Does PTSD Impair Cognition Beyond the Effect of Trauma?

Salah U. Qureshi, M.D.
Mary E. Long, Ph.D.
Major R. Bradshaw, Ph.D.
Jeffrey M. Pyne, M.D.
Kathy M. Magruder, M.P.H., Ph.D.
Timothy Kimbrell, M.D.
Teresa J. Hudson, Pharm.D.
Ali Jawaid, M.B.B.S.
Paul E. Schulz, M.D.
Mark E. Kunik, M.D., M.P.H.

This systematic review analyzed data from studies examining memory and cognitive function in subjects with posttraumatic stress disorder (PTSD), compared with subjects exposed to trauma (but without PTSD). Based on analysis of 21 articles published in English from 1968 to 2009, the conclusion is that individuals with PTSD, particularly veterans, show signs of cognitive impairment when tested with neuropsychological instruments, more so than individuals exposed to trauma who do not have PTSD.

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Epidemiological studies estimate that exposure to a traumatic event affects 50% to 70% of the general population.[1–3] Among victims of traumatic events, posttraumatic stress disorder (PTSD) is a common but serious mental health consequence. Epidemiological estimates of PTSD in the general population indicate high current (6% to 14%)[1,4,5] and lifetime[6] prevalence. PTSD is also associated with high rates of comorbid psychiatric disorders, including depression, substance abuse, psychosis, and anxiety disorders,[7–9] even after control-

Received September 3, 2009; revised December 17, 2009, and February 10, 2010; accepted March 4, 2010. Drs. Qureshi, Long, and Kunik are affiliated with the Houston Center for Quality of Care & Utilization Studies, Health Services Research and Development Service, Michael E. DeBakey Veterans Affairs (VA) Medical Center, in Houston, TX; Drs. Qureshi and Schulz are affiliated with the Neurosensory Center at Baylor College of Medicine in Houston and with the Neurology Care Line at Michael E. DeBakey VA Medical Center in Houston; Drs. Qureshi, Long, Kimbrell, and Kunik are affiliated with VA South Central Mental Illness Research, Education and Clinical Center; Drs. Bradshaw, Jawaid, and Schulz are affiliated with the Department of Neurology at Baylor College of Medicine in Houston; Drs. Pyne, Kimbrell, and Hudson are affiliated with the Center for Mental Health and Outcomes Research, Central Arkansas Veterans Healthcare System, and the Department of Psychiatry, College of Medicine, University of Arkansas for Medical Sciences; Dr. Magruder is affiliated with the Ralph H. Johnson VA Medical Center; Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC; Dr. Kunik is also affiliated with the Menninger Department of Psychiatry and Behavioral Sciences and with the Department of Medicine at Baylor College of Medicine in Houston. Address correspondence to Mark E. Kunik, M.D., M.P.H., Houston Center for Quality of Care & Utilization Studies, Michael E DeBakey VAMC (152), 2002 Holcombe, Houston, TX 77030. e-mail: mkunik@bcm.tmc.edu

ling for the symptoms these disorders share with PTSD.[10] Also, PTSD is often a chronic condition, with patients suffering symptoms several years after initial exposure to their index trauma.[11] Although a growing literature examines the effects of chronic PTSD on memory and other cognitive domains, studies of the association of PTSD and dementia are lacking. This is surprising, as PTSD, for which the memory of etiologic trauma(s) plays such a significant role in the form of intrusive thoughts, nightmares and flashbacks, has been conceptualized as a disorder of memory.[12]

PTSD and dementia share several proposed risk factors and neuroanatomical correlates. It has been reported that lower intelligence,[13–17] lower educational level,[18,19] smaller hippocampal volume,[20–23] and dysfunction of frontal and parietal cortical regions[24–27] are associated with PTSD and dementing illnesses.

Neuroanatomical changes and cognitive impairments are also reported to be present in subjects with a history of physical or psychological trauma.[28–30] Mild traumatic brain injury has been linked to oxidative stress and Alzheimer's disease.[31] Others have reported high rates of mood and anxiety disorders, with cognitive impairment associated with trauma.[32,33] It is still unclear how much of a role trauma and mood play in cognitive impairment associated with PTSD.

In this systematic review, we analyze data from studies that examined memory and cognitive function in subjects with PTSD and in control groups exposed to psychological and/or physical trauma but without PTSD. Our purpose was to identify the pattern of cognitive impairment and to examine which cognitive domains are consistently associated with PTSD when compared with trauma exposure. This will help to inform the design of future research to address cognitive impairments in this group of patients.

METHOD

We searched MEDLINE by combining the following MESH headings: stress disorder, posttraumatic, memory, dementia, cognition, and neuropsychological. The search was restricted to human adults and articles printed in English from 1968 to 2009.

We performed the initial searches, reviewed the abstracts, and excluded those that did not specifically focus on cognitive impairment. We then reviewed the full articles for the remainder and excluded those that 1) did not have a control group; 2) included only patients with acute PTSD, traumatic brain injury, schizophrenia, cerebral vascular accidents, serious medical disorders, or chemical exposure; 3) included only children and adolescents; 4) examined only memories related to trauma or trauma-related events; and 5) examined only cognitive changes after treatment of PTSD. The resulting articles were further reviewed, and, from these, we excluded review articles and those that used duplicative study samples and tested similar cognitive domains, used nonvalidated neuropsychological testing, used a single neuropsychological test beyond memory testing, and/or used only computerized testing. Finally, we excluded studies that did not have a control group exposed to trauma.

The remaining articles were independently assessed by two reviewers (SQ and ML), using the epidemiological quality tool adapted from the Jadad quality measure.[34] The tool provides a maximum score of 7; 1 point each for use of a nationally representative sample, use of a valid PTSD diagnostic tool, comparison with other psychiatric illnesses or substance abuse, accounting for the impact of depression or substance abuse, assessment of the severity of PTSD, controlling for the effects of learning-impairment on memory, and provision of established validity and reliability of all neuropsychological tests.

Data Extraction

As a first step, all neuropsychological tests in the selected articles were categorized by the mutual consensus of a neuropsychologist (MB) and a psychiatrist (SQ) as assessing some or all of five cognitive domains: attention, learning, memory, executive function, and visuospatial function (Table 1). IQ tests and those that did not fit easily into any of these domains, such as the WAIS and Spot the Word, were excluded. Some tests, like the Benton Visual Retention Test and the California Verbal Learning Test (CVLT), were assigned to more than one cognitive domain. For example, in the case of learning and memory tests like the CVLT and Auditory Verbal Learning Test (AVLT), Learning trials 1–5 were used only for learning, and Delayed Recall for memory. If only one overall result was given for these tests, then it was considered for memory unless otherwise specified.

For all articles, a test result was considered to be positive only if it showed statistically significant ($p<0.05$) impairment in the PTSD group when it was compared with a control group with psychological and/or physical trauma. It includes subjects with history of military deployment, imprisonment, combat exposure, rape, violence, child abuse, refugee status, and natural disaster; it also includes Holocaust survivors. Effect size, which is a measure of the strength of a relationship between two variables, was calculated as Cohen's *d* and/or *r* for all the significant associations wherever possible. A Cohen's *d* of less than 0.2 was considered a negligible effect size, from 0.2 to 0.4 as small, from 0.5 to 0.7 as medium, and 0.8 and above as strong. Data were not included when comparisons were made with a control group without trauma. Whenever available, results were included after controlling for confounding factors like depression, substance abuse, and learning-impairment, as they can affect cognition, particularly, memory. Approximate time since trauma was not mentioned in most studies but was estimated by the authors by incorporating historical events describing the sample.

RESULTS

Initially, the search resulted in 1,230 articles. Review of the abstracts and exclusion of studies not specifically focusing

TABLE 1. Neuropsychological Instruments and Cognitive Domains They Cover, in Studies Selected for Review

Test	Attention	Learning	Memory	Executive Function	Visuospatial
Attentional Network Task	✓			✓	
Auditory Consonant Trigrams	✓				
Auditory Verbal Learning Test		✓	✓		
Benton Facial Recognition Test					✓
Benton Visual Retention Test			✓		✓
California Verbal Learning Test		✓	✓		
Color Trail-Making Test				✓	
Comprehensive Trail-Making Test				✓	
Continuous Performance Test	✓			✓	
Continuous Visual Memory Test		✓	✓		
Controlled Oral Word Association				✓	
Digit Vigilance	✓				
Figure Classification				✓	✓
Hayling Sentence Completion Test				✓	
Judgment of Line Orientation					✓
Letter Cancellation	✓				✓
Paced Auditory Serial Addition Test	✓			✓	
Posner Visual Selective Attention Task	✓				
Rey Osterrieth Complex Figure Test			✓[a]	✓	✓
Rivermead Behavioral Memory Test			✓		
Short Category Test				✓	
Stroop Test				✓	
Sustained Attention to Response Task	✓				
Symbol Digit Modality Test				✓	
Thurstone Memory Test			✓		
Tower Of London				✓	
Trail Making Test A & B				✓	
Visual Object and Spatial Perception					✓
Verbal Fluency Test				✓	
Warrington Recognition Memory Test			✓		
Wechsler Adult Intelligence Scale					
Block Design					✓
Digit Span	✓				
Digit Forward	✓				
Digit Backward	✓				
Digit Symbol				✓	
Letter Number Sequence	✓				
Picture Arrangement	✓				✓
Picture Completion	✓				✓
Wechsler Memory Scale III			✓		
Figural Memory			✓		
Logical Memory Subtest			✓		
Spatial Span	✓				
Verbal Paired Associates		✓	✓		
Visual Memory Subsets			✓		
Wisconsin Card Sorting Test				✓	

[a] If delayed recall was tested.

on cognitive impairment left a sample of 108 articles. Examination of this group of studies and elimination of those that did not meet our inclusion criteria (see "Methods") resulted in 48 remaining articles, from which we then eliminated all but 21 articles, based on our exclusion criteria. See Table 2 for a brief description of each study and the cognitive domains examined.

Studies of Veterans

Studies of veterans are most common (n=8). Age ranges from 30 to 81 across these studies, and approximate time since trauma ranges from 7 to 65 years.

Barrett et al.[35] examined cognitive impairment in one of the largest samples of veterans from the Vietnam Experience Study. Vietnam veterans with only PTSD (N=236) were compared with those with PTSD and other psychiatric disorders (N=128), with other psychiatric disorders without PTSD (N=242) and without PTSD or other psychiatric disorders (N=1,835). Several neuropsychological tests were used, but none was significantly associated with PTSD after adjusting for demographic and military covariates including combat exposure. The authors concluded that cognitive deficits in PTSD are most likely secondary to comorbid mental health disorders.

Vasterling et al.[36] examined memory and attention in veterans who were mobilized for Operation Desert Storm. They compared veterans with PTSD (N=19) to psychopathology-free veterans (N=24), using a large battery of neuropsychological tests. Their findings include problems in sustained attention on the Continuous Performance Test commissions ($p=0.023$; $d=-0.64$, $r=-0.30$) and learning on AVLT trials ($p=0.025$; $d=-0.84$, $r=-0.39$) and Continuous Visual Memory Test learning phase ($p=0.004$; $d=-0.90$, $r=-0.41$) in veterans with PTSD. A medium-to-strong effect size was observed for these significant associations. These cognitive impairments were found to be associated with severity of PTSD symptoms, especially reexperiencing and avoidance. Memory impairment was also present on delayed recall but was not significant after controlling for initial learning.

Vasterling et al.[37] did a similar study of Vietnam veterans who served in war zones, with similar results. Veterans with PTSD (N=26) were compared with veterans without any mental disorders (N=21). Impairment in attention was noted in veterans with PTSD on Digit Span (DS) ($p=0.03$; $d=-0.05$, $r=-0.03$) and Continuous Performance Test hits ($p=0.04$; $d=-0.68$, $r=-0.32$). Although total learning was not impaired on the Continuous Visual Memory Test ($p=0.88$), total recalls on Trials 1–5 were significantly impaired on the AVLT ($p<0.01$; $d=-0.70$, $r=-0.33$) in these individuals. Impairment in both cognitive domains had a good effect size. Substance abuse and PTSD symptom severity were also taken into account in this study. The authors concluded that cognitive impairment is associated with PTSD, independent of intellectual functioning.

Yehuda et al.[38] studied learning and memory in aging combat veterans who were age 65 or older. Although the PTSD-positive group (N=30) was significantly different from the nonexposed group (without trauma; N=15) in memory and learning, when compared with the PTSD-negative group (with trauma) (N=20) this difference was not significant. However, in an analysis of a subsample population after excluding those with a history of substance abuse, they did find significant differences in the PTSD-positive (N=19) and negative (N=13) groups in learning ($p=0.03$; $d=-0.52$, $r=-0.25$) and delayed recall ($p=0.01$; $d=-0.85$, $r=-0.39$) on the CVLT, with medium-to-strong effect sizes.

Koso et al.[39] investigated memory and executive function in Bosnian combat veterans. The group found significant differences in PTSD (N=20) and non-PTSD (N=20) groups on several neuropsychological measures. They concluded that veterans with PTSD showed impairment in attention on the Sustained Attention to Response Task ($p<0.001$; $d=1.34$, $r=0.56$), memory on the Rivermead Behavioral Memory Test ($p<0.001$; $d=-2.44$, $r=-0.77$) and executive function on the Trail-Making Test A ($p<0.001$; $d=1.15$, $r=0.50$), Trail-Making Test B ($p<0.001$; $d=1.51$, $r=0.60$) and Hayling Sentence Completion Test ($p<0.001$; $d=1.41$, $r=0.58$), with strong effect size.

Gilbertson et al.[15] compared combat-exposed Vietnam-era veterans with (N=19) and without PTSD (N=24) and their monozygotic twins. The authors assessed neurocognitive functioning and found that the verbal memory measure demonstrated a significant diagnosis main effect (Cohen's $d=0.77$). Combat veterans with PTSD scored significantly lower in verbal memory ($p=0.03$) when compared with veterans without PTSD. Learning also demonstrated a significant diagnosis main effect ($t=2.13$; $p=0.04$). They also found significant diagnosis main effects on measures of attention (Cohen's $d=1.11$) and executive function (Cohen's $d=0.89$), but not in visual memory and visuospatial abilities. Combat veterans with PTSD scored lower in attention measures ($p=0.006$) and higher in executive dys-

TABLE 2. Summary of Studies and Results of Neuropsychological Tests

Study	Sample (n)	Age (Effect Size)	Cognitive Domain(s) Assessed: Attention	Learning	Memory	Executive Function	Visuospatial	Association with PTSD Severity (Duration)	Quality Score
Studies of Veterans									
Barrett et al.[35]	Vietnam veterans with PTSD only (n=236). *Control Group:* Vietnam veterans with PTSD and other psychiatric diagnosis (n=128), veterans with other psychiatric diagnosis and without PTSD (n=242) and veterans without PTSD or other current psychiatric diagnosis (n=1,835).	30–40 (NA)		−CVLT	−CVLT, ROCFT	−WCST, ROCFT	−ROCFT, BD	NA (>14 years)	5
Vasterling et al.[36]	Veterans from Operation Desert Storm with PTSD (n=19). *Control Group:* Veterans without any psychopathology (n=24).	35–36 (Medium-to-strong)	+CPT−DS, LC	+AVLT, CVMT	✷−AVLT, CVMT	−wCST, Stroop	−LC	Y (7 years)	5
Vasterling et al.[37]	Vietnam veterans with PTSD (n=26). *Control Group:* Vietnam veterans without any psychopathology (n=21).	50–51 (Medium)	+DS, CPT−LC	+AVLT −CVMT	−CVMT	−WCST, Stroop	−LC	Y/N (>25 years)	4
Yehuda et al.[38]	Aging combat veterans with PTSD and without substance abuse (n=19). *Control Group:* Aging combat veterans without PTSD and substance abuse (n=13) and veterans unexposed to combat (n=7).	65–67 (Medium-to-strong)		+CVLT	+CVLT		−BD	NA (20–60 years)	4
Koso et al.[39]	Bosnian male veterans with combat-related PTSD (n=20). *Control Group:* Bosnian male veterans without PTSD (n=20).	47 (Strong)	+SART		+RBMT	+TMT A & B, HSCT		NA (7 years)	2
Gilbertson et al.[15]	PTSD group consisting of male monozygotic twin pairs of which one was a veteran and had PTSD (n=19 pairs). *Control Group:* Non-PTSD group consisting of male monozygotic twin pairs of which one was a veteran without PTSD (n=24 pairs).	52 (Medium-to-strong)	+DS	+CVLT	✷+CVLT −CVMT	+WCST	−BFRT, VOSP	Y/N (>25yrs)	6
Samuelson et al.[40]	Veterans with PTSD and no alcohol abuse or dependence (n=37). *Control Group:* Veterans with PTSD and alcohol abuse or dependence (n=30), veterans with alcohol abuse or dependence and without PTSD (n=30) and veterans with no alcohol abuse or dependence and no PTSD (n=31).	43–48 (Medium-to-strong)	+DS, LNS, −SS	+CVLT	−CVLT, LM	+DY	−BD	NA (CND)	4
Hart et al.[41]	POWs with PTSD only (n=7). *Control Group:* POWs with PTSD and psychiatric comorbidities (n=7), POWs without PTSD and psychiatric comorbidities (n=11).	79–81 (Strong)	−DS	−AVLT	−AVLT, LMS, WRMT	+SDMT, TMTB −BNT, COWA, TMTA	−JLOT	NA (55–65 years)	4

TABLE 2. Summary of Studies and Results of Neuropsychological Tests (Continued)

Study	Sample (n)	Age (Effect Size)	Cognitive Domain(s) Assessed: Attention	Learning	Memory	Executive Function	Visuospatial	Association with PTSD Severity (Duration)	Quality Score
Studies of (Sexually/Physically) Abused Individuals									
Jenkins et al.[44]	Rape victims with PTSD (n=15). *Control Group:* Rape victims without PTSD (n=16) and non-traumatized comparison subjects (n=16).	28 (Weak)		+CVLT	+CVLT			NA (6 years)	3
Jenkins et al.[45]	Rape victims with PTSD (n=15). *Control Group:* Rape victims without PTSD (n=16) and non-traumatized comparison subjects (n=16).	27–28 (Strong)	+CPT, PASAT, DS−PVSAT			+TMTB, DY, PASAT −TMTA		NA (Approximately 8 years)	2
Stein et al.[42]	Female victims of intimate partner violence with PTSD (n=17). *Control Group:* Female victims of intimate partner violence without PTSD (n=22) and non-victimized comparison subjects (n=22).	29–34 (NA)	−DS, ACT, DV, PASAT	−CVLT, VPA	−CVLT, LM, VPA, CVMT	−TMT, COWA, Stroop, PASAT, ROCFT	−ROCFT	N (4 weeks to 2 years)	4
Bremner et al.[46]	Premenopausal abused women with PTSD (n=18). *Control Group:* Premenopausal women with abuse and without PTSD (n=10) and without abuse and PTSD (n=15).	32–34 (Medium)			WMS+ (LM) −(FM)			Y (7 years)	4
Pederson et al.[43]	Right-handed abused women with PTSD (n=17). *Control Group:* Right-handed abused women without PTSD (n=17) and women without abuse or PTSD (n=17).	24–27 (NA)			−WMS			N (CND)	4
Studies of Refugees and War Victims									
Kivling-Bodén et al.[47]	Adult refugees from former Yugoslavia with PTSD (n=21). *Control Group:* Adult refugees without PTSD (n=13).	38–39 (Strong)	+PA −PC		−BVRT, ThMT	+FC	+BD, FC, PA−PC, BVRT	Y (4 to 6 years)	3
Yehuda et al.[48]	Holocaust survivors with PTSD (n=36). *Control Group:* Holocaust survivors without PTSD (n=26) and Jewish comparison subjects (n=40).	68–70 (Medium)		+CVLT	−CVLT			NA (Approximately 60 yrs)	4
Johnsen et al.[49]	Immigrants/refugees with chronic PTSD (n=21). *Control Group:* Immigrants/refugees with similar age and ethnic profile (n=21).	37–39 (Strong)	+DB−DF, PASAT	✪− CVLT	✷− CVLT	−PASAT		Y (Approximately 9 years)	5
Studies of Undergraduates									
Twamley et al.[50]	Undergraduate students with trauma exposure and PTSD (n=38). *Control Group:* Undergraduate students with trauma exposure and without PTSD (n=105) and without trauma (n=87).	19 (NA)	−DS, DV, LNS			−TMT, WCST, COWA		N (CND)	3
Leskin et al.[51]	Undergraduate volunteers with history of trauma and PTSD (n=19). *Control Group:* Undergraduate volunteers with high history of trauma and no PTSD (n=15) and with low history of trauma and no PTSD (n=18).	20–22 (CND)	−ANT			+ANT −TMT, CTMT		Y (CND)	4

TABLE 2. Summary of Studies and Results of Neuropsychological Tests (Continued)

Study	Sample (n)	Age (Effect Size)	Cognitive Domain(s) Assessed					Association with PTSD Severity (Duration)	Quality Score
			Attention	Learning	Memory	Executive Function	Visuospatial		
Studies of Survivors of Natural Disaster									
Parslow et al.[52]	Subjects who developed PTSD after a bush fire in Australia (n=38). *Control Group:* Subjects with subthreshold PTSD (n=606) and no PTSD (n=955) after the bush fire.	27 (Weak)	+DB		+CVLT	+SDMT		Y (9 months)	3
Eren-Koçak et al.[53]	Survivors of an earthquake in Turkey with current (n=11) and past PTSD (n=14) without depression. *Control Group:* Survivors of earthquake without PTSD or depression (n=18).	33–42 (Strong)		−AVLT	−AVLT, ROCFT	+CoTMT, VF −ROCFT, SCT, Stroop	−ROCFT	NA (4 years)	2
Other Studies									
Lindauer et al.[54]	Police officers with PTSD (n=12). *Control Group:* Police officers with trauma but no PTSD (n=12).	35–37 (NA)		−CVLT	−WMS (VM), CVLT	−Stroop		Y (1.7 years)	3

−: cognitive impairment not present at p>0.05; +: cognitive impairment present at p<0.05; CND: could not be determined; Y: cognitive impairment associated with severity of PTSD symptoms; N: cognitive impairment not associated with severity of PTSD symptoms; NA: not applicable or available; ✪: results changed after controlling for depression; ✷: controlled for learning.

Strong effect size: Cohen's *d* 0.8 and above; Medium effect size: Cohen's *d* 0.5 to 0.7; Weak effect size: Cohen's *d* 0.2 to 0.4.

ACT: Auditory Consonant Trigrams; ANT: Attentional Network Task; AVLT: Auditory Verbal Learning Test; BD: Block Design; BFRT: Benton Facial Recognition Test; BVRT: Benton Visual Retention Test; COWA: Controlled Oral Word Association; CoTMT: Color Trail-Making Test; CPT: Continuous Performance Test; CTMT: Comprehensive Trail-Making Test; CVLT: California Verbal Learning Test; CVMT: California Verbal Learning Test; DB: Digit Backward; DF: Digit Forward; DS: Digit Span; DY: Digit Symbol; DV: Digit Vigilance; FM: Figural Memory; HSCT: Hayling Sentence Completion Test; LC: Letter Cancellation; LM: Logical Memory Subtest; LNS: Letter Number Sequence; PASAT: Paced Auditory Serial Addition Test; PTSD: posttraumatic stress disorder; PVSAT: Posner Visual Selective Attention Task; RBMT: Rivermead Behavioral Memory Test; ROCFT: Rey Osterrieth Complex Figure Test; SART: Sustained Attention to Response Task; SDMT: Symbol Digit Modalities Test; TMT: Trail-Making Test (A and B); VOSP: Visual Object and Spatial Perception; VPA: Verbal Paired Associates; WCST: Wisconsin Card-Sorting Test; WMS: Wechsler Memory Scale III.

function ($p=0.009$) than those without PTSD. Interestingly, veterans with PTSD did not differ significantly from their unexposed twin without PTSD on measures of verbal memory, attention, and executive function. Except for perseverative errors, none of the neurocognitive differences between PTSD and non-PTSD groups were clinically relevant. The authors suggest that cognitive deficits in PTSD are familial in nature and serve as a risk factor for PTSD in the aftermath of trauma.

Samuelson et al.[40] studied cognitive functions in veterans with PTSD and alcohol abuse. Subjects were divided into four groups, based on their PTSD and alcohol status, and their neuropsychological test scores were compared. There were 30 veterans in PTSD+/ETOH+ group, 37 veterans in PTSD+/ETOH− group, 30 veterans in PTSD−/ETOH+ group and 31 veterans without PTSD or alcohol abuse or dependence. All groups had been exposed to a similar level of trauma. On measures of attention, there was a significant main effect of PTSD on DS ($p<0.0001$; $d=-0.97$, $r=-0.43$) and Letter Number Sequencing ($p=0.01$; $d=-0.85$, $r=-0.39$) but not on Spatial Span ($p=0.57$). Similarly there was a significant main effect of PTSD on CVLT trials 1–5 ($p=0.006$; $d=-0.59$, $r=-0.29$) but not on delayed recall ($p=0.40$) or Logical Memory I and II ($p>0.2$). Among other measures, Digit Symbol had a main effect of PTSD ($p=0.001$; $d=-0.76$, $r=-0.35$) but not Block Design ($p=0.6$). All significant associations had medium-to-strong effect sizes. The authors concluded that verbal memory and attention were impaired in PTSD.

Hart et al.[41] tested World War II and Korean War veterans who were also prisoners of war (POWs). They compared POWs with PTSD-only (N=7) versus POWs with PTSD and other psychiatric comorbidities (N=7) and POWs without PTSD or psychiatric comorbidities (N=11). They found executive dysfunction with strong effect sizes on Symbol Digit ($p<0.05$; $d=-1.83$, $r=-0.67$) and Trails B ($p<0.05$; $d=1.08$, $r=0.47$) in subjects with PTSD only when compared with POWs without PTSD or other psychiatric comorbidities. They suggest that cognitive impairments in PTSD may be related to comorbid conditions and higher IQ may protect against developing PTSD.

Results of studies examining cognitive differences between veterans with and without PTSD have been mostly positive, with medium-to-strong effect sizes. Only two studies did not find any significant cognitive impairment with PTSD after controlling for confounding factors such as learning. The rest of the studies were positive, especially for attentional measures (Table 3). One reason might be the longer duration of PTSD in these studies.

Studies of Abused Individuals

The second largest group of studies (five) focuses on sexually or physically abused individuals, mostly women. Their average/mean age range is between 24 and 34 years, with approximate time since trauma ranging from a few weeks to 8 years.

Stein et al. compared neuropsychological functioning in female victims of intimate-partner violence, with (N=17) or without PTSD (N=22).[42] The subjects underwent several neuropsychological tests, but results failed to show any significant differences between trauma victims with or without PTSD. The authors reported that cognitive deficits in these subjects were subtle, regardless of PTSD status.

Pederson et al.[43] correlated memory performance and

TABLE 3. Summary of Positive and Negative Findings for Association of Cognitive Domains, by Type of Sample Subject

Cognitive Impairment	Sample	Positive	Negative
Attention	Veterans	5	1
	Abused individuals	1	1
	Refugees/war victims	2	0
	Undergraduates	0	2
	Disaster survivors	1	0
	Other	0	0
	Total	**9**	**4**
Learning	Veterans	5	2
	Abused individuals	1	1
	Refugees/war victims	1	1
	Undergraduates	0	0
	Disaster survivors	0	1
	Other	0	1
	Total	**7**	**6**
Memory	Veterans	3	5
	Abused individuals	2	2
	Refugees/war victims	0	3
	Undergraduates	0	0
	Disaster survivors	1	1
	Other	0	1
	Total	**6**	**12**
Executive Function	Veterans	4	3
	Abused individuals	1	1
	Refugees/war victims	1	1
	Undergraduates	1	1
	Disaster survivors	2	0
	Other	0	1
	Total	**9**	**7**
Visuospatial Function	Veterans	0	7
	Abused individuals	0	1
	Refugees/war victims	1	0
	Undergraduates	0	0
	Disaster survivors	0	1
	Other	0	0
	Total	**1**	**9**

hippocampal volume in women with a history of child abuse. They were divided into PTSD-and-abuse, abuse-only, and normal-control groups, with 17 subjects in each group. These subjects completed the Wechsler Memory Scale but did not demonstrate significant differences between groups with or without PTSD in immediate, delayed, and working memory.

Jenkins et al.[44] examined learning and memory in rape victims with (N=15) and without PTSD (N=16) relative to nontraumatized comparison subjects (N=16), 6 years after the initial trauma. They used CVLT and found that women with PTSD performed worse on number of words learned ($p=0.02$; $d=-0.28$, $r=-0.13$) and long-delay free recall ($p<0.01$; $d=-0.24$, $r=-0.12$) after accounting for depression and alcohol use. Although the effect size of these results is weak, the authors suggested that memory impairment was associated with PTSD diagnosis.

In another study, Jenkins et al.[45] examined attentional dysfunction in rape victims with (N=15) and without PTSD (N=16) relative to nontraumatized comparison subjects (N=16), using a wide range of neuropsychological tests. Subjects with PTSD performed significantly worse on all measures, including Paced Auditory Serial Addition Test ($p=0.001$; $d=-1.79$, $r=-0.66$), Continuous Performance Test sequential letter ($p=0.01$; $d=-1.06$, $r=-0.47$), DS total ($p=0.004$; $d=-1.19$, $r=-0.50$), Digit Symbol ($p=0.001$; $d=-1.58$, $r=-0.57$), and the Trails B ($p=0.001$; $d=1.38$, $r=0.56$). These results had strong effect size, even after accounting for depression. The authors concluded that measures of sustained and divided attention are associated with PTSD.

Bremner et al.[46] focused on verbal and visual memory in premenopausal women who were sexually abused as children. They compared results in abused women with PTSD (N=18), abused women without PTSD (N=10) and women without abuse and with PTSD (N=15). On the Logical Memory Subtest of the Wechsler Memory Scale, abused women with PTSD had lower scores in verbal memory than abused women without PTSD ($p=0.002$; $d=-0.53$, $r=-0.26$), with medium effect size. This deficit remained after controlling for depression and correlated with severity of PTSD and sexual abuse. Authors concluded that PTSD associated with childhood abuse is related to deficits in verbal declarative memory.

The overall result from this group of studies was conflicting, with three positive and two negative studies. No single cognitive domain was found to be consistently affected by PTSD (Table 3).

Studies of Refugees and War Victims

The third largest group of studies evaluated in this review was of refugees and war victims, with three studies that examined neuropsychological profiles of subjects with trauma and PTSD. The average/mean age in these studies is between 37 and 78 years, and the approximate time since trauma is calculated to be between 4 and 60 years. All studies in this group found some type of cognitive impairment associated with PTSD.

Kivling-Bodén et al.[47] studied cognitive functioning in traumatized refugees with (N=21) and without PTSD (N=13) from the former Yugoslavia. They found that participants with PTSD scored significantly lower on some measures of attention, such as Picture Arrangement ($p=0.01$; $d=-0.93$, $r=-0.42$); on measures of executive function, such as Figure Classification ($p=0.03$; $d=-0.83$, $r=-0.39$); and on measures of visuospatial function, such as Block Design ($p=0.01$; $d=-1.08$, $r=-0.47$). These measures had strong effect size; but other measures failed to show any significant differences, especially in memory, such as the Benton Visual Retention Test ($p=0.15$) and the Thurstone Memory Test ($p=0.14$). The authors reported that subjects with PTSD had significantly impaired cognitive performance.

Yehuda et al.[48] examined learning and memory by administering the CVLT in Holocaust survivors with (N=36) or without PTSD (N=26) relative to comparison subjects (N=40). The PTSD group was found to have impaired learning, with a medium effect size, as these individuals performed significantly worse than the individuals without PTSD on CVLT trials 1–5 ($p<0.05$; $d=-0.61$, $r=-0.29$). However, the difference in long-delay free recall between these groups was not significant. Authors attributed impairment in verbal learning to PTSD because of accelerated cognitive decline in this older population.

Johnsen et al.[49] analyzed memory impairments in refugees from Yugoslavia, Chile, and the Middle East, both with (N=21) and without PTSD (N=21). On measures of CVLT, learning and delayed recall were impaired in the PTSD group ($p=0.004$ and 0.002, respectively); but after controlling for learning, they found that the group difference disappeared on all recall measures. Interestingly, when depression was controlled, all the group differences on CVLT measures disappeared. Among other neuropsychological tests, only DS Backward was impaired in the PTSD group with strong effect size ($p=0.007$; $d=-1.08$), whereas DS Forward and Paced Auditory Serial Addition Test score results were not significant. The authors concluded that depression plays an important role in causing memory impairment in PTSD.

Although all studies in this group were positive, memory impairment was not present after controlling for depression and learning; however, there was evidence of attentional impairment in this population (Table 3).

Studies of Undergraduates

There were only two studies of undergraduate volunteers with PTSD, and these have conflicting results. The age range of subjects is from 19 to 22 years, with no specific duration of PTSD symptoms.

Twamley et al.[50] compared students with PTSD (N=38) versus students with trauma and without PTSD (N=105) and without trauma (N=87). They did not find significant differences in attention and executive function of participants with history of trauma, with or without PTSD. They suggested that college students with history of trauma can be resilient to its deleterious effects on cognition, irrespective of PTSD.

In another study, Leskin et al.[51] compared students with PTSD (N=19) with volunteers without PTSD with high history of trauma (N=15) and low history of trauma (N=18). They did not find significant cognitive impairments on more conventional neuropsychological tests such as the Trail-Making and Wisconsin Card-Sorting Test. However, on the Attentional Network Task, although attention was seen to be normal, executive dysfunction was noted in individuals with PTSD. The authors concluded that executive dysfunction is probably related to PTSD and dopamine irregularities.

In general, sufficient data are lacking in this group of studies; and they do not show any significant trend in cognitive impairment (Table 3).

Studies of Survivors of Natural Disaster

There were two studies of survivors of natural disaster, and both were outside the United States. The age range of subjects is between 27 and 42 years, and time since disaster is between 9 months and 4 years.

In one of the few studies that tested cognitive function before and after trauma, Parslow et al. tested a large cohort of survivors of an extensive bush fire in Australia in 2003.[52] They compared those with PTSD (N=38) with those with subthreshold PTSD (N=606) and no PTSD (N=955) after a mean duration of 9 months posttrauma. Significant impairment was found in attention on Digit Span Backward ($p<0.05$; $d=-0.10$, $r=-0.05$); Memory on CVLT ($p<0.001$; $d=-0.12$, $r=-0.06$), and executive function on the Symbol Digit Modalities Test ($p<0.05$; $d=-0.08$, $r=-0.04$); but the effect size was weak. This cognitive impairment was associated with PTSD symptoms of reexperiencing and arousal, and these can cause impairment in verbal memory. However, poorer performance on pre-trauma neurocognitive measures was more strongly associated with posttrauma PTSD symptoms.

Eren-Koçak et al.[53] examined survivors of a 1999 earthquake in Turkey and divided them into those with current (N=11), past (N=14) and no PTSD diagnoses (N=18). After excluding subjects with depression, the authors did not find significant differences ($p>0.05$) on measures of visuospatial function, learning, and memory. However, they did notice executive dysfunction on Color Trail-Making Part 1 ($p=0.024$; $d=0.96$, $r=0.41$) and 2 ($p=0.10$; $d=1.09$, $r=0.47$), and impaired Verbal Fluency in animal names ($p=0.012$; $d=-0.93$, $r=-0.42$), with strong effect size. They suggest that deficits in prefrontal organization are present, especially in individuals with current PTSD.

Although sufficient data are lacking, there is some evidence of executive dysfunction in this group (Table 3).

Other Studies

In another study, Lindaeur et al.[54] examined cognition in relation to hippocampal volume in a group of police officers with (N=12) or without PTSD (N=12), who had experienced trauma. The authors did not find significant impairment in attention, learning, and memory ($ps>0.05$) in officers with PTSD. They suggested that memory impairment in PTSD is not related to hippocampal size.

DISCUSSION

In this review, we included results from studies that compared cognitive impairment in individuals with chronic PTSD and individuals with history of trauma. Most studies were of veterans, and most studies found significant cognitive deficits. Strong evidence, especially in studies of veterans, refugees, and war victims, suggests that individuals with PTSD have poorer attention capability than individuals with a history of exposure to trauma but no PTSD. However, data regarding learning and executive dysfunction are conflicting, especially in non-veteran populations. Memory is the most commonly examined cognitive domain. It was examined in 18 studies in this review, but results have not been consistent regarding an association with PTSD, after controlling for confounding factors. Evidence for visuospatial impairment is negative. Cognitive impairment is positively correlated with severity of PTSD. Studies of abused individuals show conflicting results in most cognitive domains.

Most studies of veterans and refugees/war victims with PTSD that examined attention found it to be significantly impaired (seven studies). Interestingly, both groups consisted mostly of men, with PTSD associated with war-related trauma. Almost all these studies excluded subjects with major head trauma, but the definition of head trauma was not well defined. Many also controlled for depression and substance abuse. There were only 4 negative studies of 13 on attention. Data on other groups are lacking. These results were not surprising, as problems in the frontal lobes and limbic system have been suggested in PTSD that can cause impaired attention.[36] For instance, abnormalities of the prefrontal cortex and heightened amygdala responses have already been demonstrated in these individuals.[24–26]

Overall data on learning show conflicting results, with seven positive and six negative studies. The only exception is in the case of veterans, for whom, as with attention, most studies found learning impairment with PTSD. Not all these studies controlled for attention when examining learning. Data on other groups are lacking. Interestingly, of three studies that looked into learning in elderly individuals with PTSD, two found it to be significantly impaired.[38,48] The authors suggested that learning is affected more in elderly individuals with PTSD than in younger individuals. Prefrontal changes, reduction in hippocampus, and increased glucocorticoid levels can all be implicated as causes of impaired learning in individuals with PTSD.[20,21,26,55]

Executive function is the second most common cognitive domain examined after memory, but the results are conflicting. Of 16 studies that looked for executive dysfunction in individuals with PTSD, only 9 were positive. There seems to be some evidence of executive impairment in survivors of natural disaster, but more studies need to confirm this finding.

Memory was examined in 18 studies, and findings in 12 of these were negative. Researchers did not find significant memory impairment in PTSD subjects when they compared them with a control group with history of trauma and after controlling for depression, learning impairment, and substance abuse. Although most subjects were young adults, two of three studies of elderly subjects were also negative after controlling for confounding factors.[41,48] Unlike studies of attention and learning, most negative studies were of veterans and refugee/war victims. In other groups the results were conflicting. It seems that memory problems associated with PTSD are likely related to deficits in attention and learning. Trauma, depression, and substance abuse also play a major role; but association only with PTSD is lacking in this review.

Visuospatial impairment was not found to be associated with PTSD in 9 of 10 studies that examined this aspect. Most studies were of veterans, and all were negative.

A total of 12 studies looked into the effects of severity of PTSD symptoms on cognitive impairment; 9 found some type of correlation with severity of these symptoms and cognitive impairment.

We calculated the effect sizes of the significant associations observed in these studies. Most associations had a medium-to-strong effect size, whereas a weak effect size was observed in a few non-veteran studies. It appears that the effect sizes were not related to a particular cognitive domain but may be related to the initial insult (war trauma being stronger than other traumatic events).

This review has several limitations. We included only articles published in English. Our biggest limitation is the heterogeneity of this research in study design, method, analysis, and interpretation of results. This heterogeneity made it impossible to combine results (i.e., in a meta-analysis) in any meaningful way. Although not all studies accounted for depression or substance abuse, we included results after these confounding factors were controlled for whenever available. Also, there is significant overlap between neuropsychological tests and cognitive domains they examine. Different studies used the same test for one or more than one cognitive domain. Therefore, we cannot be very specific with our results and their implications. We did not divide cognitive domains into their subtypes (e.g., memory was not divided into explicit, implicit, verbal or nonverbal memory). Most subjects in these studies were adults, and their results cannot be generalized to children or elderly subjects, who are more vulnerable to cognitive impairment. We included only studies that had a comparison group exposed to trauma, and that could have had a major effect on our results. We expect a much stronger association of cognitive impairment with PTSD in comparison with a non-traumatized group and without accounting for confounding factors like depression and substance use. Unfortunately, duration of PTSD was not usually considered in most of these studies. Many did not account for medication use or severity of traumatic brain injury that can affect cognition. Because low intelligence and low premorbid cognitive functioning have been suggested to increase vulnerability to PTSD,[13–17] they can have confounding effects on the association between PTSD and cognitive impairment as well.

CONCLUSION

Posttraumatic stress disorder is associated with cognitive impairment, particularly in veterans when compared with individuals with history of trauma. Severity of PTSD symptoms is positively correlated with this impairment. More longitudinal follow-ups are needed in the elderly population to examine the effects of duration of PTSD on cognition, after controlling for confounding factors like trauma, mood disorders, substance abuse, medication use and traumatic brain injury.

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