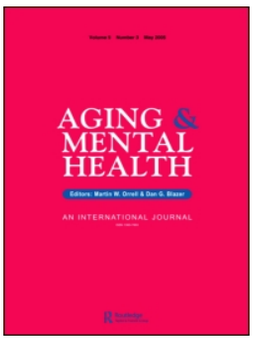

Routledge
Taylor & Francis Group

Aging & Mental Health

ISSN: 1360-7863 (Print) 1364-6915 (Online) Journal homepage: http://www.tandfonline.com/loi/camh20

Subjective rating of executive functions in mild Alzheimer's disease

Jennifer Fogarty, Erin Almklov, Michael Borrie, Jennie Wells & Robert M. Roth

To cite this article: Jennifer Fogarty, Erin Almklov, Michael Borrie, Jennie Wells & Robert M. Roth (2017) Subjective rating of executive functions in mild Alzheimer's disease, Aging & Mental Health, 21:11, 1184-1191, DOI: 10.1080/13607863.2016.1207750

To link to this article: https://doi.org/10.1080/13607863.2016.1207750

AGING & MENTAL HEALTH, 2017
VOL. 21, NO. 11, 1184–1191
http://dx.doi.org/10.1080/13607863.2016.1207750

Routledge
Taylor & Francis Group

Subjective rating of executive functions in mild Alzheimer's disease

Jennifer Fogarty[a,b], Erin Almklov[c], Michael Borrie[a,b], Jennie Wells[a,b] and Robert M. Roth[c]

[a]Department of Psychiatry and Division of Geriatric Medicine, Schulich School of Medicine & Dentistry, Western University, London, Ontario, Canada; [b]Specialized Geriatric Services, Parkwood Institute, London, Ontario, Canada; [c]Neuropsychology Program, Department of Psychiatry, Geisel School of Medicine at Dartmouth, One Medical Center Drive, Lebanon, NH, USA

ABSTRACT

Objectives: Subjective cognitive decline is considered to be a core feature of pre-Alzheimer's disease (AD) conditions, the vast majority of literature having focused on memory concerns. Neuropsychological studies have implicated executive dysfunction on objective performance measures in AD, but no research has evaluated whether individuals with AD have concerns about their executive functions and whether it differs from their caregiver's concerns. In the present study, we sought to evaluate self- and informant ratings of executive functioning in patients with mild AD.

Method: Participants were 23 patients with mild AD and 32 healthy elderly controls (HC) and their informants who completed the Behavior Rating Inventory of Executive Function – Adult version.

Results: Patients with AD and their informants reported greater executive dysfunction than the HC group and their informants, respectively, and patients reported greater difficulty than their informants. The largest effect size for both self- and informant ratings was obtained for the Working Memory scale.

Conclusions: These findings indicate that subjective cognitive concerns in mild AD extend beyond the memory domain to executive functions. That greater difficulty was endorsed by patients than their informants suggests that at least in the mild stage of AD some awareness of executive dysfunction may be maintained in some patients. Implications for clinical care are discussed.

ARTICLE HISTORY
Received 10 December 2015
Accepted 26 June 2016

KEYWORDS
Alzheimer's disease; cognitive functioning; Mild Cognitive Impairment

Introduction

Subjective cognitive decline is considered as a core criterion of Mild Cognitive Impairment (MCI) and prodromal Alzheimer's disease (AD) (Albert et al., 2011; Dubois et al., 2007; Jessen et al., 2014). The vast majority of studies on subjective cognitive decline in persons with MCI or AD have focused on memory concerns (Gifford et al., 2015; Rabin et al., 2015). This is not surprising given that memory deficit on neuropsychological testing is usually the earliest and most prominent clinical feature in persons at risk for AD (Collie & Maruff, 2000; Gainotti, Quaranta, Vita, & Marra, 2014; Salmon, 2000). Furthermore, subjective memory concerns have been reported to be predictive of conversion to MCI and dementia (Mitchell, Beaumont, Ferguson, Yadegarfar, & Stubbs, 2014).

The presence of non-memory related cognitive impairment, however, is an essential diagnostic feature of AD (Johnson et al., 2012; Libon et al., 2010; Sanchez-Benavides et al., 2014). In particular, poor performance on tests of executive functions is relatively common early in the course of AD (Johns et al., 2012; Marshall et al., 2011; Saunders & Summers, 2011). Executive functions are a set of interrelated self-regulatory control processes involved in the selection, organization, initiation, execution, and monitoring of cognitive activities, overt behaviors, and emotional responses (Roth, Isquith, & Gioia, 2005a; Stuss & Alexander, 2000).

Executive functions have been reported to contribute to the prediction of conversion from MCI to AD (Chapman et al., 2011; Gomar, Bobes-Bascaran, Conejero-Goldberg, Davies, & Goldberg, 2011). Deficits on neuropsychological measures of executive function in AD have been found to be associated with structural changes on brain imaging scans in regions such as the hippocampus, prefrontal cortex, parietal, and temporal lobes (Morgen et al., 2013; Nagata et al., 2011; Nho et al., 2012). Furthermore, executive dysfunction is associated with impairment in instrumental activities of daily living (IADL) in those with MCI and AD (Marshall, et al., 2011; Martyr & Clare, 2012).

Despite the evidence for executive dysfunction and its clinical relevance, few investigations have evaluated subjective ratings of executive functions in AD. Nonetheless, a number of studies have used the Frontal Systems Behavior Scale (FrSBe) to measure informant reports of cognitive decline in those with AD. This scale provides a total score as well as scores for three scales labelled Apathy, Disinhibition, and Executive Dysfunction (Grace & Malloy, 2002). In one study, Apathy and Executive Dysfunction were the most commonly endorsed scales by informants of patients with AD (Ready, Ott, Grace, & Cahn-Weiner, 2003). Similarly, greater subjective difficulty on these two scales was endorsed by informants of patients' mild-to-moderate as well as those with severe AD relative to healthy elderly, but only the severe AD group was abnormal on the Disinhibition scale (Stout, Wyman, Johnson, Peavy, & Salmon, 2003). Other work has indicated informant-reported abnormality for Apathy and Executive Dysfunction, but not Disinhibition, irrespective of AD severity level (Peavy et al., 2013). Rabin and colleagues evaluated both self- and informant-rated executive functions in patients with MCI (Rabin et al., 2006) using the Behavior Rating Inventory of Executive Function – Adult version (BRIEF-A Roth, Isquith, &

CONTACT Robert M. Roth Robert.M.Roth@Dartmouth.edu

Gioia, 2005b). Individuals with MCI and their informants were found to endorse greater difficulties than healthy controls and their informants on several of the scales, with both having worse scores on scales reflecting inhibitory control, cognitive flexibility, task-monitoring, initiation, Working Memory, and planning/organization. The Working Memory scale showed the largest effect size for both self and informant reports. Most of the scales showed correlations between self- and informant-reports, though the MCI group generally reported having greater difficulty than observed by informants.

In the present study, we sought to determine whether subjective executive concerns reported by patients with MCI and their informants on the BRIEF-A (Rabin et al., 2006) are also found in patients with mild AD and healthy elderly. To our knowledge, there are no studies comparing subjective ratings of executive functioning in both patients with AD and their caregivers. We hypothesized that patients with AD and their caregivers will endorse greater concern with respect to executive function than healthy elderly and their informants, especially for Working Memory as observed in patients with MCI (Rabin et al., 2006). We also predicted that, in contrast to findings for MCI, informants would endorse greater difficulty with executive functions than the patients given that reduced awareness of cognitive and functional difficulties is often reported in individuals with AD (Lehrner et al., 2015; Orfei et al., 2010). In addition, we examined the relationship between the BRIEF-A and global cognitive screening measures as well as a measure of activities of daily living (ADL). We hypothesized that similar to the findings of Rabin et al. (2006), overall cognitive function would be unrelated to BRIEF-A scores. In contrast, we predicted that poorer executive function would be associated with worse ADLs.

Method

Participants

Patients with probable mild AD were recruited from specialty geriatric outpatient clinical and research programs in London, Ontario, who were referred for neuropsychological evaluation. Diagnosis of AD was based on a clinical interview with the participant and a knowledgeable informant and a review of available medical, neurological, psychiatric, and neuropsychological test data (but not BRIEF-A scores). Of the 23 participants with AD, 22 were accompanied by either a spouse alone or both a spouse and an adult child. Only one participant with AD was accompanied by an adult child alone. Patients were diagnosed according to DSM-IV criteria (American Psychiatric Association, 2000). Functional decline was assessed using the IADL scale (Lawton & Brody, 1969). Other measures used to inform diagnosis included the Geriatric Depression Scale (GDS; Yesavage et al., 1982), Mini-Mental Status Exam (MMSE; Folstein, Folstein, & McHugh, 1975), and the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005). Consensus on diagnosis was reached between a neuropsychologist and two specialist physicians.

All participants had a functional use of the English language (using English in their work and everyday social interactions). Patients were excluded if they had psychiatric difficulties that could have an impact on cognitive function. Eight patients were taking psychotropic medications (primarily SSRIs) and two were taking cholinesterase inhibitors at the time of the evaluation.

Healthy comparison (HC) participants were recruited from community centres and through newspaper advertisement. All were administered the Dartmouth Memory and Aging Telephone Screen (Rabin et al., 2007) by a research assistant with extensive geriatric clinical experience. HCs were excluded if they had any history of psychiatric, neurological, or other medical conditions known to affect cognition. In order to be included in the HC group, participants were required to have a Clinical Dementia Rating Scale (CDR; Morris, 1993) score of zero based on an interview with them and an informant, a MMSE score of 27 or higher (Folstein et al., 1975) or a MoCA score of 26 or higher (Nasreddine et al., 2005), and no significant concerns about their cognition on interview per the participant or their informant. Informants for the 32 participants in the HC group included 12 spouses, 14 friends, 5 children, and 1 sibling. Consensus on diagnosis was reached between two neuropsychologists. Participants provided written informed consent following a protocol approval of the study by Western University's Research Ethics Board.

Procedure

The BRIEF-A consists of 75 items scored on a 3-point scale (Roth et al., 2005b). The BRIEF-A yields an overall score (GEC; Global Executive Composite) composed of two index scores (Behavioral Regulation Index (BRI) and Metacognition Index (MI)). The BRI is comprised of four clinical scales (Inhibit, Shift, Emotional Control, and Self-Monitor) and the MI is comprised of five clinical scales (Initiate, Working Memory, Plan/Organize, Task Monitor, and Organization of Materials). The measure also includes three validity scales assessing for an overly negative response style (Negativity scale), endorsement of items in an atypical manner (Infrequency scale), and inconsistent responding to similar items (Inconsistency scale). Cronbach alpha coefficients for the nine clinical scales range from .73 to .90 and one-month test−retest reliabilities ranging from .82 to .93 (Roth et al., 2005a). *T*-scores were used in the analyses, with higher scores indicating worse executive function and a $T \geq 65$ considered clinically elevated (Roth et al., 2005a).

Statistical analyses

All three validity scales were examined for the self- and informant versions of the BRIEF-A. No participants had elevated Negativity scales. The Infrequency scale was elevated for five participants (three HC and two AD) and the Inconsistency scale was elevated for two participants (one HC and one AD, the latter also elevated on the Infrequency scale). These participants (four HC and two AD) were dropped from subsequent analyses. Self-report data were missing for three participants in the AD group. *T*-scores for each of the nine BRIEF-A self-report scales and the three index scales were analyzed separately as dependent variables in multivariate analyses of variance (MANOVA; Wilk's Lambda) with diagnostic group (HC and AD) as the between-subjects factor. The same analysis was repeated for the BRIEF-A informant report. *T*-tests were used to examine differences between self- and informant-report scores for each scale in the AD sample. As in the study by Rabin and colleagues (Rabin, et al., 2006), we also examined whether the percentage of participants with scores in the clinical range in the two groups differed for the self- and informant-report forms. Significance level set at $p < .05$,

two-tailed. Effect sizes (partial eta-squared) are reported for analyses of group differences. Analyses were conducted using SPSS Statistics 21.

Results

Group differences

Table 1 presents descriptive statistics and results of statistical analyses for the participant characteristic data. The patient group was significantly older, consisted of a smaller percentage of women, and was more educated than the HC group. On cognitive screening measures, the AD group performed more poorly than the HC group, an effect that was more prominent for the MoCA than the MMSE. There were no significant correlations between any of the BRIEF-A subscales (self or informant) and overall score on the MMSE or MoCA in either sample. In addition, IADL score was not associated with either BRIEF-A scores (self or informant) or performance on cognitive screening measures in the AD group. A higher GDS score was obtained in the patient group, but the mean GDS score in both groups was well below the clinical range. Nonetheless, greater GDS score in the AD sample was associated with higher scores on the Shift ($r = .46$, $p = .042$), Self-Monitor ($r = .53$, $p = .016$), Working Memory ($r = .57$, $p = .009$), and Organization of Materials ($r = .69$, $p = .001$) scales as well as the BRI ($r = .50$, $p = .024$), MI ($r = .57$, $p = .009$), and GEC ($r = .57$, $p = .008$).

Table 2 presents the BRIEF-A self-report data. MANOVA for the three index scores was significant [$F(3, 45) = 7.99$, $p < .001$, $\eta_p^2 = .348$]. Follow-up tests indicated greater executive problems for the GEC, BRI, and MI in the AD relative to HC group (all $p \leq .01$), with effect sizes ranging from .134 to .346. MANOVA on the nine BRIEF-A self-report scales was also significant [$F(10, 38) = 5.22$, $p < .001$, $\eta_p^2 = .579$]. Univariate tests were significant for all of the scales, with the patient group endorsing more problems on all scales with the exception of Emotional Control and Organization of Materials, effect sizes ranging from .108 for Inhibit to .417 for Working Memory. MANCOVA was then conducted using age, gender, years of education, and GDS score as covariates. Results revealed that group differences for the three index scores and six of the nine scales remained significant, with only the difference on the Inhibit scale rendered non-significant.

Table 3 presents the BRIEF-A informant report data. MANOVA on the three index scores was significant [$F(3, 48) = 11.08$, $p < .001$, $\eta_p^2 = .409$], with follow-up analyses indicating greater reported executive dysfunction in the AD group for the GEC and the MI, with effect sizes of .270 and .381, respectively. MANOVA on the nine BRIEF-A scales was also significant [$F(9, 42) = 10.10$, $p < .001$, $\eta_p^2 = .684$]. Informants reported having observed greater difficulty in the AD relative to the HC group for the Shift, Initiate, Working Memory, Plan/Organize, Task Monitor, and Organization of Materials scales. Effect sizes ranged from .099 for Organization of Materials to .517 for Working Memory. When covariates were included (i.e. age, gender, education, and GDS score), group differences remained for two of the three index scores (MI and GEC), as well as the Initiate, Working Memory, Plan/Organize, and Task Monitor scales.

Clinical elevations on the BRIEF-A

Table 4 showed the percentage of participants in the AD and HC groups who obtained BRIEF-A scores in the 'clinically elevated,' range. Group differences were assessed using chi square (χ^2). On the self-report form, the percentage of individuals in the HC group with clinically elevated scales ranged from 0% (Inhibit) to 25% (Emotional Control), while in the AD group elevations ranged from 30% (Inhibit) to 70% (Working Memory). Elevations were significantly more common in the patient group for all three indices and all scales with the exception of Emotional Control. On the informant report, the percentage of participants with elevations ranged from

Table 1. Participant characteristics.

	Healthy $n = 32$		AD $n = 23$				
Characteristic	*M*	SD	*M*	SD	*F*	*p*	η_p^2
Age, yrs.	69.84	6.15	73.95	8.81	4.15	.046*	.073
Education, yrs.	13.96	2.91	15.56	2.76	4.19	.045*	.073
Gender (percentage female)	81.25		39.1		–	.001*	–
GDS	.75	.95	2.04	1.79	11.99	.001*	.185
MoCA	27.40	1.29	20.21	2.57	185.46	<.001*	.778
MMSE	28.87	.90	25.73	2.73	36.72	<.001*	.409

Note: AD = Alzheimer's disease; GDS = Geriatric Depression Scale; MoCA = Montreal Cognitive Assessment; MMSE = Mini Mental State Examination.
*Significant at $p < .05$.

Table 2. Mean BRIEF-A self-report *T* scores by diagnostic group.

	Healthy		AD		No covariates		Covariates	
BRIEF-A Scale	*M*	SD	*M*	SD	*p*	η_p^2	*p*	η_p^2
Inhibit	51.62	4.93	56.70	9.07	.012*	.120	.077	.066
Shift	55.28	7.23	63.60	10.99	.002*	.179	.010*	.137
Emotional Control	55.53	10.73	61.35	14.43	.102	.052	.402	.084
Self-Monitor	53.18	5.70	59.25	10.75	.011*	.124	.046*	.084
Initiate	49.59	8.36	63.00	17.24	<.001*	.221	.033*	.095
Working Memory	55.28	8.55	73.30	13.33	<.001*	.414	<.001*	.301
Plan/Organize	50.50	7.72	66.95	13.01	<.001*	.396	<.001*	.289
Task Monitor	53.00	8.79	64.10	9.93	<.001*	.262	.009*	.139
Organization of Materials	52.78	11.78	59.25	11.02	.054	.072	.729	.003
BRI	54.96	6.55	62.55	11.98	.005*	.148	.041*	.087
MI	52.34	8.37	67.50	13.39	<.001*	.336	.003*	.175
GEC	53.65	6.42	66.30	12.91	<.001*	.307	.002*	.183

Note: AD = Alzheimer's disease; BRI = Behavioral Regulation Index; MI = Metacognitive Index; GEC = Global Executive Composite. Covariates included age, gender, education, and Geriatric Depression Scale score.
*Significant at $p < .05$.

Table 3. Mean BRIEF-A informant report *T* scores by diagnostic group.

	Healthy		AD		No covariates		Covariates	
BRIEF-A Scale	*M*	SD	*M*	SD	*p*	η_p^2	*p*	η_p^2
Inhibit	49.50	7.48	51.91	9.50	.201	.031	.571	.007
Shift	50.76	8.30	58.34	11.35	.006*	.138	.083	.062
Emotional Control	49.36	7.81	53.26	12.33	.178	.035	.340	.019
Self-Monitor	48.26	8.57	52.04	12.47	.162	.037	.394	.015
Initiate	47.70	6.60	60.60	13.76	<.001*	.299	.025*	.102
Working Memory	51.56	7.78	70.73	10.84	<.001*	.532	<.001*	.442
Plan/Organize	46.70	5.80	61.86	11.61	<.001*	.442	<.001*	.287
Task Monitor	48.93	6.78	59.91	10.74	<.001*	.295	.008*	.140
Organization of Materials	51.26	11.69	58.65	9.74	.023*	.096	.726	.003
BRI	49.60	7.24	53.43	9.79	.088	.055	.292	.024
MI	48.93	7.33	63.39	11.13	<.001*	.396	<.001*	.233
GEC	49.23	6.31	59.08	9.81	<.001*	.288	.008*	.141

Note: AD = Alzheimer's disease; BRI = Behavioral Regulation Index; MI = Metacognitive Index; GEC = Global Executive Composite. Covariates included age, gender, education, and Geriatric Depression Scale score.
*Significant at $p < .05$.

Table 4. Percentage of adults with *T* scores ≥ 65 on BRIEF-A self- and informant report scales for diagnostic groups.

	Self-report			Informant-report		
BRIEF-A Scale	Healthy	AD	p^a	Healthy	AD	p^a
Inhibit	0	30	<.001*	3.3	12.5	.197
Shift	9.4	50	.001*	3.3	20.8	.037*
Emotional Control	25	45	.137	0	20.8	.003*
Self-Monitor	6.3	35	.008*	10	16.7	.470
Initiate	3.1	50	<.001*	3.3	33.3	.002*
Working Memory	12.5	70	<.001*	3.3	37.5	.001*
Plan/Organize	9.4	55	<.001*	3.3	37.5	.001*
Task Monitor	6.3	45	.001*	3.3	37.5	.001*
Organization of Materials	9.4	50	.001*	16.7	29.2	.273
BRI	6.3	50	<.001*	0	12.5	.024*
MI	6.3	65	<.001*	3.3	37.5	.001*
GEC	6.3	60	<.001*	3.3	29.2	.006*

Note: AD = Alzheimer's disease; BRI = Behavioral Regulation Index; MI = Metacognitive Index; GEC = Global Executive Composite.
[a]Significance tests based on likelihood ratio χ^2 with 2 degrees of freedom, two tailed.
*Significant at $p < .05$.

0% (Emotional Control) to 16.7% (Organization of Materials) for the HC group, and from 12.5% (Inhibit) to 37.5% (Working Memory, Plan/Organize and Task Monitor) for the AD group. A significantly greater percentage of participants in the AD than HC group had elevations on the three index scores and the Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, and Task Monitor scales. Groups did not differ with respect to Inhibit, Self-Monitor, or Organization of Materials.

Self versus informant report

None of the correlations between the self and informant reports reached the level of significance in the patient sample. In the HC sample, positive correlations were obtained for Emotional Control, Self-Monitor, Initiate, Working Memory, Plan/Organize, and Organization of Martials, and the Metacognition Index. Mean *T*-score differences between BRIEF-A self and informant reports in the mild AD sample ranged from 1.30 for Organization of Materials to 9.6 for Emotional Control. For all nine scales, the patient group obtained higher scores than the informants, but the difference was only statistically significant for the Inhibit ($p = .041$), Emotional Control ($p = .012$), and Self-Monitor ($p = .013$) scales. Similarly, *T*-scores were slightly higher for self than informant reports in the HC group, ranging from 2.83 for MI to 7.07 for Self-Monitor. Significantly higher *T*-scores were obtained for Emotional Control ($p = .001$), Self-Monitor ($p = .002$), Plan/Organize ($p = .029$) scales, as well as the BRI ($p = .001$), MI ($p = .05$), and GEC ($p = .007$).

Discussion

A growing body of literature has documented the presence of executive dysfunction on performance-based tests in patients with mild AD (Allain, Etcharry-Bouyx, & Verny, 2013). A small number of studies have also reported subjective difficulty with executive functioning in patients with mild or more severe AD as endorsed by their informants (Peavy et al., 2013; Ready, et al., 2003; Stout, et al., 2003). The current study evaluated subjective rating of executive functions of patients with mild AD and healthy elderly as well as their informants.

Results revealed that patients endorsed significantly greater difficulty than the comparison group on six of the nine clinical scales after taking covariates into account. Similarly, greater impairment was endorsed on four of the nine scales by the informants of the patients relative to those of the healthy elderly. Consistent across the patients and their informants were difficulties on the Initiate, Working Memory, Plan/Organize, and Task Monitor scales. The patients also showed significant elevations on the Shift and Self-Monitor scales. Neither patients nor their informants reported significant problems on the Organization of Materials scale. Further inspection of data showed that the percentage of cases within each group exhibiting clinically elevated BRIEF-A scores indicated that patients with mild AD and their informants were more likely to endorse clinically meaningful executive problems than the comparison group and their informants for nearly all of the scales.

The largest effect size in both the self- and informant-report data was for the Working Memory scale. Similarly, this

scale showed the highest percentage of clinical elevations within the mild AD group per self-report, as well as being tied with two other scales (Plan/Organize and Task Monitor) for being most frequently elevated per the informant report. A similar pattern of findings was reported for elderly with MCI (Rabin et al., 2006), suggesting that Working Memory may be especially vulnerable to the underlying pathology of AD. This is consistent with findings for performance-based measures indicating that deficits in Working Memory can be observed early in the course of AD and are often evident in amnestic and non-amnestic MCI (Chen et al., 2001; Klekociuk & Summers, 2014; Lafleche & Albert, 1995; Saunders & Summers, 2011).

Our sample of patients with mild AD reported having greater difficulty with executive functions than observed by their informants across the nine BRIEF-A scales, though this was only statistically significant for the Inhibit, Emotional Control, and Self-Monitor scales. This is consistent with a prior study that found greater endorsement of executive problems on the BRIEF-A by patients with MCI than their informants (Rabin et al., 2006), as well as some other work that has reported greater memory concern in patients with MCI than their informants (Buckley et al., 2015). Our findings appear counterintuitive, however, given elevated rates of unawareness of cognitive deficits in samples of patients with MCI and AD (Orfei et al., 2010; Ott et al., 1996) and evidence of less concern about general cognitive functioning in patients with AD relative to their informants as assessed by the Everyday Cognition (ECog) questionnaire (Rueda et al., 2015). Interestingly, results of the Rueda et al. study also indicated that their AD sample endorsed somewhat greater difficulty on the ECog than patients with early or late MCI. It should be noted that these other studies assessed participants' awareness of memory, functional deficits, or general cognitive functioning rather than executive functions. There is evidence indicating that awareness may vary across cognitive domains (Schoo, van Zandvoort, Biessels, Kappelle, & Postma, 2013). Thus, it may be that awareness of difficulties with executive functions is particularly salient for our highly educated sample. Further research examining whether there are dissociations in the awareness of patients with mild AD in terms of cognitive domains such as executive functions and memory will, therefore, be informative.

It is possible that our mild AD sample consisted mainly of individuals with relatively well preserved awareness, which may be due in part to the sample consisting of individuals who were relatively early in the disease state, as reflected by their scores on cognitive screening measures. Prior work has found that at least a subset of individuals with mild AD retains adequate awareness of their cognitive abilities (Orfei et al., 2010). Furthermore, our patients were generally well educated, which could reflect a higher level of cognitive reserve; greater reserve having been previously found to be related to better awareness in mild dementia (Spitznagel & Tremont, 2005).

Worse executive functions on the BRIEF-A was associated with greater self-rated depression in our patient group, and others have reported that increased awareness of cognitive deficits is associated with worse symptoms of depression in patients with mild dementia (Spitznagel, Tremont, Brown, & Gunstad, 2006). Furthermore, no significant correlations were observed between self and informant reports in the mild AD group, though significant problems were endorsed by both. This raises the question as to the extent to which subjective executive function concerns reflect actual problems with executive functions versus other contributors. There is evidence that worse subjective executive function is related to structural changes of the frontal lobe in some other clinical populations (Garlinghouse, Roth, Isquith, Flashman, & Saykin, 2010; kawada et al., 2009). On the other hand, recent work has found that in a community sample of non-demented older adults greater concern with respect to executive functioning was associated with variables such as physiological anxiety, neuroticism, fear of aging, and symtoms of depression (Meltzer et al., in press). Thus, similar to performance-based tests of cognition, there can be multiple contributors to subjective cognitive concerns. Research employing a multivariate approach to identifying contributors to subjective executive function, including both biological and psychological measures, will be needed. Clinically, however, it is likely that the specific combination of contributors, and their respective degree of etiological relevance to subjective cognitive concerns, will vary among patients thus informing individualized care.

Ability to complete IADLs was not associated with either BRIEF-A scores (self or informant) or performance on cognitive screening measures in our mild AD group. This finding may be due to the relatively mild nature of their subjective executive dysfunction, per self and informant report, as well as the mild general cognitive impairment observed on the MMSE and MoCA. Some studies have noted relationships between performance-based tests of executive functions and specific aspects of IADLs in mild AD (Hall et al., 2011). Thus, while our sample size did not permit us to conduct such a fine grained analysis, future studies would benefit from examining whether subjective executive functioning is related to specific IADLs in this population.

Our observation of concerns about executive functions in patients with mild AD has implications for patient care and management. As our findings and those of others (Orfei et al., 2010) indicate, at least some individuals with mild AD may retain some awareness of their cognitive problems. This should reinforce the importance of not dismissing cognitive concerns in individuals with mild AD just because they have a diagnosis of dementia, especially given that greater awareness of cognitive and functional limitations can be associated with psychological distress (Maki et al., 2012), including distress during neuropsychological testing irrespective of actual performance (Lai, Hawkins, Gross, & Karlawish, 2008). Furthermore, while many interventions for individuals with mild AD tend to focus on the caregiver (Gitlin, 2012), treatment planning should take into consideration the patient's level of awareness and include them along with family members in shared decision making, as appropriate (Graff et al., 2006). That subjectively worse executive functioning was related to greater depression in our patient, sample suggests that clinicians should carefully assess for depressive symptoms in this population, as identification and treatment of depressive symptoms may lead to improved quality of life (Baquero & Martin, 2015).

The results of the present investigation should be interpreted in the context of its limitations. The sample sizes of both participant groups were modest and thus the findings require replication in a larger sample. There was also a significant gender disparity between the groups, with considerably more women in the healthy than patient group. Although this

did not appear to impact our findings, evidence that women are more likely to report subjective memory concerns than men (Tomita et al., 2014) indicates the need for further research to determine whether such gender differences are also present for subjective rating of executive functions. In addition, as noted above our sample had on average greater than a high school level of education. Thus, the findings may not apply to a more heterogeneous group of individuals with lower levels of education. In addition, as noted above, our AD patients were very early in the disease, thus our findings for the BRIEF-A may not apply to patients with more severe dementia. Finally, our HC group did not have neuropsychological testing as part of their diagnostic work up, thus we cannot completely rule out the possibility that the HC group included individuals with MCI. Neither HC participants nor their informants had concerns about their cognitive or functional abilities, a core diagnostic criteria for MCI, thus it is unlikely that our findings are accounted for by failure to use neuropsychological testing to exclude individuals with the condition. Nonetheless, future research should examine the BRIEF-A in a larger sample of elderly HC participants, including those that have shown normal cognitive function on neuropsychological testing.

Together, the present findings indicate that patients with mild AD have concerns with respect to their executive functions as manifested in their everyday lives, which is also observed by their informants albeit to a lesser degree. Additional research will be required to identity factors (e.g. cognitive reserve, awareness of illness, global, or focal brain atrophy) that may differentiate those with mild AD who have concerns about their executive functions from those that do not. Furthermore, given prior research indicating that prediction of conversion to AD is enhanced when using informant report (Rabin et al., 2012) or both informant- and self-reports (Gifford et al., 2014) of cognitive functioning, longitudinal research will be needed to determine whether subjective rating of executive functioning by patients, their informants, or their combination provide better prediction of deterioration in functioning over time.

Acknowledgments

The authors thank Sarah Woolmore-Goodwin, M.Sc., and Thida Han, M.Sc. for assistance with data collection for the healthy controls and with data entry. Thanks go to Betsy Schaefer and Kaitlin Stefanovich for assistance with data entry. Thanks also go to Kevin Hansen for providing comments on an earlier draft of this paper.

Disclosure statement

Robert Roth is an author of the BRIEF-A and receives royalties from the publisher. For the remaining authors, no conflicts of interest were declared.

Funding

Portions of this research were supported by seed funding from the Schulich School of Medicine & Dentistry, Department of Psychiatry, Western University, London, Ontario, Canada.

References

Albert, M.S., DeKosky, S.T., Dickson, D., Dubois, B., Feldman, H.H., Fox, N.C., … Phelps, C.H. (2011). The diagnosis of Mild Cognitive Impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia*, *7*(3), 270−279. doi:10.1016/j.jalz.2011.03.008

Allain, P., Etcharry-Bouyx, F., & Verny, C. (2013). Executive functions in clinical and preclinical Alzheimer's disease. *Revue Neurologique (Paris)*, *169* (10), 695−708. doi:10.1016/j.neurol.2013.07.020

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (revised, 4th ed.). Washington, DC: American Psychiatric Press.

Baquero, M., & Martin, N. (2015). Depressive symptoms in neurodegenerative diseases. *World Journal of Clinical Cases*, *3*(8), 682−693.

Buckley, R., Saling, M., Ellis, K., Rowe, C., Maruff, P., Macaulay, L.S., … Ames, D. (2015). Self and informant memory concerns align in healthy memory complainers and in early stages of Mild Cognitive Impairment but separate with increasing cognitive impairment. *Age and Ageing, 44*(6), 1012−1019. doi:10.1093/ageing/afv136

Chapman, R.M., Mapstone, M., McCrary, J.W., Gardner, M.N., Porsteinsson, A., Sandoval, T.C., … Reilly, L.A. (2011). Predicting conversion from Mild Cognitive Impairment to Alzheimer's disease using neuropsychological tests and multivariate methods. *Journal of Clinical & Experimental Neuropsychology, 33*(2), 187−199. doi:10.1080/13803395.2010.499356

Chen, P., Ratcliff, G., Belle, S.H., Cauley, J.A., DeKosky, S.T., & Ganguli, M. (2001). Patterns of cognitive decline in presymptomatic Alzheimer disease: A prospective community study. *Archives of General Psychiatry, 58*(9), 853−858. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11545668

Collie, A., & Maruff, P. (2000). The neuropsychology of preclinical Alzheimer's disease and Mild Cognitive Impairment. *Neuroscience & Biobehavioral Reviews, 24*(3), 365−374. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10781696

Dubois, B., Feldman, H.H., Jacova, C., Dekosky, S.T., Barberger-Gateau, P., Cummings, J., … . Scheltens, P. (2007). Research criteria for the diagnosis of Alzheimer's disease: Revising the NINCDS-ADRDA criteria. *Lancet Neurology, 6*(8), 734−746. doi:10.1016/s1474-4422(07)70178-3

Folstein, M.F., Folstein, S.E., & McHugh, P.R. (1975). "Mini mental state": A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189−198. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1202204

Gainotti, G., Quaranta, D., Vita, M.G., & Marra, C. (2014). Neuropsychological predictors of conversion from Mild Cognitive Impairment to Alzheimer's disease. *Journal of Alzheimer's Disease, 38*(3), 481−495. doi:10.3233/jad-130881

Garlinghouse, M.A., Roth, R.M., Isquith, P.K., Flashman, L.A., & Saykin, A.J. (2010). Subjective rating of working memory is associated with frontal lobe volume in schizophrenia. *Schizophrenia Research, 120*, 71−75. doi:10.1016/j.schres.2010.02.1067

Gifford, K.A., Liu, D., Damon, S.M., Chapman Iv, W.G., Romano Iii, R.R., Samuels, L.R., Jefferson, A.L. (2015). Subjective memory complaint only relates to verbal episodic memory performance in Mild Cognitive Impairment. *Journal of Alzheimer's Disease, 44*(1), 309−318. doi:10.3233/jad-140636

Gifford, K.A., Liu, D., Lu, Z., Tripodis, Y., Cantwell, N.G., Palmisano, J., … Jefferson, A.L. (2014). The source of cognitive complaints predicts diagnostic conversion differentially among nondemented older adults. *Alzheimer's & Dementia, 10*(3), 319−327. doi:10.1016/j.jalz.2013.02.007

Gitlin, L. (2012). Good news for dementia care: Caregiver interventions reduce behavioral symptoms in people with dementia and family distress. *American Journal of Psychiatry, 169*(9), 894−897. doi:10.1176/appi.ajp.2012.12060774

Gomar, J.J., Bobes-Bascaran, M.T., Conejero-Goldberg, C., Davies, P., & Goldberg, T.E. (2011). Utility of combinations of biomarkers, cognitive markers, and risk factors to predict conversion from Mild Cognitive Impairment to Alzheimer disease in patients in the Alzheimer's disease neuroimaging initiative. *Archives of General Psychiatry, 68*(9), 961−969. doi:10.1001/archgenpsychiatry.2011.96

Grace, J., & Malloy, P.F. (2002). *Frontal Systems Behavior Scale (FrSBe)*. Lutz, FL: Psychological Assessment Resources.

Graff, M.J., Vernooij-Dassen, M.J., Thijssen, M., Dekker, J., Hoefnagels, W.H., & Rikkert, M.G. (2006). Community based occupational therapy for patients with dementia and their care givers: Randomised controlled trial. *British Medical Journal, 333*(7580), 1196. doi: 10.1136/bmj.39001.688843.BE.

Hall, J.R., Vo, H.T., Johnson, L.A., Barber, R.C., & O'Bryant, S.E. (2011). The link between cognitive measures and ADLs and IADL functioning in

mild Alzheimer's: What has gender got to do with it? *International Journal of Alzheimers Disease, 2011*, 1–6. doi:10.4061/2011/276734

Jessen, F., Amariglio, R.E., van Boxtel, M., Breteler, M., Ceccaldi, M., Chetelat, G., … Wagner, M. (2014). A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimer's & Dementia, 10*(6), 844–852. doi:10.1016/j.jalz.2014.01.001

Johns, E.K., Phillips, N.A., Belleville, S., Goupil, D., Babins, L., Kelner, N., … Chertkow, H. (2012). The profile of executive functioning in amnestic Mild Cognitive Impairment: Disproportionate deficits in inhibitory control. *Journal of the International Neuropsychological Society, 18*(3), 541–555. doi:10.1017/s1355617712000069

Johnson, J.K., Gross, A.L., Pa, J., McLaren, D.G., Park, L.Q., & Manly, J.J. (2012). Longitudinal change in neuropsychological performance using latent growth models: A study of Mild Cognitive Impairment. *Brain Imaging and Behavior, 6*(4), 540–550. doi:10.1007/s11682–012-9161–8

Kawada, R., Yoshizumi, M., Hirao, K., Fujiwara, H., Miyata, J., Shimizu, M., … Murai, T. (2009). Brain volume and dysexecutive behavior in schizophrenia. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 33*(7), 1255–1260. doi:10.1016/j.pnpbp.2009.07.014

Klekociuk, S.Z., & Summers, M.J. (2014). Lowered performance in working memory and attentional sub-processes are most prominent in multi-domain amnestic Mild Cognitive Impairment subtypes. *Psychogeriatrics, 14*(1), 63–71. doi:10.1111/psyg.12042

Lafleche, G., & Albert, M.S. (1995). Executive function deficits in mild Alzheimer's disease. *Neuropsychology, 9*(3), 313–320. doi:10.1037/0894-4105.9.3.313

Lai, J.M., Hawkins, K.A., Gross, C.P., & Karlawish, J.H. (2008). Self-reported distress after cognitive testing in patients with Alzheimer's disease. *Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 63*(8), 855–859.

Lawton, M.P., & Brody, E.M. (1969). Assessment of older people: Self-maintaining and instrumental activities of daily living. *The Gerontologist, 9*, 179–186. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/5349366

Lehrner, J., Kogler, S., Lamm, C., Moser, D., Klug, S., Pusswald, G., … Auff, E. (2015). Awareness of memory deficits in subjective cognitive decline, Mild Cognitive Impairment, Alzheimer's disease and Parkinson's disease. *International Psychogeriatrics, 27*(3), 357–366. doi:10.1017/s1041610214002245

Libon, D.J., Xie, S.X., Eppig, J., Wicas, G., Lamar, M., Lippa, C., …Wambach, D.M. (2010). The heterogeneity of Mild Cognitive Impairment: A neuropsychological analysis. *Journal of the International Neuropsychological Society, 16*(1), 84–93. doi:10.1017/s1355617709990993

Maki, Y., Amari, M., Yamaguchi, T., Nakaaki, S., & Yamaguchi, H. (2012). Anosognosia: Patients' distress and self-awareness of deficits in Alzheimer's disease. *American Journal of Alzheimer's Disease and Other Dementias, 27*(5), 339–345. doi:10.1177/1533317512452039

Marshall, G.A., Rentz, D.M., Frey, M.T., Locascio, J.J., Johnson, K.A., & Sperling, R.A. (2011). Executive function and instrumental activities of daily living in Mild Cognitive Impairment and Alzheimer's disease. *Alzheimer's & Dementia, 7*(3), 300–308. doi:10.1016/j.jalz.2010.04.005

Martyr, A., & Clare, L. (2012). Executive function and activities of daily living in Alzheimer's disease: A correlational meta-analysis. *Dementia and Geriatric Cognitive Disorders, 33*(2–3), 189–203. doi:10.1159/000338233

Meltzer, E.P., Kapoor, A., Fogel, J., Elbulok-Charcape, M.M., Roth, R.M., Katz, M.J., … Rabin, L.A. (in press). The association of psychological, cognitive, and functional variables with self-reported executive functioning in a sample of non-demented community-dwelling older adults. *Applied Neuropsychology: Adult*. doi:10.1080/23279095.2016.1185428

Mitchell, A.J., Beaumont, H., Ferguson, D., Yadegarfar, M., & Stubbs, B. (2014). Risk of dementia and Mild Cognitive Impairment in older people with subjective memory complaints: Meta-analysis. *Acta Psychiatrica Scandinavica, 130*(6), 439–451. doi:10.1111/acps.12336

Morgen, K., Frolich, L., Tost, H., Plichta, M.M., Kolsch, H., Rakebrandt, F., … Meyer-Lindenberg, A. (2013). APOE-dependent phenotypes in subjects with Mild Cognitive Impairment converting to Alzheimer's disease. *Joural of Alzheimer's Disease, 37*(2), 389–401. doi:10.3233/jad-130326

Morris, J.C. (1993). The Clinical Dementia Rating (CDR): Current version and scoring rules. *Neurology, 43*(11), 2412–2414. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8232972

Nagata, T., Shinagawa, S., Ochiai, Y., Aoki, R., Kasahara, H., Nukariya, K., & Nakayama, K. (2011). Association between executive dysfunction and hippocampal volume in Alzheimer's disease. *International Psychogeriatrics, 23*(5), 764–771. doi:10.1017/s1041610210002164

Nasreddine, Z.S., Phillips, N.A., Bedirian, V., Charbonneau, S., Whitehead, V., Collin, I., … Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for Mild Cognitive Impairment. *Journal of the American Geriatrics Society, 53*(4), 695–699. doi:10.1111/j.1532-5415.2005.53221.x

Nho, K., Risacher, S.L., Crane, P.K., DeCarli, C., Glymour, M.M., Habeck, C., … Saykin, A.J. (2012). Voxel and surface-based topography of memory and executive deficits in Mild Cognitive Impairment and Alzheimer's disease. *Brain Imaging and Behavior, 6*(4), 551–567. doi:10.1007/s11682-012-9203-2

Orfei, M.D., Varsi, A.E., Blundo, C., Celia, E., Casini, A.R., Caltagirone, C., & Spalletta, G. (2010). Anosognosia in Mild Cognitive Impairment and mild Alzheimer's disease: Frequency and neuropsychological correlates. *American Journal of Geriatric Psychiatry, 18*(12), 1133–1140. doi:10.1097/JGP.0b013e3181dd1c50

Ott, B.R., Lafleche, G., Whelihan, W.M., Buongiorno, G.W., Albert, M.S., & Fogel, B.S. (1996). Impaired awareness of deficits in Alzheimer disease. *Alzheimer Disease & Associated Disorders, 10*(2), 68–76. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8727167

Peavy, G.M., Salmon, D.P., Edland, S.D., Tam, S., Hansen, L.A., Masliah, E., … Hamilton, J.M. (2013). Neuropsychiatric features of frontal lobe dysfunction in autopsy-confirmed patients with Lewy Bodies and "pure" Alzheimer disease. *American Journal of Geriatric Psychiatry, 21*(6), 509–519. doi:10.1016/j.jagp.2012.10.022

Rabin, L.A., Roth, R.M., Isquith, P.K., Wishart, H.A., Nutter-Upham, K.E., Pare, N., … Saykin, A.J. (2006). Self- and informant reports of executive function on the BRIEF-A in MCI and older adults with cognitive complaints. *Archives of Clinical Neuropsychology, 21*(7), 721–732. doi:10.1016/j.acn.2006.08.004

Rabin, L.A., Saykin, A.J., Wishart, H.A., Nutter-Upham, K.E., Flashman, L.A., Pare, N., & Santulli, R.B. (2007). The memory and aging telephone screen: Development and preliminary validation. *Alzheimer's & Dementia, 3*, 109–121. doi:10.1016/j.jalz.2007.02.002.

Rabin, L.A., Smart, C.M., Crane, P.K., Amariglio, R.E., Berman, L.M., Boada, M., … Sikkes, S.A. (2015). Subjective cognitive decline in older adults: An overview of self-report measures used across 19 international research studies. *Journal of Alzheimer's Disease, 48*(Suppl 1), S63–S86. doi:10.3233/jad-150154

Rabin, L.A., Wang, C., Katz, M.J., Derby, C.A., Buschke, H., & Lipton, R.B. (2012). Predicting Alzheimer's disease: Neuropsychological tests, self-reports, and informant reports of cognitive difficulties. *Journal of the American Geriatrics Society, 60*(6), 1128–1134. doi:10.1111/j.1532-5415.2012.03956.x

Ready, R.E., Ott, B.R., Grace, J., & Cahn-Weiner, D.A. (2003). Apathy and executive dysfunction in Mild Cognitive Impairment and Alzheimer disease. *American Journal of Geriatric Psychiatry, 11*(2), 222–228. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12611752

Roth, R.M., Isquith, P.K., & Gioia, G.A. (2005a). Executive function: Concepts, assessment and intervention. In G.P. Koocher, J.C. Norcross, & S.S. Hill (Eds.), *Psychologists' desk reference* (2 ed., pp. 38–41). New York, NY: Oxford University Press.

Roth, R.M., Isquith, P.K., & Gioia, G.A. (2005b). *Behavior Rating Inventory of Executive Function - Adult version (BRIEF-A)*. Lutz, FL: Psychological Assessment Resources.

Rueda, A.D., Lau, K.M., Saito, N., Harvey, D., Risacher, S.L., Aisen, P.S., … Farias, S.T. (2015). Self-rated and informant-rated everyday function in comparison to objective markers of Alzheimer's disease. *Alzheimer's & Dementia, 11*(9), 1080–1089. doi:10.1016/j.jalz.2014.09.002

Salmon, D.P. (2000). Disorders of memory in Alzheimer's disease. 95. In L.S. Cermak (Ed.), *Handbook of neuropsychology: Memory and its disorders.* (2nd., Vol. *2*, pp. 155–195). Amsterdam: Elsevier.

Sanchez-Benavides, G., Pena-Casanova, J., Casals-Coll, M., Gramunt, N., Molinuevo, J.L., Gomez-Anson, B., … Blesa, R. (2014). Cognitive and neuroimaging profiles in Mild Cognitive Impairment and Alzheimer's disease: Data from the Spanish Multicenter Normative Studies (NEURONORMA Project). *Journal of Alzheimer's Disease, 41*(3), 887–901. doi:10.3233/jad-132186

Saunders, N.L., & Summers, M.J. (2011). Longitudinal deficits to attention, executive, and working memory in subtypes of Mild Cognitive Impairment. *Neuropsychology, 25*(2), 237–248. doi:10.1037/a0021134

Schoo, L.A., van Zandvoort, M.J., Biessels, G.J., Kappelle, L.J., & Postma, A. (2013). Insight in cognition: Self-awareness of performance across cognitive domains. *Applied Neuropsychology: Adult, 20*(2), 95–102. doi:10.1080/09084282.2012.670144

Spitznagel, M.B., & Tremont, G. (2005). Cognitive reserve and anosognosia in questionable and mild dementia. *Archives of Clinical*

Neuropsychology, 20(4), 505–515. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15896563

Spitznagel, M.B., Tremont, G., Brown, L.B., & Gunstad, J. (2006). Cognitive reserve and the relationship between depressive symptoms and awareness of deficits in dementia. *Journal of Neuropsychiatry and Clinical Neurosciences, 18*, 86–190. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16720795

Stout, J.C., Wyman, M.F., Johnson, S.A., Peavy, G.M., & Salmon, D.P. (2003). Frontal behavioral syndromes and functional status in probable Alzheimer disease. *American Journal of Geriatric Psychiatry, 11*(6), 683–686. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/14609810

Stuss, D.T., & Alexander, M.P. (2000). Executive functions and the frontal lobes: A conceptual view. *Psychological Research., 63*(3–4), 289–298. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11004882

Tomita, T., Sugawara, N., Kaneda, A., Okubo, N., Iwane, K., Takahashi, I., … Yasui-Furukori, N. (2014). Sex-specific effects of subjective memory complaints with respect to cognitive impairment or depressive symptoms. *Psychiatry and Clinical Neurosciences, 68*(3), 176–181. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/24895733

Yesavage, J.A., Brink, T.L., Rose, T.L., Lum, O., Huang, V., Adey, M., & Leirer, V. O. (1982). Development and validation of a geriatric depression screening scale: A preliminary report. *Journal of Psychiatric Research, 17*(1), 37–49. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7183759