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TITLE: Automated Neuropsychological Assessment Metrics Version 4 (ANAM4): Examination of Select Psychometric Properties and Administration Procedures

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14. ABSTRACT The ability to accurately and efficiently monitor the neurocognitive status of US warfighters under diverse operational and experimental conditions is of critical importance to the ongoing mission and network-centered initiatives of the United States military. The Automated Neuropsychological Assessment Metrics (ANAM) is a computer assisted tool for evaluating neurocognitive performance with demonstrated effectiveness for application in diverse military operational and research testing scenarios. The primary objective of this project is to examine select psychometric and administration properties of the newly-released ANAM4. Four studies are proposed that will 1) examine common use practices and determine the effect of specific administration procedures on ANAM4 performance, 2) assess the test-retest reliability of individual ANAM4 tests, 3) examine the validity of the ANAM4 mood scale, and 4) develop a representative military normative dataset. Data collection is complete for Studies 1, 2 and 3; data analysis and manuscript preparation is underway for all three studies. An amendment requesting approval of Study 4 has been submitted and we are currently coordinating with test sites.				
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INTRODUCTION

The ability to accurately and efficiently monitor neurocognitive status of U.S. warfighters under diverse operational and experimental conditions is of critical importance to the ongoing mission and network-centered initiatives of the U.S. military. The Automated Neuropsychological Assessment Metrics Version 4 (ANAM4) is a computer-assisted tool for evaluating neurocognitive performance with demonstrated efficacy for application in diverse military operational and research testing scenarios. The primary objective of this multi-study project is to examine select psychometric and administration properties of the ANAM4. This project includes four studies that will 1) examine common use practices and determine the effect of specific administration procedures on ANAM4 performance (Study 1), 2) assess the test-retest reliability of individual ANAM4 tests (Study 2), 3) examine the validity of the ANAM4 mood scale (Study 3), and 4) develop a representative military normative dataset (Study 4).

Body

This project was funded 01 December 2007. The approved study timeline/SOW is presented in **Table 1** (with task order revised Oct 2009).

Progress made during the funding period (01 December 2007 - 30 November 2009), corresponding to Tasks 1-7, was reported in the 2009 Annual Report. **Progress made during the 01 December 2009 - 30 November 2010 funding period, corresponding to Tasks 1-13, is reported below.**

Initial USARIEM Human Use Review Committee (HURC) approval for this project was received on 14 June 2007 (initial approval pending modification given on 23 May 2007). However, approval for Study 4 (normative data collection) was tabled on 11 January 2008 by the HURC due to the lack of a confirmed site(s) for data collection and potential duplicative efforts and other current research endeavors. A request to revise Study 4 was submitted to the Grant COR and the modification to the grant was approved on 16 February 2010. An Amendment to approve revised objectives and procedures for Study 4 was submitted the USARIEM HURC on 09 June 2010. Approval was granted pending modifications to the proposed study plan/protocol. A revised protocol is being prepared for submission within the next month.

TABLE 1: STATEMENT OF WORK: *Study Timeline*

Year 1	Months 1-2	Task 1	Plan and finalize logistics for Phase I (Studies 1-3)
	Months 3-12 (Dec 2008)	Task 2	Subject recruitment, data collection and data management for Studies 1-3
Year 2	Month 13-14	Task 3	Perform preliminary data analyses for Study 3
	Month 15-24 (Dec 2009)	Task 4	Complete data collection for Study 1
		Task 5	Perform preliminary data analyses for Study 1
		Task 6	Continue recruitment, data collection and data management for Study 2 & 3
		Task 7	Complete data collection for Study 3
Year 3	Month 25-36 (Dec 2010)	Task 8	Complete data collection for Study 2
		Task 9	Plan and finalize logistics for Phase II (modified Study 4)
		Task 10	Complete data analyses for Studies 1, 2, 3
		Task 11	Preparation of journal manuscript(s) for Studies 1, 2, 3
		Task 12	Preparation of Project report for Studies 1, 2, 3
		Task 13	Set-up data management procedures for Study 4
		Task 14	Initiate data collection procedures for Study 4
Year 4	Month 37-48 (Dec 2011)	Task 15	Carry out data collection procedures for Study 4
		Task 16	Perform preliminary data analyses for Study 4
		Task 17	Complete data collection procedures for Study 4
Year 5	Month 49-60 (Dec 2012)	Task 18	Complete data analyses for Study 4
		Task 19	Prepare Study 4 manuscript for peer review
		Task 20	Preparation of Project Final Report

Task 1 (Month 1-2)**Plan and finalize logistics for Phase I (Studies 1-3) – COMPLETED**

All logistical aspects for HURC approved studies (Studies 1-3) have been confirmed. Recruitment procedures, equipment, testing facilities, and other data collection elements have been finalized and are now complete.

Task 2 (Month 3-12) Subject recruitment logistics, data collection and data management for Studies 1-3 – COMPLETED

Subject recruitment, data collection and data management efforts have been completed for Studies 1-3. Recruitment of both Human Research Volunteers and Civilians was effective and efficient.

Task 3 (Month 15-24) Perform preliminary data analyses for Study 3– COMPLETED

All preliminary data analyses for Study 3 have been completed. Initial analyses suggested that additional participants would be necessary to explore noted differences between military and civilian participants on discrete on mood measures. Thus an amendment (#4, 14 July 2009) to increase enrollment from 50 to 80 participants was submitted and approved. Higher-level analyses are nearing completion on this expanded sample.

Task 4 (Month 15-24) Complete data collection for Study 1– COMPLETED

Study 1 involves the examination of common use practices and specific administration procedures (individual or group administration, practice or no practice, single session or two sessions) on ANAM4 task performances. Our recruitment goal for Study 1 was 90 participants, 30 participants per condition. This goal has been reached.

Table 2. Study 1 Enrollment

# Participants Enrolled	90
# Participants Completed	86*

**NOTE: 15 participants completed the ANAM4 without practice test modules; 15 participants completed the ANAM4 in a group setting and 15 participants completed the ANAM4 in two administration sessions. The remaining 41 participants served as controls for these discrete administration scenarios (individual administration using practice test modules and completed in a single testing session). Thus each condition had at least 30 participants, as required.*

Task 5 (Month 15-24) Perform preliminary data analyses for Study 1– COMPLETED

Preliminary analyses (sample characterization and demographic analyses) on the Study 1 data set have been completed.

Task 6 (Months 15-24) Subject recruitment, data collection and data management for Studies 2 & 3 – COMPLETED

Our recruitment goal for Study 2 was 90 participants, 30 participants per condition (days 1 & 7 / days 1 & 30 / 7 consecutive day retest). Recruitment goal for Study 3 was 80 participants. Recruitment goals were reached for Studies 2 and 3 and data collection has been completed for these studies.

Task 7 (Months 15-24) Complete data collection for Study 3– COMPLETED

Data collection for Study 3 is complete.

TABLE 3. Study 3 Enrollment

# Participants Enrolled	113
# Participants Completed	77

Task 8 (Months 25-36) Complete data collection for Study 2- COMPLETED

Data collection for Study 2 is complete.

TABLE 4. Study 2 Enrollment

# Participants Enrolled	99
# Participants Completed	92

Task 9 (Months 25-36) Plan and finalize logistics for Phase II (modified Study 4) – IN PROGRESS

The Study 4 protocol has been finalized and submitted for HURC review and approval. A total of 8 states have been identified for recruitment purposes. We are currently working to establish and connect with appropriate contacts in each state to begin the process of identifying, selecting, and scheduling individual units within each state.

Task 10 (Months 25-36) Complete data analyses for Studies 1, 2, 3- IN PROGRESS

Preliminary data analyses have been completed for each of the studies. We are currently conducting higher-level analyses for data within each of these studies.

Task 11 (Months 25-36) Preparation of journal manuscript(s) for Studies 1, 2, 3 – IN PROGRESS

Manuscripts for each of these studies are in draft form and are waiting for completion of higher-level analyses to finalize and submit to peer-reviewed journals.

Task 12 (Months 25-36) Preparation of project report for Studies 1, 2, 3 – IN PROGRESS

This task will be completed pending submission of manuscripts for peer review.

Task 13 (Months 25-36) Initiate Phase II, Study 4 - IN PROGRESS

Study 4, as originally conceptualized for this grant, has already been conducted as part of ongoing efforts within the DoD to develop normative ANAM 4 data for use within a military-specific population. While recent efforts have worked to establish normative reference data for Active Duty personnel, to our knowledge, no representative normative dataset exists for Army National Guard (ARNG) personnel. Thus, we revised Study 4 to focus specifically on the development of an accurate and reliable dataset of normative performance values, including means, standard deviations, median scores, reaction time, accuracy and throughput values, for a battery of ANAM4 tests (inclusive of the ANAM4TBI task battery) using standardized administration procedures developed in Study 1, with a geographically diverse, representative adult population of US ARNG personnel.

An Amendment requesting approval of a revised Study 4 plan was submitted to the USARIEM HURC on 09 June 2010. We are currently responding to comments from the USARIEM HURC and plan to submit a revised protocol to the HURC within a month. We have initiated contacts with Army National Guard Headquarters staff members in three of the eight identified states and are moving forward with coordinating approvals and on-site logistics.

Task 14 (25-36) Initiate data collection procedures for Study 4 – PENDING

Task 15 (37-48) Carry out data collection procedures for Study 4 - PENDING

Task 16 (37-48) Perform preliminary data analyses for Study 4 - PENDING

Task 17 (37-48) Complete data collection procedures for Study 4 - PENDING

Task 18 (49-60) Complete data analyses for Study 4 - PENDING

Task 19 (49-60) Prepare Study 4 manuscript for peer review - PENDING

Task 20 (49-60) Preparation of Project Final Report - PENDING

KEY RESEARCH ACCOMPLISHMENTS

Key research accomplishments during the current study period include:

- Recruitment and data collection have been completed for Studies 1, 2 and 3.
- Data analysis and manuscript preparation for Studies 1, 2 and 3 are underway.
- Continuing Review report was reviewed and approved by the USARIEM HURC (19 April 2010).
-

REPORTABLE OUTCOMES

1. Reports, manuscripts, abstracts (Abstracts are included in the Appendix)

- Product Line Review Presentation:
 - Proctor SP and Heaton KJ. Automated Neuropsychological Assessment Metrics Version 4 (ANAM4): Examination of Select Psychometric Properties and Administration Procedures. Psychological Health: Neuropsychological Testing, Product Line Review. Frederick, MD, 4 February 2010.
- Conference Presentations:
 - Proctor, S. Prospective Assessment of Neuropsychological Functioning Associated with Military Deployments. Invited talk at the conference 'Issues and Challenges with Rapid Neuropsychological Assessment', University of Toronto Concussion Program, University of Toronto, Toronto Canada, 10-11 Dec 2009
 - Kryskow E, Proctor S, Maule A, Heaton K. Automated Neuropsychological Assessment Metrics (ANAM4) Mood Scale is a reliable and valid measure of mood state in a military sample. *Abstract*. 12th Annual Force Health Protection Conference, Phoenix, AZ, 10-11 August 2010.
 - Maule A, Proctor S, Kryskow E, Heaton K. Automated Neuropsychological Assessment Metrics Version 4 (ANAM4) is robust to differences in several common administration practices. *Abstract*. 12th Annual Force Health Protection Conference, Phoenix, AZ, 10-11 August 2010.

2. Degrees and research training opportunities

One graduate-level student, two master's-level students, and two undergraduate students have been trained to administer the study protocol for this project.

3. Collaborative funding applications related to work supported by this award

The following funded projects are directly related to the work supported by this award:

- “Eye-Tracking Rapid Attention Computation (EYE-TRAC)” (USARIEM Protocol # H09-07; Site PI: Heaton). This project was funded as a CDMRP Advanced Technology Award in FY08. This project includes an ANAM4 task battery (ANAM 4 TBI Battery) as part of the protocol, with ANAM 4 data being collected at 4 time points, allowing for computation of test-retest reliability across a 2 week interval and sensitivity of the ANAM4 TBI battery to differentiate performance between a rested and fatigued (24 hour sleep deprivation) state. The following presentations have included preliminary results from this study:
 - Heaton KJ, Kryskow EW, Maule A, Ghajar J, Murata J. Eye tracking evidence for fatigue-related decrements in attention within a healthy military sample. 12th Annual Force Health Protection Conference, Phoenix, AZ, 10-11 August 2010. (See abstract in the Appendix)
- “An Investigation of the Effects of Head Impacts Sustained during Collegiate Boxing Participation on Central and Peripheral Nervous System Function” (USAFA Protocol # FAC2007010H, PI: MAJ Brandon Doan, USAFA), was funded in part by an AMEDD Advanced Medical Technology Initiative (AAMTI) award to Dr. Heaton and includes use of the ANAM4. Data from this project have been presented as described below:
 - Heaton KJ, Neurocognitive Performance During an Intercollegiate Boxing Bout: Preliminary Results. Presented at the Neurocognitive Assessment Tool (NCAT) State of Knowledge Conference, Walter Reed Army Research Institute, Silver Spring, MD, 26 January 2010.
 - Heaton KJ, Doan B, Brininger T, Hanna M, Butler M, Wile A, Self B, Kryskow E, Adam G. Neurocognitive Function Changes After Repeated Mild Head Impacts During Intercollegiate Boxing. *Abstract*. 12th Annual Force Health Protection Conference, Phoenix, AZ, 10-11 August 2010.
 - Butler M, Doan B, Hanna M, Adam G, Wile A, Self B, Heaton K, Brininger T, Kryskow E. “An Investigation of Head Accelerometry, Cognitive Function, and Brain Blood Flow during Intercollegiate Boxing and its Impact Regarding Head Injury Assessment in Combat.” *Abstract*. National Academy of Neuropsychology (NAN) Conference, Vancouver, British Columbia, 13-16 October 2010.
- “Validation of Select Neurobehavioral Assessments for Concussion/Mild Traumatic Brain Injury (MTBI)” (USARIEM #H09-08), was intramurally funded (MRMC RAD3) to Drs. Proctor and Heaton (co-PIs). This study seeks to validate the ANAM4TBI Battery against a standard neuropsychological screening battery for traumatic brain injury. The project is ongoing.

4. Related projects and collaborations initiated

- “Mild traumatic brain injury characterization with multi-modal neuroimaging compared to EEG and fNIRS” (USARIEM Protocol H10-08) (PI: Dr. Carole Palumbo, USARIEM; Co-I: Dr. Heaton)
- “Quantification of head sweating during rest and exercise in the heat” (USARIEM Protocol H08-09) (PI: Ms. Catherine O’Brien, USARIEM; Research Associate: Dr. Heaton)
- “Microclimate cooling carrying approach march load” (USARIEM Protocol H09-19) (PI: Mr. Bruce Cadarette, USARIEM; Research Associate: Dr. Heaton)
- “Microclimate cooling for air soldier flight crew” (USARIEM Protocol 11-08-H) (PI: Mr. Bruce Cadarette, USARIEM; Research Associate: Dr. Heaton)
- “Analyses of ANAM4 TBI predeployment assessment data: USARIEM-OTSG research collaborative” (USARIEM Protocol 11-07-H) (PI: Dr. Proctor; Co-I: Dr. Heaton)
- “Identifying Biomarkers That Distinguish Posttraumatic Stress Disorder and Mild Traumatic Brain Injury Using Advanced Magnetic Resonance Spectroscopy” (2007-P-002458/9; Brigham and Women’s Hospital) Department of Defense U.S. Army Medical Research and Materiel Command Congressionally Directed Medical Research Programs, 2009 Psychological Health and Traumatic Brain Injury Research Program Award (PI: Dr. Alexander Lin, Brigham and Women’s Hospital; Co-I: Dr. Heaton)
- “Noninvasive Cerebral Glutamate Monitoring in Veterans with Traumatic Brain Injury” Harvard Catalyst Pilot Grant, (PI: Dr. Alexander Lin, Brigham and Women’s Hospital; Co-I: Dr. Heaton)

CONCLUSIONS

There has been significant progress in this current funding period. We completed all recruitment and data collection for three of the four studies. Data from these studies have been presented at professional conference and manuscripts are currently in preparation for submission to peer-reviewed journals. An amendment to approve Study 4 has been submitted and work is underway to coordinate with Army National Guard state headquarter offices in eight states for access to appropriate units.

Data from this project will contribute to ongoing efforts to validate the ANAM4 and inform use of this assessment tool and interpretation of testing results within a military population.

APPENDIX

ABSTRACT for invited talk at the conference 'Issues and Challenges with Rapid Neuropsychological Assessment', University of Toronto Concussion Program, University of Toronto, Toronto Canada, 10-11 Dec 2009

Prospective Assessment of Neuropsychological Functioning Associated with Military Deployments

CORRESPONDING AUTHOR: Susan P. Proctor, D.Sc. U.S. Army Research Institute of Environmental Medicine, Kansas St. Bldg. 42, Natick, MA 01760, USA

In this presentation, two prospective epidemiological studies designed to examine neuropsychological performance changes related to deployment will be described. In each study, assessments were conducted prior to deployment and then within several months of return from deployment. Also, each study included a comparison group of soldiers not deployed over the study period. One study focused on a peacekeeping mission to Bosnia, while the other study involved a war-zone deployment mission to Iraq.

Although increasing medical attention is being focused on better understanding the physical and mental health consequences of deployment and the underlying risk and resilience factors, there are many knowledge gaps. Prospective evaluation of neuropsychological performance patterns following varying deployment scenarios, and thus occupational settings, can provide further insight for more targeted protection, prevention, and treatment strategies.

[The views expressed in this presentation are those of the author and do not reflect the official policy of the Dept of the Army or the Department of Defense.]

NOTE: Aspects of the research studies described in this presentation have been reported on previously at several conferences and in published articles (Vasterling et al., 2006; Proctor et al., 2009).

-Vasterling JJ, Proctor SP, Amoroso PJ, Kane R, White RF. Neuropsychological outcomes of Army personnel following deployment to the Iraq War. JAMA 2006; 296:519-529.

-Proctor SP, Heaton KJ, Dos Santos KD, Rosenman ES, Heeren T. Prospective assessment of neuropsychological functioning and mood in US Army National Guard personnel deployed as peacekeepers. Scandinavian Journal of Work, Environment and Health 2009; 35:349-360.

Abstract for Force Health Protection Conference, August 2010

Automated Neuropsychological Assessment Metrics (ANAM4) Mood Scale is a reliable and valid measure of mood state in a military sample.

Kryskow EM, Proctor SP, Maule A, Heaton KJ

USARIEM

Mood assessment is critical for monitoring soldier health, performance, and operational readiness since altered mood is frequently associated with illness and injury. This study examined the reliability and validity of the Mood Scale (AMS) module of the Automated Neuropsychological Assessment Metrics Version 4 (ANAM4) in a sample of 86 military and civilian participants. AMS was compared to two validated mood measures.

The AMS demonstrated strong internal consistency for all 7 subscales ($\alpha = .71-.92$); convergent validity was demonstrated by significant correlations between AMS subscales and comparable subscales on the Neurobehavioral Evaluation System Version 3 and Profile of Mood States (e.g., Depression subscales $r = .81$ and $.83$, $p < .01$, respectively). Significant effects for gender and military status also were noted on the vigor, restlessness, tension and anger subscales.

The AMS module of the ANAM4 is a reliable, valid measure of mood state in a military and civilian sample.

The views expressed in this presentation are those of the authors and do not reflect the official policy of the Department of the Army or the Department of Defense.

Abstract for Force Health Protection Conference, August 2010

The Automated Neuropsychological Assessment Metrics Version 4 (ANAM4) is robust to differences in several common administration practices

Maule A, Proctor SP, Kryskow E, Heaton KJ

USARIEM

The Automated Neuropsychological Assessment Metrics Version 4 (ANAM4) is a computerized neurocognitive test battery used in clinical, research, and military settings. Given requirements of these diverse environments, a variety of administration procedures have been utilized. However, the effect of different administration practices on task performance is unclear. This study examined the impact of several administration practices on task performance in a sample of 83 military and civilian participants: individual versus group administration, use of practice tests, and completion of the full battery in one session versus two shorter sessions.

Participants taking ANAM4 individually in a single session with practice tests served as controls. No significant differences in task performance across test modules were noted, suggesting the ANAM4 is robust to a variety of administration practices. However, variability in task performance was significantly elevated in non-controls ($F=4.189-17.000$; $p=0.046-0.0001$). Thus further investigation of effects of different administration practices is warranted.

The views expressed in this presentation are those of the authors and do not reflect the official policy of the Department of the Army or the Department of Defense.

Abstract for Force Health Protection Conference, August 2010

Eye tracking evidence for fatigue-related decrements in attention within a healthy military sample

Heaton KJ, Kryskow EW, Maule A

USARIEM

Ghajar J, Murata J

Brain Trauma Foundation

Previous research has linked performance on a visual tracking paradigm with impaired attention following mild brain injury. However assessment of brain injury must also account for non-injury sources of attention deficits, including fatigue. This study examined the effects of 26h of sleep deprivation on circular visual tracking performance in 30 healthy military participants.

Results indicate good test-retest reliabilities (14 days) on visual tracking indices: standard deviations of radial and tangential errors, horizontal and vertical gains and mean phase (.74-.90, $p < .001$). Changes in SDs of radial and tangential error and horizontal gain after 26h sleep deprivation were small but statistically significant and therefore provided evidence of sensitivity. Concurrent validity was demonstrated through significant correlations between visual tracking performance and impaired performance on multiple tests of reaction time, learning and memory. Thus this novel approach utilizing a visual tracking paradigm may provide a reliable and valid measure of fatigue-related attention impairment.

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