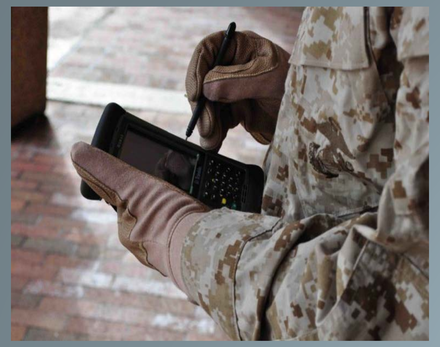

Development of an Objective, Functional Biomarker of Invisible Wounds of War for Use by Providers

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Abstract

Post deployment stress is marked by high rates of post-traumatic stress, depression, insomnia, and other mental health conditions that may go undiagnosed and therefore untreated. In the military, there is often under-reporting or over-reporting of symptoms indicative of mental or physical health problems associated with impaired performance. Assessments based on self-reported symptoms are not always effective in detecting underlying psychological conditions or problems. This study examined the potential for using computerized neurocognitive tests (CNTs) as an objective biomarker of functional impairment in a functioning, non-clinical, military population in order to complement subjective reporting of symptoms. Although, extensive neuropsychological testing can be performed for research purposes, this is often difficult in clinical practice as there are relatively few neuropsychologists; time and cost is often prohibitive, and traditional measures may only detect severe impairment. CNTs using precise speed and accuracy measures hold the promise of being more sensitive, as well as being more easily disseminated and utilized in a variety of healthcare settings. This research aimed to determine if neurocognitive functioning was associated with emotional and somatic distress in a sample of combat veterans. Differences for those with and without significant symptoms of PTSD, Depression, Insomnia, and Anger were compared across seven neurocognitive tests. Sensitivity and specificity of the tests were also determined. Medium to small effect sizes were found on cognitive performance for all psychological factors. Results suggest that the CNT provided a reliable and sensitive measure that has the potential for being utilized by clinicians for initial diagnosis, treatment disposition, and potentially assessing improvement and return to work determinations.

Introduction

Currently, there are no standardized, objective assessments or biomarkers available for predicting or determining diagnostic cut-offs for psychological conditions or problems such as PTSD, Depression, Insomnia, Anger, or post-concussive symptoms. CNT data was collected from active duty personnel using the Defense Automated Neurobehavioral Assessment (DANA). DANA is a CNT that was developed for the Department of Defense (DoD) as a clinical decision support tool for assessing neurobehavioral functioning both in-field and in-clinic. This research investigates the general assumption that various risk factors (PTSD, Depression, Insomnia, anger, pain, etc.) lead to significantly slower and less accurate (throughput) performance on cognitive tests. DANA's primary purpose is to assist providers in determining current level of cognitive functioning and to track recovery over time. This study analyzed DANA's ability to operate as an objective neurocognitive biomarker for cognitive impairment that is associated with PTSD, Depression, Insomnia, Anger, and post-concussive symptoms (3+ or 0-1). The study also determined the sensitivity and specificity of DANA neurocognitive measures to discriminate the accurate diagnosis for this population.

Question 1: Do CNT tests or composite scores correspond to diagnostic cut-offs for PTSD, Depression, Insomnia, Anger, or post-concussive symptoms for 0-1 or 3 or more concussions?

Question 2: Which CNT tests and composite scores are most closely associated with diagnostic cut-offs for PTSD, Depression, Insomnia, Anger, or post-concussive symptoms for 0-1 or 3 or more concussions?

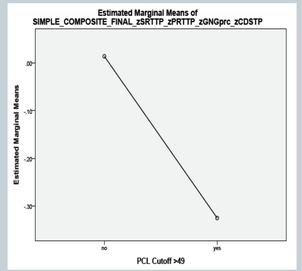
Methods

DANA Standard military version CNT was administered on hand-held devices to 646 active duty service members from the 2nd Marine Expeditionary Force. The battery included assessments for emotional distress (PCL-m, PHQ-8, anger); postconcussive symptoms (based on a revised NSI-22; insomnia (PSQI), and neurocognitive functioning (Simple Reaction Time – SRT; Procedural Reaction Time – PRT); Go-NoGo (GNG), Spatial Rotation Discrimination (SRD), Code Substitution Learning (CDS), Code Substitution Delayed (CDD), and Sternberg Running Memory (STN). Following IRB-approved consenting of participants, testing took about 40 minutes. Subjects were generally between the ages of 19-22, and were either Never Deployed, Previously Deployed (more than one year prior to testing), or Recently Deployed (within six months of testing). Throughput (TP) was calculated for each neurocognitive measure (number of correct responses in one minute). A Simple Composite Score based on four simple reaction time tests was calculated by averaging the z scores of SRT TP; PRT TP; GNG% and CDS [(zSRT TP + zPRT TP,+ zGNG% + zCDS) / 4]. A Complex Composite Score was the average of the z scores for the three more cognitively tasking tests SRD TP; CDD %; and STN% [(zSRD TP + zCDD % + zSTN%) / 3]. The Total Composite Score was the average of the two composite scores [(Simple + Complex) / 2]. Cut-offs and measures for each symptom were as follows: PTSD (PCL-m >49), Depression (PHQ-8 >10), Anger (DSI >1SD), and insomnia (PSQI>11).

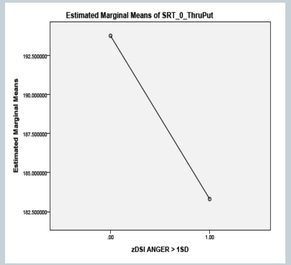
Results

General Linear Modeling was used for between-group ANOVA to compare groups above and below the diagnostic cut-off for each symptom. Generalized Linear Modeling (with Wald statistic and Robust Estimator) was utilized to confirm significance when groups were associated with unequal variances per Levene's test of homogeneity. Medium to small effect sizes were found on CNT performance for all psychological factors. Receiver Operating Characteristic (ROC) curve analyses was done to measure sensitivity and specificity of the measures for the different diagnostic cut-offs. See table and figures for details. The z score for SRT TP showed significant differences for all factors. The Simple Composite was more sensitive than the Complex Composite Score overall. Details of the findings are presented.

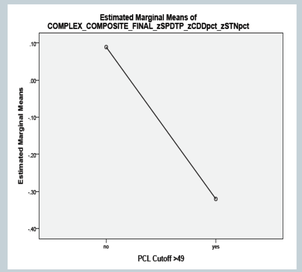
Simple Composite Score for **PTSD**
(F= 7.342, P=.007, η^2_p=.018)



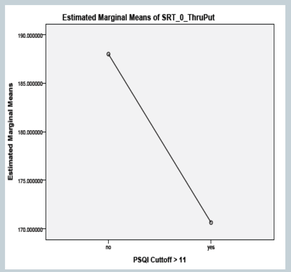
Simple Reaction Time Throughput for **ANGER** (F=11.795, P=.001, η^2_p=.018)



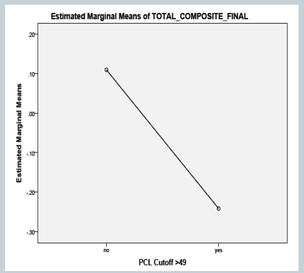
Complex Composite Score for **PTSD**
(F= 10.878, P=.001, η^2_p=.037)



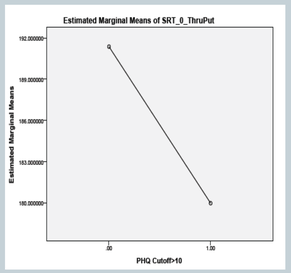
Simple Reaction Time Throughput for **INSOMNIA**
(F= 6.207, P=.013, η^2_p=.017)



Total Composite Score for **PTSD**
(F= 10.190, P=.002, η^2_p=.036)



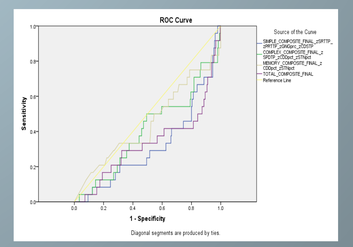
Simple Reaction Time Throughput for **DEPRESSION**
(F= 7.740, P=.006, η^2_p=.018) (Wald=5.458, DF=1, P=.019



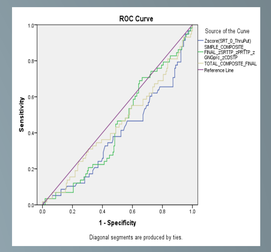
Sensivity and Specificity of zSRT_TP and Total Composite Scores

Diagnostic Cut-Off	Measure	Level	Sensitivity	Specificity
For 3 plus lifetime concussions	Total Composite	½ SD below mean	.70	.80
	Total Composite	1 SD below mean	.87	.93
For Insomnia (ISI>12)	zSRT_TP	½ SD below mean	.66	.84
(Total Composite Score was not predictive)	zSRT_TP	1 SD below mean	.79	.91
For PTSD (PCL>49)	Total Composite	½ SD below mean	.64	.90
	Total Composite	1 SD below mean	.92	.96
DEPRESSION (PHQ>10),	zSRT_TP	½ SD below mean	.63	.73
(Total Composite Score was not predictive)	zSRT_TP	1 SD below mean	.75	.86
For >MODERATELY HEAVY COMBAT EXPOSURE	zSRT_TP	½ SD below mean	.70	.83
(Total Composite Score was not predictive)	zSRT_TP	1 SD below mean	.82	.91
	zSRT_TP	½ SD below mean	.70	.83
	zSRT_TP	1 SD below mean	.82	.91
For Anger -Somatic (Neurobehavioral Symptom Inventory) > 1SD	zSRT_TP	½ SD below mean	.64	.77
(Total Composite Score was not predictive)	zSRT_TP	1 SD below mean	.77	.88
For Balance Symptoms (Neurobehavioral Symptom Inventory) > 1SD	zSRT_TP	½ SD below mean	.64	.74
(Total Composite Score was not predictive)	zSRT_TP	1 SD below mean	.80	.87

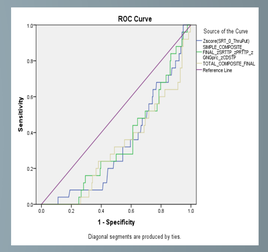
ROC curves for >3 lifetime concussions (Simple and Total Composite Scores were significant to <.01)



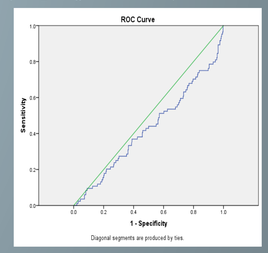
ROC curves for Insomnia (ISI >12)
(zSRT_TP was significant to <.05)



ROC curves for PTSD (PCL-M>49)
(zSRT_TP, Simple, and Total significant to <.05)



ROC curves for Depression (PHQ-8 >10)
(zSRT_TP significant to <.05)



ROC curves for Anger (NSI >1SD)
(zSRT_TP significant to <.05)