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ANAM4 TBI Reaction Time-Based Tests Have Prognostic Utility for Acute Concussion

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ABSTRACT The Concussion Restoration Care Center has used the Automated Neuropsychological Assessment Metrics version 4 Traumatic Brain Injury (ANAM4 TBI) battery in clinical assessment of concussion. The study's aim is to evaluate the prognostic utility of the ANAM4 TBI. In 165 concussed active duty personnel (all ultimately returned to duty) seen and tested on the ANAM4 TBI on days 3 and 5 (median times) from their injury, Spearman's ρ statistics showed that all performance subtests (at day 5) were associated with fewer days return-to-duty (RTD) time, whereas concussion history or age did not. Kruskal–Wallis statistics showed that ANAM4 TBI, loss of consciousness, and posttraumatic amnesia were associated with increased RTD time; ANAM4 TBI reaction time-based subtests, collectively, showed the largest effect sizes. A survival analysis using a Kaplan–Meier plot showed that the lowest 25% on the reaction time-based subtests had a median RTD time of 19 days, whereas those in the upper 25% had a median RTD time of approximately 7 days. Results indicate that until validated neurocognitive testing is introduced, the ANAM4 TBI battery, especially reaction time-based tests, has prognostic utility.

INTRODUCTION

In August 2010, providers at the Concussion Restoration Care Center (CRCC) began using the Automated Neuropsychological Assessment Metrics version 4 Traumatic Brain Injury (ANAM4 TBI) battery in clinical assessment of its patients as they recovered from concussion/mild TBI (mTBI). A concussion/mTBI is a traumatic brain injury having normal structural imaging (if imaging is done), a loss of consciousness (LOC) of no more than 30 minutes, and/or alteration of consciousness (AOC) or post-traumatic amnesia (PTA) of no more than 24 hours.¹ Between August 2010 and December 2011, the ANAM4 TBI battery, a computerized neurocognitive test was administered to over 800 patients at the CRCC.^{2,3} The CRCC use of ANAM4 TBI is in a moni-

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toring paradigm, administered on intake and periodically across re-evaluation days to support assessment of injury progression and resolution. Although used at the CRCC with anecdotal support from the CRCC providers, the use of ANAM4 TBI battery as a prognostic (predictive) tool for time to return to duty (RTD) has not been empirically evaluated and there are differences in recommendations for its optimal use.⁴ The study reported here is an examination of the ANAM4 TBI battery as a prognostic tool.

DoD Instruction (DoDI 6490.11, dated Sept. 18, 2012), the document outlining U.S. Department of Defense (DoD) care for in-theater concussion care, targets cognitive testing as a focus issue.¹ There is accumulating literature addressing the utility of neurocognitive testing for screening, diagnosis, and RTD evaluation following concussion in military settings. The Military Acute Concussion Evaluation (MACE), a DoD-developed tool, has some degree of sensitivity and specificity as a screening tool for field-level medical personnel when used within 12 hours postinjury. This conclusion was drawn from a population of military personnel from Iraq and using a standard cutoff score of <25, which yielded 20% sensitivity for all cases and 88% specificity.5 At longer durations postinjury, such as within 72 hours, the ANAM4 TBI battery may have added value in assisting diagnosis of concussion, delivering added value above the MACE. However, beyond 1 week, ANAM4 TBI utility as a diagnostic tool is severely limited.^{6,7} The ANAM4 TBI is being used with some success in forward deployed settings to evaluate RTD following concussion.4

CRCC RTD Criteria

In accordance with established clinic practices, 3 main criteria are used in the determination of whether and when a patient returns to regular military duty following diagnosis of concussion (unpublished CRCC brief overview OCT 2011, unreferenced).

- (1) Symptom resolution: Patient's concussion-related symptoms (e.g., headache) have resolved.
- (2) Stress test: Patient must also be symptom-free following an exertion stress test. At the CRCC, this is conducted by increasing the patient's heart rate to 65%–85% of maximum heart rate for a period of 2 minutes. Patients are asked to run on a treadmill while wearing standard issue body armor (a flak tactical vest with ballistic resistant plates, weighing approximately 40 lb). Patients are asked to report symptoms at the conclusion of the test. Based on the CRCC database records, the exertion stress test has 16.9% failure rate (i.e., positive report of symptoms).
- (3) ANAM4 TBI simple reaction time (SRT) subtest: Patient's ANAM4 TBI SRT score in milliseconds is tracked. Generally, a score <300 ms serves as an acceptable criterion indicating neurocognitive recovery.

These criteria are recorded in patient records with each assessment and weighed along with the providers' clinical assessment in the measure of fitness (unpublished CRCC brief overview OCT 2011, unreferenced).

Clinical Questions

As part of developing an individualized treatment plan and monitoring its progress, the CRCC clinicians use the ANAM4 TBI to evaluate patient neurocognitive status. A key indicator in this use of ANAM4 TBI is the SRT subtest. The aim of this study was to improve clinical practice and develop better treatment plans at the CRCC at Camp Leatherneck, Afghanistan, through concerted evaluation of the ANAM4 TBI. The study was approved by the Joint Combat Casualty Research Team as a Performance Improvement Project. The focus of this project is to address the following questions: Does the SRT test, as currently used, act as the best neurocognitive indicator of recovery trajectory available to the CRCC clinicians within the ANAM4 TBI? Does performance on SRT at presentation predict a patient's recovery time? Does information such as age, self-reported blast exposure, prior concussion history, reported LOC, or PTA provide equally relevant (and easier to access) prognostic information?

METHODS

This study received institutional review board (IRB) approval from the U.S. Army Medical Research and Material Command, including a waiver of informed consent (IRB number M-10166). This study followed guidelines detailed in the U.S. Central Command (CENTCOM) Human Research Protection Program.

Record Screening

CRCC records from August 2010 to November 2011 were screened from the CRCC patient database for the following

criteria: diagnosed with concussion by a CRCC provider, seen at the CRCC within 1 week of injury, no prior concussions treated at the CRCC, eventual RTD, and no reported musculoskeletal injuries that would hinder performance on the test. Patient records were only included if there were at least 2 administrations of the ANAM4 TBI within a week following the injury (tested at days 3 and 5 postinjury; median times) and SRT scores for the first and the second administration showed SRT number correct response rate >80% (33 out 40 trials). Researchers surmised that 80% number correct responses to a simple, single response test had adequate face validity, indicating the patient could understand and execute directions while exercising sufficient motor and response control (9 records were excluded for this reason). From an initial set of 816 patients records available, 165 records remained for analysis after applying exclusion/inclusion criteria. The majority of records not included in analysis were from patients who were cleared for RTD at the initial assessment, yielding no second assessment to use in this evaluation and to inform the objective of this study.

Instrument

The ANAM4 TBI is a computer-based neuropsychological assessment consisting of 9 tests. The first 2 subtests reflect sleep and mood rather than neurocognitive ability and are outside the scope of this report. Those subjective scales are followed by 7 neurocognitive performance-based subtests (in order): SRT, code substitution (CDS), procedural reaction time (PRO), mathematical processing (MTH), matching-to-sample (M2S), CDS delayed (CDD), and simple reaction time 2 (SR2).

Simple Reaction Time

The subject clicks the left mouse button (single-button response) when an asterisk stimulus is presented on the screen. This stimulus is presented at different intervals for 40 trials and reaction time for each trial is recorded. This subtest assesses reaction time.

Code Substitution

A static display of digits 1 through 9 appears in a row at the top of the screen with a unique symbol above each digit. A series of 72 probes appears at the bottom of the screen, each showing a pairing of a single digit and symbol in the same fashion as the static display at the top of the screen. The subject uses the left mouse button to indicate if the pairing in the probe matches a pairing in the static display above and the right mouse button if the pairing in the probe does not match a pairing in the static display above. Subjects are informed that the static display will be referenced in a later task, but the display will not be represented. This subtest assesses visual search, sustained attention, and encoding.

Procedural Reaction Time

A series of single digits (2, 3, 4, or 5) is presented in 32 trials. The subject uses the left mouse button to indicate the digit is "low" (2 or 3) or the right mouse button to indicate the digit is "high" (4 or 5). This subtest assesses reaction time and processing efficiency associated with following a simple set of mapping rules.

Mathematical Processing

A series of 3 single-digit operator arithmetic mathematical equations (e.g., "3 + 4 - 1") is presented in 20 trials. The subject uses the left mouse button to indicate the answer is less than 5 or the right mouse button if the answer is greater than 5. This subtest assesses basic computational skills, concentration, and working memory.

Matching-to-Sample

A series of 4×4 matrices with cells in a 2-colored pattern appears in 20 trials. Following each stimulus, a pair of slightly different 4×4 matrices appears side-by-side. The subject uses the left or right mouse button to indicate which matrix in the pair matches the previous stimulus. This subtest assesses spatial processing and visuospatial working memory.

CDS Delayed

A series of 36 probes appears in the same fashion as the CDS subtest. The subject responds in the same fashion as in the CDS subtest using memory of the static display from the CDS subtest, presented approximately 10 minutes before and not represented.

Simple Reaction Time 2

A subtest identical to the SRT subtest.

ANAM4 TBI Administration at the CRCC

The ANAM4 TBI was administered to the CRCC patients following initial physical examination and intake by Navy Hospital Corpsmen and before examination by a physician. The battery was administered by the Corpsmen in a quiet room without auditory or visual distractions on individual laptops with a computer mouse, provided to the CRCC by the ANAM testing office. The CRCC personnel instructed patients to give an honest effort and ensured that patients were familiar with the mouse and computer setup. After the battery was completed, Corpsmen escorted patients to the CRCC waiting area for a short period before seeing the physician. Physicians reviewed the ANAM SRT score as part of the clinical process.

Data Analyses

In typical use of ANAM4 TBI, reaction time and accuracy are combined into a single outcome measure of "throughput." Throughput is a speed–accuracy product reflecting performance across both dependent variables.⁸ Throughput is derived from number correct divided by mean reaction time. Throughput was selected as the key variable to remain metric consistent with previous published literature on the ANAM4 TBI and to allow comparison between subtests.^{6,7,9}

Data were processed using Microsoft Office Excel and Access 2007. Analyses were conducted on Microsoft Office Excel 2007 and StatView software (SAS Institute, Cary, North Carolina). Descriptive statistics are presented for a variety of demographic measures, number of reported concussions in the past 12 months (excluding number of concussions 90 days before injury), and number of days between injury and RTD. Although the skew of the throughput data was within normal range, we used a conservative approach of Spearman's ρ correlation coefficients, a nonparametric statistic that is insensitive to outliers, followed-up with z-score tests to determine whether ρ values were statistically significantly different from each other. Nonparametric survival analyses using Kaplan-Meier plots and Kruskal-Wallis statistics were used to assess differences in time to RTD based on subtest performance and categorical factors.

RESULTS

Most records were from patients who were male (99%) and Marines (78%). 20% of records were from Army personnel, and 2% were from Navy personnel. Patients ranged from 19 to 41 years old, with a median age of 22 years old (22%); most were under 25 years old (78%). The most represented rank was E-3 (43%). Approximately 146 (89%) patients reported no prior concussions in previous 12 months; 15 (10%) reported 1 concussion, and 2 (1%) reported 2 to 4 concussions within the previous 12 months. 100 (61%) patients reported no blast exposure in the previous 12 months; 27 (15%) reported a single blast exposure event; 38 (23%) reported more than a single blast exposure. Improvised explosive device blast exposure was the most common mechanism of injury, accounting for nearly 86% of injuries. Other leading causes of injury were rocket propelled grenades (2%) and vehicle accidents (2%). Blunt head trauma from objects falling or from martial arts sparring accounted for the remaining 10%. Approximately 76% of all concussions occurred when the patient was in a vehicle. Approximately 16% of records listed co-occurring injuries including post-traumatic headache, minor shrapnel wounds, lower extremity sprains, and neck and back sprains. The sample did not include patients held back from duty because of co-occurring injuries. Approximately 51% reported no LOC at the time of injury, 40% reported LOC following injury, and 9% were uncertain as to whether they had lost consciousness.

Exploratory data analysis of days to RTD shows a trend toward a positive-skew in the distribution (skewness = 1.4) with corresponding differences in the mode (7 days), median (10 days), and mean (12 days) to RTD. All subjects in the sample completed care; none were evacuated from theater because of concussion. Descriptive statistics for each subtest are shown in Table I. ANAM4 TBI subtest throughput

Subtest	Mean	SE	Median
Session 1			
SRT	145.76	4.993	146.56
CDS	41.49	1.06	41.76
PRO	70.27	2.15	74.15
MTH	16.14	0.49	15.40
M2S	23.32	0.73	22.84
CDD	31.51	1.16	29.58
SR2	134.62	5.51	133.91
Session 2			
SRT	175.35	6.28	203.34
CDS	43.60	1.05	43.90
PRO	83.25	2.43	92.94
MTH	17.70	0.81	16.04
M2S	27.62	0.85	27.43
CDD	37.87	1.31	36.46
SR2	167.4	6.71	208.01

TABLE I.Postinjury ANAM4 TBI Throughput Descriptive
Statistics (N = 165)

variables tended to be positively skewed at first administration and negatively skewed at second administration. RTD was also a positively skewed variable.

Relationship Between ANAM4 TBI Subtests, Clinical Information, and RTD

For sessions 1 and 2, Spearman's ρ correlation coefficients were calculated for each performance subtest, age, blast exposures, and concussion history (last 12 months and before 12 months). Results show that performance on each ANAM4 TBI subtests and number of days RTD significantly covary at both the first and second postinjury ANAM4 TBI, p values < 0.03. Of greatest note, the second administration of the SR2 subtest correlates with days to RTD, ρ (corrected for ties) = -0.52, p < 0.0001, as does the second administration of the SRT subtest, ρ (corrected for ties) = -0.50, p < 0.0001, and second administration of the PRO subtest, ρ (corrected for ties) = -0.50, p < 0.0001. Spearman's ρ coefficients showed no statistically significant relationship between age, self-reported blast exposures, concussion history in both 12 months before injury and before a year before injury are documented in Table II, which is consistent with similar findings.⁹

Assuming independent samples, *z*-score tests revealed the highest magnitude ρ statistic, session 2 SR2, does in fact differ significantly from the next highest magnitude ρ statistics, session 2 SRT and session 2 PRO: z = 2.29, p < 0.05, and z = 2.54, p < 0.05, respectively. However, session 2 SRT and session 2 PRO do not differ, z = 0.25, p = ns.

To evaluate whether LOC, PTA, or mechanism of injury factors related to RTD time, Kruskal–Wallis tests for *K*-independent samples were performed (as these were nominal rather than ordinal variables): LOC (yes, no, uncertain), H = 7.86, df = 2, p < 0.05; PTA (yes, no, uncertain), H = 6.935, df = 2, p < 0.05; Mechanism of Injury (Improvised explosive device, motor vehicle accident, other combat, other blunt trauma), H = 0.95, df = 3, p = ns.

TABLE II.	ANAM4 TBI Performance Subtests at Sessions 1
and 2, and	Concussion History and RTD Time $(N = 165)$

ANAM4 TBI Subtest	ρ^{a}	z-Value ^a
Session 1		
SRT	-0.37***	-4.37
CDS	-0.23**	-2.91
PRO	-0.35***	-4.49
MTH	-0.31***	-3.92
M2S	-0.32***	-4.14
CDD	-0.18*	-2.25
SR2	-0.39***	-4.99
Session 2		
SRT	-0.50***	-6.42
CDS	-0.43***	-5.55
PRO	-0.50***	-6.40
MTH	-0.31***	-3.91
M2S	-0.37***	-4.68
CDD	-0.39***	-5.00
SR2	-0.52***	-6.61
Age/Concussion History		
Age, Years	-0.07	-0.94
No. of Blast Exposures	-0.10	-1.26
No. of Concussions 12 Months Prior	-0.07	-0.93
No. of Concussions Before 12 Months	-0.01	-0.73

*p < 0.05; **p < 0.01; ***p < 0.0001. ^aCorrected for ties.

Clinical Utility of SRT, SR2, PRO Subtests, LOC, and PTA

The clinical utility of the significant findings was evaluated. The 3 ANAM subtests that accounted for the greatest amount of variance, LOC, and PTA were selected for further evaluation. To compare ANAM4 TBI subtests, LOC, and PTA, each patient's ANAM4 TBI scores were categorized according to quartile ranking. A Kruskal–Wallis test for *K*-independent samples were performed for session 2 SR2, H = 47.207, df = 3, p < 0.0001; session 2 SRT, H = 52.02, df = 3, p < 0.0001; and session 2 PRO, H = 54.53, df = 3, p < 0.0001. Using the H statistic to calculate effect sizes for session 2 SR2, session 2 SRT, session 2 PRO, LOC, and post-traumatic headache revealed the following: session 2 SR2, w = 0.535; session 2 SRT, w = 0.561; session 2 PRO, w = 0.575; LOC, w = 0.218; and PTA, w = 0.205. Kruskal–Wallis tests for the ANAM subtests showed larger effect sizes than LOC and PTA.

Survival curves with a Kaplan–Meier plot (shown in Figs. 1 and 2) were constructed for session 2 SRT, session 2 SR2, session 2 PRO, LOC, and PTA to examine the performance patterns associated with these quartiles over time to RTD. Visual inspection of survival plots and of median times to RTD for each patient subgroup (shown in Table III) showed that for all 3 ANAM4 TBI subtests, the principal difference was between the poor performers (0%–25%) and top performers (76%–99%). For example, on the session 2 SR2 subtest, poor performers took a median time of 19 days to RTD. Meanwhile, top performers took a median time of 7.5 days to RTD. A visual inspection of the survival plot and median times to RTD for LOC showed a difference of 3 days

Kaplan-Meier Cum. Survival Plot for: Session 2 Simple Reaction Time (SRT)



Kaplan-Meier Cum. Survival Plot for: Session 2 Simple Reaction Time 2 (SR2)



Kaplan-Meier Cum. Survival Plot for: Session 2 Procedural Reaction Time (PRO)



FIGURE 1. Kaplan-Meier cumulative survival plot showing percentage of patients in care as a function of days since injury, broken down by performance (by percentile ranking) on either the SRT (Top), SR2 (Middle), or PRO (Bottom) ANAM4 TBI subtests.

for median time to RTD between groups (NO LOC, 8 days; YES LOC, 11 days). Patients reporting uncertainty about LOC took a median of 10 days to RTD. Logrank tests for ANAM and LOC Kaplan–Meier plots were statistically significant, p < 0.01. Median RTD time for those with PTA (11 days) was significantly longer than for those without PTA (8 days), the logrank test for PTA was not statistically significant, p = ns.

To streamline the current use of the ANAM 4 TBI battery and promote an evidence-based approach to its application at



Kaplan-Meier Cum. Survival Plot: Loss of Consciousness (LOC)

FIGURE 2. Kaplan–Meier cumulative survival plot showing percentage of patients in care as a function of days since injury, broken down by self-reported LOC (Top) and PTA (Bottom).

TABLE III.	Median RTD, Categorized by Performance Quartile
on Se	ected Session 2 ANAM4 TBI Subtests ($N = 165$)

ANAM4 TBI Subtest	0%-25%	26%-50%	51%-75%	76%-99%
SRT	19 Days	10 Days	8 Days	8 Days
SR2	19 Days	10 Days	7 Days	8 Days
PRO	19 Days	10 Days	7 Days	8 Days

the CRCC, a proposed guide is shown in Figure 3. This proposed guide was developed using the RTD times from Figure 3 in combination with the range of scores based on quartiles. For example, on session 2 PRO subtest, those individuals in the lowest 25% scored lower than 58. The median time for those individuals to RTD according to

ANAM Subtest	Score Ranges (Throughput)		
Session 2 SR2	< 83	83-239	> 239
Session 2 SRT	< 98	98-246	> 246
Session 2 PRO	< 58	58-92	> 92
Median Time Return to Duty	19 days	10 days	8 days

*Applicable when patients take the ANAM4 TBI battery the first time (Session 1) within approximately 96 hours following injury and take the test a second time (Session 2) within one week following injury.

FIGURE 3. Proposed clinical guide for the use of the ANAM4 TBI.

the lower portion of Figure 3 was 19 days—nearly twice the median RTD time of 10 days seen within the remainder of the cohort.

DISCUSSION

A sample of 165 patients diagnosed with concussion/mTBI were administered the ANAM4 TBI battery twice within a week of injury as part of routine clinical protocol. Analyses of ANAM4 TBI subtest throughput indicate that on all subtests and across the first 2 administration sessions of this battery patients' performance corresponded with time to RTD and ANAM4 TBI at second administration showed greatest utility as a prognostic indicator. Among the tests, SR2 showed the strongest association in both first and second administrations. Furthermore, those individuals who performed most poorly (i.e., lowest 25%) on the SR2 at second administration took a median of 19 days to recover, whereas the top 25% recovered in a median time of 7 to 8 days. The reaction timebased ANAM4 TBI subtests outperformed LOC as a predictor of time to RTD. These results support continued use of the ANAM4 TBI battery as a prognostic tool for RTD time in concussion/mTBI patients at the CRCC. It is important to note that this use of the repeated ANAM testing at the CRCC as a surveillance tool is unique and that results suggest the second administration of the ANAM4 TBI is of greatest utility as a prognostic indicator.

To our knowledge, this is the first study to date showing that ANAM4 TBI has utility as a prognostic tool for RTD following concussion in a military setting. Results from SRT tests are consistent with findings from other populations,^{9–13} showing that an elevated reaction time was a marker consistent with concussion in the right clinical setting. It is important to note that SRT tests and the related construct and vigilance are also sensitive to other factors such as practice,¹⁴ fatigue, or environmental factors.^{15,16} SRT tests are valuable, provided fatigue and environmental factors are accounted for before testing. Practice effects are present but minimal for SRT and may be attributable to task learning; examining the second postinjury ANAM4 TBI should help mitigate any confounding effects of practice. This study corroborates findings that PRO is sensitive to concussion.^{6,9} Both SRT/SR2 and PRO reflect reaction time with minimal cognitive processing demand. Other computer-based tests in ANAM4 TBI and in other batteries can be expected to demand a greater level of processing and may correspond to RTD in more complex relations, when incorporating education history and other individual differences. These relational models are not yet established and available.

Results from demographic and history considerations independent of ANAM4 TBI performance suggest that clinical information such as a lifetime history of concussion, recent blast exposures, or age has limited clinical utility compared with neurocognitive testing-based reaction time. Concussion history data are consistent with some, but not all, previous results from sports concussion literature on the cumulative effects of concussion. Prior research showed evidence that 1 or 2 previous concussions do not affect recovery on neuropsychological testing or symptom reporting.^{16,17} However, athletes with prior concussions are at statistically increased risk for a future concussion.¹⁸⁻²¹ Other research has shown that athletes with 3 or more previous concussions performed worse on verbal memory tests than athletes with fewer concussions.^{22,23} Given the majority of patients reported overall low lifetime history of concussion or blast exposure, a lack of significance is to be expected. Regarding negative findings associated with age, some research shows high school athletes might recover more slowly than university or professional athletes.²³⁻²⁶ Given that the age of the sample was post high school, the observed pattern of results is consistent with the literature.

Two anticipated results were findings that RTD time differed significantly for those individuals with a reported LOC or PTA. Research from sports concussion literature shows that LOC, among other factors, may predict longer recovery time.²⁷ Moreover, some head injury grading systems, such as that recommended by American Academy of Neurology, rely heavily on LOC to rate the severity of a concussion.^{28–30} Although significant, LOC does not appear to be as effective an indicator of time to RTD when compared to SRT. Even stronger is the evidence PTA is associated with injury severity and is associated with functional outcomes such delays in return to work and cognitive impairment.^{31–33} Although ANAM showed a stronger association, results reported here support the use of LOC or PTA as an indicator of severity in austere settings where extensive testing is limited.

Limitations

This study had limitations that must be considered, especially given the clinical impact of continued use of ANAM. The study's most notable limitation is that SRT was incorporated into the RTD criteria, leading to a potential for circular logic. This was addressed by using SR2 and PRO in the analysis (two measures not used in RTD determination). Future process improvements or research studies could further evaluate these limitations. Another limitation is sole use of postconcussive testing without use of baselines or normative data sets.34 Comparison to baseline or normative data was outside the scope of this project, but it may be worthy of follow-up investigation. A missing element in ANAM4 TBI is a measure of effortwe used a proxy for effort in this article. An additional follow-up study could examine more thoroughly relative differences in value (between subtests) and target opportunities to achieve efficiencies in testing by removing or replacing subtests that yield relatively less value. There is value from a clinical perspective in shortening or eliminating less useful testing. That focus was not pursued for this report because of a change that would have been required in the CRCC clinical practice to test those questions.

CONCLUSION

This study of 165 cases shows that computer-based testing is able to capture useable data that otherwise would have required over 80 hours of clinician time for test administration. The study shows computer-based testing can capture reaction time to millisecond-level accuracy unlike technician-based testing, which is typically limited to second-level accuracy. This work shows means for conducting empirics-based clinical practice performance improvement in a deployed setting, showing initial evidence for utility in practice that otherwise had not been shown. There are opportunities for improvements in computer-based testing, but evidence reported here shows value already realized in the current battery of tests, value that is scalable to very large populations such as that of the DoD. This report supports the CRCC clinician use of the SRT tests in their initial and follow-up assessments of concussion. As part of a broader neuropsychological exam, tests of reaction time have value and are consistent with processing speed assessment intended in DoDI 6490.11.

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REFERENCES

- Department of Defense: DoD Policy Guidance for Management of Mild Traumatic Brain Injury/Concussion in the Deployed Setting. Washington, DC, Undersecretary of Defense for Personnel and Readiness. Available at http://www.pdhealth.mil/tbi.asp; accessed April 23, 2013.
- Friedl KE, Grate SJ, Proctor SP, Ness, JW, Lukey BJ, Kane RL: Army research needs for automated neuropsychological tests: monitoring soldier health and performance status. Arch Clin Neuropsychol 2007; 22 (Suppl 1): S7–14.
- Reeves DL, Winter KP, Bleiberg J, Kane RL: ANAM genogram: historical perspectives, description, and current endeavors. Arch Clin Neuropsychol 2007; 22 (Suppl 1): S15–37.
- 4. Office of the Surgeon General: The DoD ANAM Program: A Critical Review of Supporting Documentation. Falls Church, VA, Neurocognitive Assessment Branch, Proponency Office for the Rehabilitation & Reintegration, Office of the Surgeon General, August 2011. Available at www .propublica.org/documents/item/268330-the-dod-anam-program-a-criticalreview-of; accessed December 5, 2012.
- Coldren RL, Kelly MP, Parish RV, Dretsch M, Russell ML: Evaluation of the Military Acute Concussion Evaluation for use in combat operations more than 12 hours after injury. Mil Med 2010; 175(7): 477–83.
- Coldren RL, Russell ML, Parrish RV, Dretsch M, Kelly MP: The ANAM lacks utility as a diagnostic or screening tool for concussion more than 10 days following injury. Mil Med 2012; 177(2): 179–83.
- Ivins BJ, Kane R, Schwab KA: Performance on the automated neuropsychological assessment metrics in a nonclinical sample of soldiers screened for mild TBI after returning from Iraq and Afghanistan: a descriptive analysis. J Head Trauma Rehabil 2009; 24(1): 24–31.
- Thorne DR: Throughput: a simple performance index with desirable characteristics. Behav Res Methods 2006; 38: 569–73.
- Kelly MP, Coldren RL, Parish RV, Dretsch MN, Russell ML: Assessment of acute concussion in the combat environment. Arch Clin Neuropsychol 2012; 27(4): 375–88.

- Luethcke CA, Bryan CJ, Morrow CE, Isler WC: Comparison of concussive symptoms, cognitive performance, and psychological symptoms between acute blast-versus nonblast-induced mild traumatic brain injury. J Int Neuropsychol Soc 2011; 17: 36–45.
- McCrea M, Prichep L, Powell MR, Chabot R, Barr WB: Acute effects and recovery after sport-related concussion: a neurocognitive and quantitative brain electrical activity study. J Head Trauma Rehabil 2010; 25(4): 283–92.
- Warden DL, Bleiberg J, Cameron KL, et al: Persistent prolongation of simple reaction time in sports concussion. Neurology 2001; 57: 524–6.
- Bleiberg J, Halpern EL, Reeves D, Daniel JC: Future directions for the neuropsychological assessment of sports concussion. J Head Trauma Rehabil 1998; 13(2): 36–44.
- Eonta SE, Carr W, McArdle JJ, et al: Automated Neuropsychological Assessment Metrics: repeated assessment with two military samples. Aviat Space Environ Med 2011, 82(1): 34–9.
- Murphy PJ: Fatigue Management During Operations: A Commander's Guide. Puckapunyal, VIC, Australia, Australian Defence Force Psychology Organisation and the Defence Science and Technology Organisation, 2002. Available at http://www.defence.gov.au/health/ about/docs/Fatigue_Management_Handbook.pdf; accessed December 5, 2012.
- Lowe M, Harris W, Kane RL, Banderet L, Levinson D, Reeves D: Neuropsychological assessment in extreme environments. Arch Clin Neuropsychol 2007; 22(Suppl 1):S89–99.
- Iverson GL, Echemendia RJ, Lamarre AK, Brooks BL, Gaetz MB: Possible lingering effects of multiple past concussions. Rehabil Res Pract 2012; 2012: 316575.
- Delaney JS, Lacroix VJ, Leclerc S, Johnston KM: Concussions during the 1997 Canadian Football League season. Clin J Sport Med 2000; 10(1): 9–14.
- Gerberich SG, Priest JD, Boen JR, Straub CP, Maxwell RE: Concussion incidences and severity in secondary school varsity football players. Am J Public Health 1983; 73(12): 1370–75.
- Guskiewicz KM, McCrea M, Marshall SW, et al: Cumulative effects associated with recurrent concussion in collegiate football players: the NCAA Concussion Study. JAMA 2003; 290(19): 2549–55.
- 21. Zemper ED: Two-year prospective study of relative risk of a second cerebral concussion. Am J Phys Med Rehabil 2003; 82(9): 653–9.
- 22. Iverson GL, Brooks BL, Lovell MR, Collins MW: No cumulative effects for one or two previous concussions. Br J Sports Med 2006; 40(1): 72–5.
- Collins MW, Lovell MR, Iverson GL, Ide T, Maroon J: Examining concussion rates and return to play in high school football players wearing newer helmet technology: a three-year prospective cohort study. Neurosurgery 2006; 58(2): 275–86.
- Field M, Collins MW, Lovell MR, Maroon J: Does age play a role in recovery from sports-related concussion? A comparison of high school and collegiate athletes. J Pediatr 2003; 142(5): 546–53.
- Lang DA, Teasdale GM, Macpherson P, Lawrence A: Diffuse brain swelling after head injury: more often malignant in adults than children? J Neurosurg 1994; 80(4): 675–80.
- Pellman EJ, Lovell MR, Viano DC, Casson IR: Concussion in professional football: recovery of NFL and high school athletes assessed by computerized neuropsychological testing-part 12. Neurosurgery 2006; 58(2): 263–74.
- Asplund CA, McKeag DB, Olsen CH: Sport-related concussion: factors associated with prolonged return to play. Clin J Sport Med 2004; 14(6): 339–43.
- Kelly JP, Rosenberg JH: The development of guidelines for the management of concussion in sports. J Head Trauma Rehabil 1998; 13(2): 53–65.
- 29. Kelly JP: Loss of consciousness: pathophysiology and implications in grading and safe return to play. J Athl Train 2001; 36(3): 249–52.
- Torg J: Athletic Injuries to the Head, Neck, and Face. St. Louis, MO, Mosby, 1991.

- Russell WR, Smith A: Post-traumatic amnesia in closed head injury. Arch Neurol 1961; 5: 4–17.
- 32. van der Naalt J, van Zomeren AH, Sluiter WJ, Minderhoud JM: One year outcome in mild to moderate head injury: the predictive value of acute injury characteristics related to complaints and return to work. J Neurol Neurosurg Psychiatry 1999; 66: 207–13.
- 33. Shores EA: Comparison of the Westmead PTA Scale and the Glasgow Coma Scale as predictors of neuropsychological outcome following extremely severe blunt head injury. J Neurol Neurosurg Psychiatry 1989; 52: 126–7.
- Vincent A, Roebuck-Spencer T, Gilliland K, Schlegel R: Automated Neuropsychological Assessment Metrics (v4) Traumatic Brain Injury Battery: military normative data. Mil Med 2012; 177(3): 256–69.

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14. ABSTRACT The Concussion Restoration Care Center has used the Automated Neuropsychological Assessment Metrics version 4 Traumatic Brain Injury (ANAM4 TBI) battery in clinical assessment of concussion. The study's aim is to evaluate the prognostic utility of the ANAM4 TBI. In 165 concussed active-duty personnel (all ultimately returned to duty) seen and tested on the ANAM4 TBI on days 3 and 5 from their injury, Spearman's rho statistics showed that all performance subtests (at day 5) were associated with fewer days return to duty (RTD), while concussion history or age did not. Kruskal- Wallis statistics showed that ANAM4 TBI and loss of consciousness were associated with increased RTD time; ANAM4 TBI reaction time-based subtests, collectively, showed a larger effect size. A survival analysis using a Kaplan-Meier plot showed that the lowest 25% on the reaction time-based subtests had a median RTD time of 19 days, while those in the upper 25% had a median RTD time of approximately 7 days. Results indicate that until validated neurocognitive testing is introduced, the ANAM4 TBI, especially reaction time based tests, has prognostic utility.						
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