Complex Figure copy and memory scores, Boston Naming Test and Controlled Oral Word Association Test.[24] Moreover, it has been found that three subtests from the KBNA were able to correctly distinguish 98% of individuals with mild dementia from individuals without dementia.[25]

The present study evaluated the ability of the 12 core subtests of the KBNA to distinguish between the cognitive profiles of individuals with MCI and individuals with SMC associated with depression. The subtests of the KBNA that have the greatest potential for distinguishing these profiles are the episodic memory subtests (Word List 1 and 2 Recall, Word List 2 Recognition, Complex Figure 1 and 2 Recall and Complex Figure 2 Recognition)[7,19,26] as these have clearly been shown to identify individuals with mild dementia.[25] It is not clear, however to what degree other KBNA subtests may contribute to the discrimination of MCI and depressed individuals with SMC. In order to address this question, we conducted a retrospective study based on data obtained from a clinical database.

Method

Data selection

The data were selected from a database of clients referred for neuropsychological assessment to the Neuropsychological Consultation Service of the Baycrest Centre for Geriatric Care or the Sunnybrook Health Sciences Centre in Toronto, Ontario. Participants were referred by their general practitioner to a memory clinic to be seen by a neurologist, psychiatrist, or geriatrician and neuropsychologist. Data were entered without personal identifying information; participants being identified only by an alphanumeric code. Database information included age, gender, education, medical diagnoses, neuropsychological test data including raw and age-corrected standard scores for all subtests of the KBNA and other neuropsychological tests, primary diagnoses relevant to the differential diagnosis (e.g. MCI, depression, Alzheimer's disease, etc.) and additional medical conditions or diagnoses (e.g. hypertension, cerebrovascular dementia, diabetes) being medically treated at the time of the assessment. The primary diagnosis was based on consensus diagnoses obtained from the consulting neurologists, neuropsychologists, and/or psychiatrists and supporting evidence based on neuroimaging and laboratory studies as well as reports from allied health professionals such as speech-language pathologists or occupational therapists.

Consensus diagnosis of MCI was made if there was the presence of: a subjective memory complaint (preferably corroborated by another informant), objective evidence of memory impairment, preserved general cognitive function, preserved Activities of Daily Living (ADLs) and no dementia.[14,27] Diagnosis of depression was based on DSM-IV criteria[28] obtained from a clinical interview although information from self-report inventories or structured inventories (e.g. SCIDS, Beck Depression Inventory (BDI-II)) may have been administered as ancillary measures to support the diagnosis. The database was searched for all participants with a primary diagnosis of depression or MCI. Participants with a primary diagnosis of depression but without secondary diagnosis of MCI were assigned to group DEP. Participants with a primary diagnosis of MCI but without secondary diagnosis of depression were assigned to group MCI. Participants' data were excluded if any of the following additional diagnoses were present; dementia, head injury, stroke, alcoholism, seizure disorder, schizophrenia, substance abuse, or neurodegenerative disorders.

Twenty-seven participants met the selection criteria for MCI (group MCI) and 28 for depression (group DEP). All participants included in group DEP were, or had been, treated for a major depressive disorder at the time of assessment. The median BDI-

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II score for group DEP was 17 (range 4 - 34) and for group MCI was 8 (range 0-12). Only one person in the group DEP scored four and the next lowest score was 14, resulting in very little overlap between the two groups. Participants in group DEP and group MCI both had subjective memory complaints; no participants in group DEP were being treated with cholinesterase inhibitors at the time of testing, compared to two participants from group MCI. The composition of group MCI with respect to type of MCI was as follows: MCI-anmestic n = 22; MCI-amnestic-multiple domain n = 5.

Description of the 12 subtest scaled scores of the KBNA

Sequences (SEQ). This subtest measures attention and mental control. There are four tasks: reciting the months of the year forward and backwards (measures sustained attention and ability to manipulate information), naming letters that rhyme with the word key, naming printed capital letters that contain curved lines (both measures of working memory) and counting backwards by fours (measure of focused attention).

Spatial Location (SPLOC). This subtest measures spatial memory for location and can be an indication of the examinees spatial working memory capacity. The examinee is presented with figures containing three to seven dots placed on either a 3x3 or a 4x4 matrix. The examinee views each figure for ten seconds and must replicate each figure by placing the correct number of dots in their correct location.

Word List 1 Recall (WL1). This subtest measures encoding and retrieval prior to consolidation. The examinee is read a list of 12 words and then is asked to recall as many of the words as possible. The word list is read to the examinee four times with free recall being required after each presentation. The total number of words recalled across the four trials was used to calculate the examinees age-corrected score.

Complex Figure 1 Recall (CF1). This subtest measures the encoding of visual information. A diagram of a complex figure is presented and the examinee is asked to copy the figure. Then the diagram is removed and the examinee is required to immediately reproduce the complex figure from memory.

Word List 2 Recall (WL2). This is a measure of episodic recall of learned, verbal information. The examinee is requested to recall the 12 words presented in Word List 1 after a 15-20 minute delay using free recall and cued recall paradigms.

Complex Figure 2 Recall (CF2). This measures retrieval of episodic information in the visual modality. The examinee must reproduce the abstract figure presented and copied in Complex Figure 1 after a 15-20 minute delay.

Word List 2 Recognition (WLREC). This measures retention of verbal information learned in Word List 1. The examinee is asked to recognize the 12 words from Word List 1 from a list containing the 12 target words and 24 non-target words.

Complex Figure 2 Recognition (CFREC). This measures retention of visual memory for detail and location. First the examinee must recognize isolated parts of the abstract figure presented in Complex Figure 1 among 3 distracters. The examinee must then place each isolated part of the figure in its correct location when presented with the general contour of the figure.

Complex Figure 1 Copy/Clocks (CF1/C). This is a measure of visuoconstruction ability. In addition the Clocks test measures semantic memory, executive function, specifically planning and organization. In Complex Figure 1 Copy the examinee copies the abstract figure with the figure in view. In Clocks, the examinee must produce a free drawn clock with a specific time, the numbers and time to a pre-drawn contour, and a copy of a clock stimulus that is in view.

Phonemic Verbal Fluency (PHF). This measures the ability to produce as many words as possible in one minute beginning with a letter of the alphabet (C).

Semantic Verbal Fluency (SEMF). This test measures the ability to produce as many words as possible in one minute that belong to a particular semantic category (first names and animals).

Practical Problem Solving/Conceptual Shifting (PPS/CS). Practical Problem Solving is a measure of cognitive competency and flexibility and Conceptual Shifting measures the ability to recognize similarities between objects and the ability to shift attention. Practical Problem Solving requires the examinee to generate two different responses to how they would react in scenarios representing situations of urgency or emergency. Conceptual Shifting requires the examinee to identify two different physical similarities between three of four line drawings that share similar physical attributes (e.g. size, shading, shape) and to characterize this similarity.

Total Index Score. The Total Index (KBNA-TI) score of the KBNA represents a composite of performance on the 12 KBNA subtests scores listed above. The score is presented as a T-score (M = 50, SD = 10).

Other measures. In addition to the KBNA scores listed above the following scores were also extracted from the database: Full Scale IQ (FSIQ) form either the Wechsler Adult Intelligence Scale-III (WAIS-III) or Wechsler Abbreviated Scale of Intelligence (WASI); the age-corrected score from the Boston Naming Test (BNT); the age-corrected score of the Trail Making Test A and B (TMTA and TMTB); the age-corrected score for the Digit Span subtest of the WAIS-III and the Global Deterioration Scale (GDS) score. The GDS is a 7-point rating scale used as a measure of the severity of cognitive impairment with a low score of 1 indicating no cognitive decline to a high score of 7 indicating very severe cognitive decline.[29]

Statistical analyses

The age-corrected scaled scores for each subtest of the KBNA were used in the data analyses, thereby controlling for the effect of age. The age-corrected scaled scores are transformed scores with a mean of 10 and standard deviation of 3. A Multivariate Analysis of Covariance (MANCOVA) was performed with the scores of the 12 subtests of the KBNA as the dependent measures, group (DEP vs. MCI) as a between subject factor and, because the norms for the KBNA are not education corrected, education as a covariate. Multiple, between-group comparisons for each subtest were performed using the Bonferroni correction. In addition, univariate effects sizes (Cohen's d) were calculated for the between-group differences on the 12 dependent measures. A forward stepwise logistic regression was performed to determine which of the 12 subtests of the KBNA best classified group membership. All analyses were done using a statistical software package (SPSS version 16.0).

Statistical analysis of the BNT, TMTA, TMTB and Digit Span was based on age-corrected scaled scores (M = 10; SD = 3). Between-group differences for FSIQ were performed using a Student's t-test. In order to analyze within-group, FSIQ vs. KBNA-TI differences, the FSIQ was converted to a T-score using a linear transformation based on the z-score equivalent of the FSIQ. For example, an FSIQ of 112 is equivalent to a z-score of +.8 and this translates to a T-score of 58 (e.g. (10 x .8) + 50). The FSIQ-KBNA-TI difference was then analyzed using a within-subjects', Student's t-test.

Results

Demographic factors

Group MCI was significantly older (M = 77.2 years, SD = 7.3) than group DEP (M = 69.7 years, SD = 9.9), $F(1, 54)$ = 10.01, p = 0.003. This difference in age was corrected prior to analysis by use of age-corrected subtest scaled scores in the analyses. Group MCI also had more years of education (M = 15.2, SD = 2.9) than group DEP (M = 13.3, SD = 3.2), $F(1, 54)$ = 5.74, p = 0.02. The gender composition of group DEP (male = 15; female = 13) and group MCI (male = 12; female = 15) was not significantly different, χ^2 = .89, p = .35. The median GDS rating was significantly lower for group MCI (MDN = 3.0; rating = mild cognitive decline) than for group DEP (MDN = 2.0; rating = very mild cognitive decline), *Mann-Whitney* U = 126.5, p < .0001.

The MCI group scored significantly lower on KBNA-TI index (M = 41.0; SD = 7.9) than did the DEP group (M = 50.6; SD = 14.9), $t(53)$ = 2.95, p = .005. There were no significant differences on the other neuropsychological measures. The mean FSIQ of groups MCI (M = 112.7; SD = 13.1) and DEP (M = 108.4; SD = 17.8) did not differ significantly, $t(53)$ = 1.01, p = .32. The mean BNT score for group MCI was 10.5 (SD = 3.7) and 11.2 (SD = 3.3) for group DEP, $t(53)$ = .75, p = .46. The mean TMTA score for group MCI was 8.6 (SD = 2.8) and 8.3 (SD = 3.5) for group DEP, $t(53)$ = .28, p = .78. The mean TMTB score for group MCI was 8.0 (SD = 3.8) and 7.7 (SD = 3.8) for group DEP, $t(53)$ = .23, p = .82. The mean Digit Span score for group MCI was 10.6 (SD = 3.0) and 10.5 (SD = 2.9), $t(53)$ = .12, p = .90.

Overall ability of the KBNA to distinguish MCI from DEP

Because of the significant between-group difference in education, this variable was entered as a covariate in the MANCOVA. Education had no significant effect on the overall MANCOVA (*Wilks'* Λ = .76, $F(1,12)$ = 1.05, p = .42), but education did have a significant effect on the following subtest scores; Sequences (F = 5.45, p = .02), Complex Figure 2 Recall (F = 4.60, p = .04), and Complex Figure 2 Recognition (F = 4.16, p = .05).

Table 1 shows the mean performances on the 12 subtests of the KBNA for the DEP and MCI participants. The MANCOVA was significant, *Wilks'* Λ = .36, F(12, 41) = 6.16, $p < 0.001$, η^2 = 0.64. The DEP group obtained significantly higher scores than the MCI group on the Word List 1 Recall (WL1), Complex Figure 1 Recall (CF1), Word List 2 Recall (WL2), Complex Figure 2 Recall (CF2), Word List Recognition (WLREC) and Complex Figure 2 Recognition (CFREC) subtests (experiment-

Table 1: Descriptive statistics and individual subtests results of education corrected MANCOVA. Univariate effect sizes given as Cohen's d statistic corrected for sample size

KBNA subtest	Group	Mean (95% CI)	*SD*	*F(1,52) p*	Cohen's *d* (95% CI)
Sequences	MCI	11.67 (10.72-12.62)	2.40	.35	+.36
	DEP	10.71 (9.60-11.83)	2.87	*.56*	(-.18, +.89)
Spatial Location	MCI	10.22 (9.19-11.26)	2.62	2.67	+.52
	DEP	8.79 (7.72-9.85)	2.75	*.11*	(-.01, +1.06)
Word List 1 Recall	MCI	7.52 (6.69-8.35)	2.10	17.46	-1.19
	DEP	10.89 (9.60-12.18)	3.33	*.001*	(-1.76, -.62)
Complex Figure 1 Recall	MCI	5.59 (4.69-6.50)	2.29	29.76	-1.35
	DEP	9.82 (8.39-11.25)	3.68	*.001*	(-1.94, -.77)
Word List 2 Recall	MCI	6.04 (4.92-7.16)	2.84	31.65	-1.58
	DEP	11.07 (9.75-12.39)	3.40	*.001*	(-2.19, -.98)
Complex Figure 2 Recall	MCI	5.52 (4.86-6.18)	1.67	30.67	-1.32
	DEP	9.50 (8.01-10.99)	3.84	*.001*	(-1.90, -.73)
Word List 2 Recognition	MCI	6.07 (4.91-7.24)	2.95	24.44	-1.39
	DEP	10.46 (9.20-11.72)	3.25	*.001*	(-1.98, -.80)
Complex Figure 2 - Recognition	MCI	5.19 (4.50-5.87)	1.73	39.84	-1.54
	DEP	9.36 (8.07-10.65)	3.32	*.001*	(-2.14, -.94)
Complex Figure 1 Copy / Clocks	MCI	11.11 (9.66-12.56)	3.66	.02	+.15
	DEP	10.57 (9.16-11.99)	3.65	*.89*	(-.39, +.68)
Phonemic Verbal Fluency	MCI	10.15 (8.92-11.38)	3.11	.50	+.36
	DEP	8.96 (7.67-10.26)	3.40	*.48*	(-.17, +.90)
Semantic Verbal Fluency	MCI	8.30 (7.12-9.47)	2.97	2.07	-.24
	DEP	9.25 (7.49-11.01)	4.54	*.16*	(-.77, +.29)
Practical Problem Solving/ Conceptual Shifting	MCI	10.56 (9.45-11.67)	2.81	.30	+.23
	DEP	9.86 (8.65-11.06)	3.11	*.59*	(-.30, +.76)

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wise with Bonferonni correction $p < .05$; each individual comparison $p < .004$). No other significant between group differences were obtained. It is important to note however, that the DEP participants performed within the average range on all measures when compared to the age-matched normative sample used to validate the KBNA, and that the MCI participants were impaired on all memory measures relative to the normative sample of the KBNA.

Table 1 shows the Effect Sizes (Cohen's *d*) and 95% Confidence Intervals of the differences between the groups' DEP and MCI performances on the 12 Subtests of the KBNA. Negative effect sizes indicate that group MCI scored lower than group DEP and positive effect sizes indicate the reverse. The six subtests on which the DEP group scored significantly higher than the MCI group (WL1, CF1, WL2, CF2, WLREC and CFREC) all had large effect sizes ranging from 1.19 – 1.58. Non-significant tests comparisons fell in the range of small to medium effect sizes.

Ability of the KBNA subtests to predict group membership

Table 2 summarizes the results of the forward, step-wise logistic regression. Five subtests of the KBNA, Sequences (SEQ), Complex Figure 1 Immediate Recall (CF1), Word List 2 Delayed Recall (WL2), Complex Figure 2 Recognition (CFREC), and Spatial Location (SPLOC), correctly classified 96.4% (95% CI 91.4 – 99.9%) of the DEP and MCI individuals. A pattern of relatively poor performance on SEQ and SPLOC subtests and good performance on CF1, CFREC, and WL2 best predicted DEP group membership. In contrast, relatively poor performance on CF1, CFREC, and WL2 but good performance on SEQ and SPLOC subtests best predicted group MCI membership.

In order to address the issue of the effect of using the KBNA memory tests to partially identify members of the MCI group during the initial clinical diagnosis, two additional logistic regression analyses were performed. The first analysis included only those memory test scores that were included in the first analysis above, namely; CF1, CFREC and WL2. The second analysis included all memory test scores from the KBNA; WL1, WL2, WLCFREC, CF1, CF2 and CFREC.

Entering memory test scores CF1, CFREC and WL2 into a logistic regression correctly classified 87.3 % (95% CI 76.0 – 93.7%) of the sample. Entering all memory test scores, WL1, WL2, WLREC, CF1, CF2, and CFREC, into a logistic

Table 2: Results of forward, step-wise logistic regression

Step	Variables	B	S.E.	Wald	df	Sig.	Odds Ratio Exp(B) (95% C.I.)
1	Word List 2 – recall	.54	.14	14.03	1	.0001	1.72 (1.30 – 2.29)
	Constant	-4.54	1.26	12.98	1	.0001	.01
2	Spatial location	-.52	.20	6.43	1	.011	.60 (.40 - .89)
	Word list 2 - recall	.74	.21	12.63	1	.0001	2.09 (1.39 – 3.14)
	Constant	-1.27	1.68	.58	1	.28	.43
3	Spatial location	-.85	.31	7.72	1	.005	.43 (.23 - .78)
	Word list 2 - recall	.58	.22	7.23	1	.007	1.78 (1.17 – 2.72)
	Complex figure 2 - recognition	.74	.27	7.31	1	.007	2.09 (1.22 – 3.57)
	Constant	-1.73	1.70	1.04	1	.308	.18
4	Spatial location	-1.24	.44	8.10	1	.004	.29 (.12 - .68)
	Complex figure 1- recall	.65	.34	3.68	1	.055	1.91 (.99 – 3.71)
	Word list 2 – recall	.47	.22	4.66	1	.031	1.60 (1.04 – 2.45)
	Complex figure 2 - recognition	.67	.31	4.62	1	.032	1.95 (1.06 – 3.60)
	Constant	-1.51	1.93	.61	1	.434	.22
5	Sequences	-1.37	.73	3.50	1	.062	.26 (.06 – 1.07)
	Spatial location	-1.80	.82	4.83	1	.028	.17 (.03 - .82)
	Complex figure 1 – recall	1.58	.91	3.01	1	.083	4.88 (.82 – 29.23)
	Word list 2 – recall	1.14	.59	3.68	1	.055	3.13 (.98 – 10.02)
	Complex figure 2 - recognition	1.19	.67	3.13	1	.077	3.30 (.88 – 12.36)
	Constant	2.92	3.49	.70	1	.403	18.54

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regression correctly classified 89.1% (95% CI 80.5 – 97.3%). Compared to using all memory scores to assign class membership, using only three memory test scores (CF1, CFREC and WL2) and the SEQ and SPLOC subtest scores, improved overall diagnostic accuracy by 7.3%. The greatest impact the inclusion of the SEQ and SPLOC had on diagnostic accuracy was to increase specificity, i.e. improving correct identification of DEP group membership. The sensitivity of using all memory test scores to identify MCI was .926 (95% CI .766 – .979) and specificity of identifying DEP was .857 (95% CI .685 - .943). In contrast, addition of the SEQ and SPLOC scores improved sensitivity by .038 to .963 (95% CI .817 - .993) but increased specificity by .106 to .964 (95% CI .823 - .994).

Associations of the KBNA scores with other test scores

Significant correlations obtained between the FSIQ and KBNA-TI for group MCI, $r(25) = .70$, $p < .001$, and for group DEP, $r(26) = .85$, $p < .001$. Although the two groups did not differ in their mean FSIQ scores, the FSIQ (converted to T-scores) was significantly higher than the KBNA-TI scores within both group MCI, $M = 17.3$; $SD = 6.5$, $t(26) = 13.9$, $p < .001$ and within group DEP ($M = 4.9$; $SD = 7.9$, $t(27) = 3.3$, $p = .003$. The effect size of the within-group difference was greater for group MCI, Cohen's d = 2.9, 95% CI 1.87 – 3.32, than for group DEP, *Cohen's d* = .60, 95% CI .06 – 1.14, however.

Performance on the KBNA was associated with the level of rated severity of cognitive decline. The KBNA-TI score was negatively correlated with the Global Deterioration Scale rating (where a higher score signifies greater disability), $r(53) = -.66$, $p < .001$. The probability of being assigned to the MCI group, based on the logistic regression formula, was positively correlated with the GDS rating (where a higher probability is associated with greater cognitive decline), $r(53) = .40$, $p = .003$.

Within group DEP, no significant correlations obtained between the BDI score and the SEQ ($r = -.14$, $p = .62$), SPLOC ($r = .1$, $p = .74$), CF1 ($r = -.02$, $p = .95$), WL2 ($r = -.14$, $p = .64$), CFREC ($r = .03$, $p = .92$) or KBNA-TI ($r = -.01$, $p = .982$) scores. Insufficient number of group MCI participants were administered the BDI to justify calculating correlations between the BDI and KBNA scores.

Discussion

The primary goal of this study was to determine which subtests of the Kaplan-Baycrest Neurocognitive Assessment (KBNA) best distinguished individuals diagnosed with depression and reporting subjective memory complaints from those with a diagnosis of MCI. The memory measures, Word List 1 and 2, Complex Figure 1 and 2, Word List 2 Recognition and Complex Figure 2 Recognition, and the non-verbal measures of Sequences (attention control) and Spatial Location (spatial working memory) were best at discriminating individuals with depression from those with MCI. The memory subtests were the only ones to show significant, between-group differences, however and the depression group scored higher than the MCI group on all significant measures.

The participants' scores on the five subtests of the KBNA were able to assign group membership with an accuracy of 96.4%. Relatively poor performances on subtests of visual working memory and attention control, but good performances on tests of visual and verbal episodic memory, were best at identifying individuals with depression. The reverse pattern best identified individuals with MCI. Leach[25] showed that the Complex Figure 1, Word List Recognition and Semantic Verbal Fluency subtests could correctly classify 98% of individuals with mild dementia and without dementia. Except for the Complex Figure 1 subtest, the subtests that distinguish depression from MCI are different from those that distinguish mild dementia from individuals without dementia.

The performance of the group with treated depression was average and none of the group scores could be classified in the impaired range despite subjective cognitive complaints by all group members. This is in line with results reported by Fischer and colleagues[4] who found differences in subjective cognitive complaints present in depressed versus non-depressed individuals, but with no differences between depressed and non-depressed individuals on objective neuropsychological tests. The Fischer et al study may have failed to find significance due to lack of power as both the depressed group and non-depressed control group were small (n = 17 and 19 respectively). We did find evidence that although they were not psychometrically impaired, our group with depression may have suffered a modest decline in cognitive performance. When the depressed group's overall performance on the KBNA was compared to expected performance based on their FSIQ scores, there was evidence that depression resulted in a moderate and significant decline in cognitive performance. Nevertheless, we found no correlation between level of depression (assessed by available BDI scores) and any of the KBNA subtest scores included in the regression formula. Also, the effect size of the FSIQ versus KBNA-TI difference was within the range of effect sizes reported in meta-analyses of studies that included depressed individuals and non-depressed controls[23] as well as between elderly patients with either early or late-depression and elderly controls.[10] This FSIQ versus KBNA-TI difference was significantly less than that expressed by the MCI group, however. The MCI group was impaired on measures of memory but impairments in other domains reported by other authors[1,3,8,17,18,20] were not shown on the other subtests of the KBNA.

In the present study, the KBNA was capable of discriminating the MCI and depression groups based on the pattern of specific test scores. Not surprisingly, the memory test scores resulted in a large proportion (87.3%) of individuals classified correctly. But addition of scores on non-verbal memory, representing attention control (Sequences subtest) and spatial working memory (Spatial Location subtest) increased overall classification accuracy by 7.6% and increased specificity (i.e. identifying depressed individuals) by 10.6%. Although the increase in specificity may not appear large, it has significant, clinical ramifications. Assume that 1000 individuals are seen and there is equal pre-test probability, i.e. 0.5, of being assessed as depressed or MCI. If only the memory tests were used to diagnose, then 72 individuals would be incorrectly identified as MCI and 37 incorrectly identified as depressed. If the five subtests identified in the regression formula in Table 2 were used, then only 18 would be misdiagnosed as MCI and 18 as depressed. This represents a 75% reduction in false-positive rate and 49% reduction in the false-negative rate.

The practical application is as follows: If the differential diagnosis is between depression and MCI, then the pattern of KBNA test scores can facilitate assignment of an individual to the most probable diagnosis. Three conditions must be met in order to use the regression formula, however. First, the patient in question must be similar in demographic features to those utilized in this study. Second, the differential must be between MCI amnestic or amnestic-multiple domain MCI and depression and not non-amnestic MCI and depression. Third, the regression cannot be used indiscriminately as a screen. It would be inappropriate to apply it to an individual without subjective memory complaint and then, based on the output of the regression formula, claim support for a diagnosis of depression or MCI. If the purpose is to screen for cognitive impairment, then the method and data provided by Leach[25] is more appropriate.

Applying the obtained scores to the logistic regression formula in Table 2 will yield the natural logarithm of the odds, *ln*(odds), of being classified as depressed. The *ln*(odds) then can be transformed to a probability by using the formula; $p(\text{dep}) = e^{ln(odds)} / (1 + e^{ln(odds)})$. Here are two examples of the application to the results taken from individuals belonging to group MCI and DEP. Client-1 is a 67-year-old woman with 14 years of education, a FSIQ of 116, an MMSE of 29 and a BDI of 17. She obtained the following scores on the KBNA subtests; SEQ = 7, SPLOC = 6, CF1 = 12, WL2 = 18 and CFREC = 6. Applying the latter scores to the logistic regression formula yields *ln*(odds) of 29.254 which is equivalent to a probability of 1.00 that her cognitive performance represented the effects of depression. Client-2 is a 74-year-old woman with 15 years of education, a FSIQ of 118, an MMSE of 28 and no history of depression and no evidence of depressive symptomatology on interview. Client-2 obtained the following KBNA scores; SEQ = 13, SPLOC = 5, CFL1 = 2, WL2 = 4 and CFREC = 3. The logistic regression for Client-2 yielded *ln*(odds) of -12.545 or a probability of having depression (relative to MCI) of 3.56×10^{-6} and as this probability is low Client-2 is best categorized as MCI.

Our groups tend to be older and well-educated but this is in keeping with the clientele we generally serve. We corrected for the effect of age by using age-corrected scores thereby eliminating the need for entering age as a covariate in the MANCOVA. Based on the database used, education accounts for only 5 – 6 % of the variance in KBNA scores and therefore needs no correction for practical application.

Limitations and future research

Although observed power was high, the combined effect of a small sample size and use of multiple comparisons would have decreased the power to find statistical significance of moderate to small effect sizes. Second, the KBNA was used, in small part, along with other information, including other neuropsychological tests, clinical interviews, imaging data, and expert consensus to diagnose the MCI participants. This could possibly have affected the results by inflating the between group differences and thereby enhancing the predictive ability of the KBNA for determining MCI group membership. Regardless, we found that the addition of non-memory tests yielded an incremental increase in overall diagnostic accuracy and was most beneficial for increasing the identification of the depressed individuals. The increase in specificity of adding the tests of attention, mental control and spatial working memory would result in fewer false-positives (i.e. identifying depressed individuals as MCI). Assignment to the depression group was not influenced by the KBNA results, as this was solely dependent on a diagnosis of depression. Moreover, no attempt was made to refine the data prior to analysis by rejecting participants that were outliers of either group; selection was based only on the diagnoses entered in the database. Despite this, the possibility remains that selection bias could have influenced the results of the present study, to rule out this possibility this study's results should be replicated with a larger sample size and with a sample of MCI participants who received their diagnoses of MCI entirely independently of the KBNA. This could be done by applying the regression formula reported in this study to a new set of participants diagnosed with MCI or depression, independently of their scores on the KBNA, in order to cross-validate the findings of the current study.

Conclusion

This initial inquiry into the KBNA's ability to distinguish the cognitive profiles of MCI and depression has been promising. The KBNA was able to correctly classify 96.4% of the participants in this study. Should this finding be replicated, taking into account the aforementioned limitations, the KBNA could be used as a time and cost effective tool for distinguishing the two conditions. This would have great clinical implications as distinguishing depression from MCI is imperative due to their differing treatment plans and prognoses.

Conflict of Interest

The first author has no known conflict of interest. Both the second author and Baycrest Centre for Geriatric Care are in contractual agreement with PsychCorp to receive royalties from sales of the KBNA.

References

1. Engmann B. Mild cognitive impairment in the elderly. GeroPsych. 2011; 24: 71-6.
2. Steffens DC, Potter GG. Geriatric depression and cognitive impairment. Psychol Med. 2008; 38: 163-75.
3. Belleville S, Chertkow H, Gauthier S. Working memory and control of attention in persons with Alzheimer's disease and mild cognitive impairment. Neuropsychology. 2007; 21: 458-69.
4. Fischer C, Schweizer TA, Atkins JH, et al. Neurocognitive profiles in older adults with and without major depression. Int J Geriatr Psychiatry. 2008; 23: 851-6.
5. Defrancesco M, Marksteiner J, Deisenhammer EA, Hinterhuber H, Weiss EM. Association of mild cognitive impairment (MCI) and depression. Neuropsychiatrie. 2009; 23: 144-50.
6. Panza F, Frisardi V, Capurso C, et al. Late-life depression, mild cognitive impairment, and dementia: Possible continuum. Am J Geriatr Psychiatry. 2010; 18: 98-116.
7. Dierckx E, Engelborghs S, De Raedt R, De Deyn PP, Ponjaert-Kristoffersen I. Differentiation between mild cognitive impairment, Alzheimer's disease and depression by means of cued recall. Psychol Med. 2007; 37: 747-55.
8. Zihl J, Reppermund S, Thum S, Unger K. Neuropsychological profiles in MCI and in depression: Differential cognitive dysfunction patterns or similar final common pathway disorder? J Psychiatr Res. 2010; 44: 647-54.
9. Bhalla RK, Butters MA. Cognitive functioning in late-life depression. BCMJ. 2011; 53: 357-60.

10. Herrmann LL, Goodwin GM, Ebmeier KP. The cognitive neuropsychology of depression in the elderly. Psychol Med. 2007; 37: 1693-1702.
11. Steffens DC. Separating mood disturbance from mild cognitive impairment in geriatric depression. Int Rev Psychiatr. 2008; 20: 374-81.
12. Sheline YI, Barch DM, Garcia K, et al. Cognitive function in late life depression: Relationships to depression severity, cerebrovascular risk factors and processing speed. Biol Psychiatry. 2006; 60: 58-65.
13. Modrego PJ, Ferrandez J. Depression in patients with mild cognitive impairment increases the risk of developing dementia of Alzheimer type: A prospective cohort study. Arch Neurol, 2004; 61: 1290-3.
14. Petersen RC, Doody R, Kurz A, et al. Current concepts in MCI. Arch Neurol. 2001; 58: 1985-92.
15. Mitchell AJ. Is it time to separate subjective cognitive complaints from the diagnosis of mild cognitive impairment? Age Ageing. 2008; 37: 497-9.
16. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. Arch Neuro. 1999; 56: 303-8.
17. Alladi S, Arnold R, Mitchell J, Nestor P, Hodges JR. Mild cognitive impairment: Applicability of research criteria in a memory clinic and characterization of cognitive profile. Psychol Med. 2006; 36: 507-15.
18. Lonie JA, Herrmann LL, Donaghey CL, Ebmeier KP. Clinical referral patterns and cognitive profile in mild cognitive impairment. Br J Psychiatry. 2008; 192: 59-64.
19. Kavé G, Heinik J. Neuropsychological evaluation of mild cognitive impairment: Three case reports. Clin Neuropsychol. 2004; 18: 362-72.
20. Nordlund A, Rolstad S, Hellström P, Sjögren M, Hansen S, Wallin, A. The Goteborg MCI study: Mild cognitive impairment is a heterogeneous condition. J Neurol Neurosurg Psychiatry. 2005; 76: 1485-90.
21. Petersen RC. Mild Cognitive Impairment. New York: Oxford University Press; 2003.
22. Sikkes SAM, van den Berg MT, Knol DL, et al. How useful is the IQCODE for discriminating between Alzheimer's disease, mild cognitive impairment and subjective memory complaints? Dement Geriatr Cogn Disord. 2010; 30: 411-6.
23. Zakzanis KK, Leach L, Kaplan E. On the nature and pattern of neurocognitive function in major depressive disorder. Neuropsychiatry Neuropsychol Behav Neurol. 1998; 11: 111-9.
24. Leach L, Kaplan E, Rewilak D, Richards B, Proulx G. Kaplan Baycrest Neurocognitive Assessment Manual. San Antonio, TX: Psychological Corporation; 2000
25. Leach L. The diagnostic prediction of the Kaplan-Baycrest Neurocognitive Assessment for identification of mild dementia. Arch Clin Neuropsych. 2010; 25: 359-70.
26. Foldi NS, Brickman AM, Schaefer LA, Knutelska, ME. Distinct serial position profiles and neuropsychological measures differentiate late life depression from normal aging and Alzheimer's disease. Psychiatry Res. 2003; 120: 71-84.
27. Petersen RC, Morris JC. Clinical Features. In RC Petersen, editors. Mild cognitive impairment: Aging to Alzheimer's disease. New York: Oxford University Press; 2003. p. 15-40.
28. APA. Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR, 4th ed., text revision. American Psychiatric Association: Washington, DC; 2000.
29. Reisberg B, Ferris SH, de Leon MJ, Crook T. The Global Deterioration Scale for assessment of primary degenerative dementia. Am J Psychiatry, 1982; 139: 1136-9.