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Pattern of Cognitive Impairment in Older Veterans with Post Traumatic Stress Disorder Evaluated at a Memory Disorders Clinic

R. Scott Mackin, PhD, Julia A. Lesselyong, PsyD, and Kristine Yaffe, MD

Department of Psychiatry, University of California, San Francisco

Abstract

OBJECTIVE—We determined the pattern of clinically significant cognitive impairment (CI) among older veterans with Post Traumatic Stress Disorder (PTSD) evaluated in a memory disorders clinic.

METHODS—Data was collected from 19 ethnically diverse veterans. Cognitive functioning in six domains (verbal learning, memory, attention, language, executive functioning, and information processing speed) was assessed.

RESULTS—The majority of veterans (57%) demonstrated CI on a measure of single trial list learning, 44% exhibited CI on short delay memory for lists, and 31% exhibited CI in long delay memory for lists. CI on measures of memory for stories (14%) and executive functioning (6%) were less common and none of the participants demonstrated CI on measures of attention, language, or information processing speed.

CONCLUSIONS—CI on measures of single trial list learning and memory for lists are common in older PTSD patients evaluated in a memory disorders clinic and are likely to contribute to functional deficits.

Keywords

Cognitive deficits; cognitive impairment; Post Traumatic Stress Disorder; older adults; veterans; memory; learning; single trial learning; executive dysfunction; information processing speed; attention; language

INTRODUCTION

Cognitive dysfunction is often described as a frequent consequence of PTSD with lower performance on measures of attention, verbal learning, and memory being most commonly reported, but executive dysfunction and reductions in information processing speed having also being documented (Samuelson et al., 2006, Vasterling et al., 2002, Sachinvala et al., 2000, Kanagaratnam and Asbjornsen, 2007). However, these performance inefficiencies attributed to PTSD are often subtle and usually fall within the normal range of cognitive functioning (Twamley et al., 2009). As such, it is difficult to determine the extent to which the observed cognitive inefficiencies associated with PTSD are clinically significant,

Address reprint requests to: R. Scott Mackin, Ph.D. University of California, San Francisco, Department of Psychiatry and Langley Porter Psychiatric Institute, 401 Parnassus Avenue, Box F-0984, San Francisco, CA 94143-0984 USA, Tel: (415) 476-7067, Fax: (415) 502-6364.

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typically defined as performance falling 1.5 standard deviations below age matched peers (Schink et al.), and therefore likely to contribute to functional impairment and/or warrant accommodations for treatment.

An improved understanding of the pattern of clinically significant cognitive impairment (CI) in older adults with PTSD is particularly salient given a recent report demonstrating that veterans with PTSD have a nearly a two-fold increased risk for dementia when compared to veterans without PTSD (Yaffe et al.). However, to date, relatively few studies have evaluated cognitive functioning specifically in older adults with PTSD. Of these studies, inefficiencies of verbal learning and memory have again been consistently reported (Yehuda et al., 2006, Golier et al., 2006, Yehuda et al., 2004, Golier et al., 2002), but the extent to which these cognitive inefficiencies represent clinically significant CI in these domains has not been clarified. Further, cognitive functioning in other domains such as language, information processing speed, and attention has not typically been evaluated. As a consequence, very little is currently known about the extent and pattern of CI in older adults with PTSD.

Identifying the pattern of CI in older adults with PTSD could inform our understanding of the impact of these symptoms on functional status and suggest treatment modalities that could lead to improved functional and health outcomes. The present study was conducted to determine the pattern of CI in a sample of older adults with PTSD who were referred for evaluation at a memory disorders clinic. Based on previous reports of raw score inefficiencies on measures of learning and memory in older adults with PTSD we hypothesized that CI in these cognitive domains would be most commonly impairments in our sample. A secondary goal of this study was to report on the clinical characteristics of this sample as a hypothesis generating exploration of potential contributory factors to CI in older adults with PTSD.

METHODS

Participants

We assessed veterans evaluated at the San Francisco Veterans Affairs Memory Disorders Clinic between 2006 and 2009 for a diagnosis of PTSD. Of the 272 new patients seen in clinic for a multidisciplinary evaluation consisting of a geriatric psychiatrist and neuropsychologist, 24 (9%) were diagnosed with current PTSD utilizing Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) criteria. Of these, 5 were excluded from study participation due to insufficient neuropsychological data and the remaining 19 individuals comprised our study sample. Participants were not financially compensated for their participation in this study.

Measurements

Demographic information (age, years of education, race) was obtained for each participant by self-report or medical record review. Origin of PTSD symptoms (combat related vs non-combat) and PTSD onset (acute vs delayed) was identified from medical record review. PTSD onset was categorized as acute (symptoms occurring within 12 months of traumatic event) or delayed (symptoms occurring after 12 months of traumatic event) from medical record review. Additional clinical information regarding history of head injury, major depressive disorder, substance abuse disorder, and seizure disorder was also obtained for each participant from medical record review. Similarly, the presence of cardiovascular risk factors (hypertension, diabetes, coronary artery disease, dyslipidemia, and history of stroke) was obtained from the patient's medical records as was information regarding current psychotropic and cognitive enhancing medication use. Depressive symptoms were measured with the 15-item Geriatric Depression Scale (GDS) (Yesavage et al., 1982). The Committee

on Human Research at the University of California, San Francisco and the Committee for Research and Development at the San Francisco VA approved the study.

Cognitive Tests

Measures of cognitive functioning were administered by a licensed neuropsychologist. All participants completed neuropsychological assessment in a single session. Raw scores for each cognitive test were converted to Z scores using normative data for age matched peers. Cognitive impairment was defined as performance falling 1.5 standard deviations below age matched peers for each of the 12 cognitive tests. Unless specified otherwise the normative data utilized to calculate z scores for each cognitive test was obtained from the test manual. Global cognitive status was measured with the Mini-Mental State Exam (MMSE)(Folstein et al., 1983).

Verbal Learning and Memory

California Verbal Learning Test –Second Edition (CVLT II): The CVLT II (Delis, 2000) is a measure of verbal learning and memory for lists of information. The number of items recalled correctly for the first and total learning trials were utilized as measures of verbal learning. Measures of memory included the total number of correct responses on the short and long delay recall trial.

Logical Memory subtests of the Wechsler Memory Scale - Revised(Wechsler, 1997):

These subtests assess learning and memory for semantically related verbal information (stories). The number of correctly recalled story units for both stories for the immediate recall trial (Logical Memory I total score) was utilized as a measure of verbal learning and the total number of correct responses on the delayed recall trial (Logical Memory II total score) was utilized as a measure of verbal memory.

Attention

Wechsler Adult Intelligence Scale-Revised Digit Span subtest (Wechsler, 1981): This test assesses auditory attention. The outcome variable utilized was the total number of correct responses.

Information Processing Speed

Trail Making Test Part A (Reitan and Wolfson, 1993): This test is a measure of information processing speed. The time required to complete the task was utilized as the outcome variable(Heaton R, 2004).

Language

The Boston Naming Test (BNT)(Kaplan et al., 1983): The BNT is a commonly utilized measure of confrontation naming ability and the total number of correct responses was utilized as the outcome variable(Heaton R, 2004).

Semantic Fluency Test (Benton et al., 1983): This test is a measure of semantic fluency and the total number of correct responses was utilized as the outcome variable(Heaton R, 2004).

Controlled Oral Word Association Test (COWAT) (Benton et al., 1983): The COWAT is a measure of speed of phonemic fluency. The total number of correct responses for the three trials was utilized as the outcome variable(Heaton R, 2004).

Executive Functioning

Trail Making Test Part B(Reitan and Wolfson, 1993): This test is a measure of executive functioning. The primary outcome variable was the time required to complete the task(Heaton R, 2004).

RESULTS

The demographic and clinical characteristics of the sample are provided in Table 1. The mean age of the patients was 69.0 years (SD=9.9; range = 56 to 88 years) and the mean level of education was 14.1 years (SD=2.9) with 63% of participants self-reporting White race, 32% were African American, and 5% were Asian. Seventeen participants (89%) reported experiencing acute onset PTSD and 14 individuals (74%) reported experiencing combat related PTSD. The mean MMSE score for the sample was 25.6 (SD=3.5) and the mean GDS was 5.4 (SD=3.4). A majority of participants (79%) were taking anti-depressant medications, 6 participants (32%) were taking cognitive enhancing medication, and 3 participants (16%) were taking anxiolytic medications. Four individuals (21%) had a history of head injury, 6 (32%) had a history of substance abuse, 1 (5%) had a history of seizure disorder, and 14 (74%) had a history of major depressive disorder. Eight participants (42%) had been diagnosed with hypertension, 6 (32%) with coronary artery disease, 5 (26%) with dyslipidemia, 7 (37%) with diabetes, and 1 participant had a history of stroke (5%).

The mean age corrected z scores for each cognitive test is provided in Table 2. Performance on single trial list learning was impaired for 57% of the sample. Across the five learning trials of the list learning task and on the measure of verbal learning for stories none of the veterans demonstrated CI. With regard to memory performance, 44% of the sample demonstrated CI on short delay recall and 31% demonstrated CI on long delay recall of lists. Fourteen percent of the sample demonstrated CI on memory for stories and 6% demonstrated impairment on a measure of executive functioning (Trail Making Test Part B). No patient had CI on tests of attention, language, or information processing speed.

As single trial list learning was the most commonly observed CI in this sample we evaluated the degree to which performance on this test correlated with other cognitive measures. Single trial list learning was significantly correlated with total list learning ($r=0.57$, $p=0.05$) in our sample but was not significantly associated with performance on other cognitive tests. Further, to evaluate the relationship between clinical characteristics and one trial list learning, we conducted correlation analyses and no statistically significant associations were identified. Similarly, to explore the association between cognitive performance on other measures and clinical characteristics additional correlation analyses were conducted. Hypertension was associated with poorer performance on both the short ($r=-0.56$; $p=0.02$) and long delay recall ($r=-0.67$, $p<0.01$) memory of the list learning test. Performance on the learning trial for stories was negatively correlated with history of previous head injury ($r=-0.58$, $p=0.03$) but other indices of cognitive functioning were not associated with demographic variables (age, education), PTSD onset (acute/delayed) or type of PTSD (combat, non-combat), history of substance abuse, depressive symptom severity (GDS), or the total number of cerebrovascular risk factors ($p>0.05$ for all).

Discussion

The primary goal for this study was to gather data on the pattern of cognitive deficits and proportion with clinically significant cognitive impairment among older adults with PTSD evaluated at a memory clinic. A secondary goal for this study was to report on the clinical characteristics of older veterans with PTSD in order to determine potential contributors to cognitive deficits in this patient population in larger studies. Our primary results indicate

that: 1) Clinically significant deficits on single trial list learning test and verbal memory test for lists of information were common in older veterans with PTSD, 2) Clinically significant deficits in verbal learning for stories and measures of executive dysfunction were less common, and 3) With the exception of hypertension and history of head injury, the observed cognitive deficits were largely unrelated to demographic and clinical characteristics, however we interpret these findings cautiously given our small sample size.

In our sample, cognitive impairment was demonstrated by 57% of participants on a test of single trial list learning. Performance inefficiencies in one trial learning have been suggested previously in studies evaluating raw score differences between PTSD and normal comparison subjects in older adults (Yehuda et al., 2004), however to our knowledge this is the first study to document the frequency to which these inefficiencies represent clinically significant CI relative to same age peers. These findings suggest that older adults with PTSD may commonly show functional consequences when faced with tasks requiring a single learning trial for lists of information. In contrast, when evaluating learning for lists of information over several trials, none of the participants in our sample demonstrated clinically significant impairment which was unexpected given previous studies (Yehuda et al., 2004). Another unexpected finding was that none of the participants in our sample demonstrated impairment on measures of verbal learning for semantically related information (stories), which was anticipated given previous findings demonstrating reduced efficiency in learning of semantically related word pairs in older adults with PTSD (Yehuda et al., 2006).

Our results also indicate that a large proportion of patients in this sample demonstrated CI on measures of memory for lists of information after a short delay (44%) and long delay (31%). Again, results documenting performance inefficiencies in these areas with older adults with PTSD have been reported earlier (Golier et al., 2006, Yehuda et al., 2004, Golier et al., 2002), however our findings are important as they document that clinically significant CI in these domains. In contrast, performance on measures of memory for more structured information (stories) was impaired in only 14% of the sample. Again, these results suggest that memory impairments in older adults with PTSD may be more common for lists of information rather than more structured semantically related information, i.e. stories. Additionally, with the exception of a small proportion of participants exhibiting CI on one measure of executive functioning (6%), CI on measures of language, attention, and information processing speed were not exhibited in our PTSD sample. Given that patients were evaluated in the context of a memory disorders clinic this lack of impairment in other cognitive domains is notable, particularly given that deficits in these domains are commonly seen in memory disorder clinics due to effects of neurodegenerative diseases such as Alzheimer's disease (Lonie et al., 2009).

A number of previous studies have suggested that concurrent psychiatric diagnoses, such as depression and substance abuse, can largely account for cognitive inefficiencies observed in individuals with PTSD (Neylan et al., 2004). Consistent with previous studies (Marcinko et al., 2006), our preliminary data suggests that many of these comorbidities are quite common in older adults with PTSD with 74% of participants in our sample having a history of depression, 35% having substance abuse histories, and 25% having past head injuries. In older adults with PTSD, the potential for neurodegenerative disease to contribute to cognitive deficits is also an important factor and participants in our study had cardiovascular risk factors and a significant number of participants were taking cognitive enhancing medication. However, in our study, cognitive performance was not associated with demographic variables, PTSD characteristics (early vs late onset; combat vs non-combat), current depression severity, medication use, or total number of cardiovascular risk factors. Overall, with the exception of hypertension and history of head injury, which are commonly

associated with cognitive dysfunction in older adults (Guskiewicz et al., 2005, Saxby et al., 2003) and also shown to be related to cognitive functioning in our sample, the clinical characteristics of our sample were largely unrelated to cognitive performance. These preliminary findings suggest that further study of factors contributing to CI in older adults with PTSD are warranted in order to delineate the potential etiology of CI in this patient group. We do, however, recognize that given our small sample size we were limited in our ability to identify specific risk factors for CI and these preliminary findings should be interpreted cautiously.

Overall, we believe that the identification of clinically significant CI in older veterans with PTSD represents a strength of this investigation, however there are several limitations to our study that should be discussed in relation to our findings. First, and perhaps most significant, the sample size was quite small and limited to male veterans evaluated at a memory disorders clinic. As a result, our findings may not be generalizable to the larger population and the rates of memory impairment exhibited in our sample may be higher than in the general population of older adults with PTSD. Further, given our sample size our ability to identify clinical risk factors for CI was limited. Additionally, we did not utilize a structured rating scale to classify the severity of PTSD symptoms in our sample which would have enabled us to more clearly identify whether the cognitive deficits correlate with PTSD symptoms. Also, by design, we did not utilize a non-psychiatric comparison group in this study as our primary aim was to determine the pattern of clinically significant cognitive impairment in older veterans with PTSD referred for evaluation at a memory disorders clinic with a secondary aim of identifying other clinical characteristics of this sample that might influence cognitive functioning. As a result, however, we recognize that our ability to differentiate the impact of PTSD on CI from other clinical characteristics was limited and future studies investigating CI in older adults with PTSD would benefit from utilizing non-psychiatric control groups. Lastly, we utilized medical chart review to obtain clinical information for our sample of PTSD participants and previous studies have documented the potential for this information to be less accurate than more direct means of obtaining clinical information (Luck et al., 2000).

CONCLUSIONS

We believe our results offer compelling preliminary data to suggest that clinically significant cognitive impairments of single trial learning and memory impairment are common in older veterans with PTSD; whereas deficits in other cognitive domains were less common. In our sample older veterans exhibited a number of risk factors for CI however cognitive performance was largely unrelated to demographic or clinical variables with the exception of a strong relationship of measures of memory to hypertension and history of head injury. Continued study of clinically significant CI in older adults with PTSD represents a critical aspect of delineating contributors to functional decline and improving treatments in this patient population.

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Table 1

Clinical and demographic characteristics of older veterans with PTSD (n=19)

Age (years)	69.0 (SD=9.9)
Education (years)	14.1 (SD=2.9)
Mini Mental State Exam	25.6 (SD=3.5)
Geriatric Depression Scale	5.4 (SD=3.4)
Current Cognitive Enhancing Medication	6 (32%)
Current Anti-Depressant Medication	15 (79%)
Current Anxiolytic Medication	3 (16%)
Combat Related PTSD	14 (74%)
Onset of PTSD (Acute)	17 (89%)
History of Head Injury	4 (21%)
History of Substance Abuse	6 (32%)
History of Seizure Disorder	1 (5%)
History of Major Depression	4 (21%)
Coronary Artery Disease	6 (32%)
Hypertension	8 (42%)
Dyslipidemia	5 (26%)
Diabetes	7 (35%)
History of Stroke	1 (5%)

Table 2

Neuropsychological test performance of older veterans with PTSD (n=19)

Neuropsychological Domain/Tests	Z score Mean (SD)	Cognitive Impairment
Language		
Boston Naming Test	0.10 (.47)	0%
Semantic Fluency (Animal Naming)	0.09 (.75)	0%
Controlled Oral Word Association Test	0.09 (.57)	0%
Attention		
WAIS-R Digit Span	-0.77 (.51)	0%
Executive Functioning		
Trail Making Test Part B	0.10 (.72)	6%
Information Processing Speed		
Trail Making Test Part A	0.09 (.68)	0%
Learning		
WMS-R Logical Memory I	0.22 (.75)	0%
CVLT Trial 1	-1.75 (1.13)	57%
CVLT Trials 1-5 Total	0.09 (.66)	0%
Memory		
WMS-R Logical Memory II	-0.10 (1.06)	14%
CVLT II Short Delay Free Recall	-1.13 (0.95)	44%
CVLT II Long Delay Free Recall	-0.82 (0.94)	31%

Note: WAIS-R = Wechsler Adult Intelligence Scale-Revised; CVLT II = California Verbal Learning Test-Second Edition; WMS-R = Wechsler Memory Scale - Revised