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TITLE: iANAM: The Ability to "Visualize" Headache, Sleep Disturbance, and mTBI

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14. ABSTRACT The purpose of this research was to integrate simultaneously collected eye movement data with computerized cognitive assessment data (ANAM). Not having access to ANAM application programming interface (API) required developing an ANAM analog to integrate with eye movement data. Following transition to a new co-Investigator (Co-I) proximal to the end of Year 1, a matching-to-sample (M2S) analog task integrated with eye-movement data was created within the Co-I's lab using the Unity game engine. M2S is a subtest within the ANAM Military mTBI battery that is sensitive to mTBI recovery. The focus of Year 2 was to develop a single ANAM analog task. Multiple builds (10) of the analog M2S + eye-movement data were completed. In total, 31 participants were recruited and 17 completed all testing associated with the final version of the analog M2S + eye-movement data. Data collection is now complete.		

15. SUBJECT TERMS			
Eye-tracking, eye-movements, fixations, saccades, Automated Neuropsychological Assessment Metrics (ANAM), Portable Automated Rapid Testing (PART), computerized cognitive task, matching-to-sample (M2S), MATLAB, mild traumatic brain injury (mTBI), headache, pain, sleep disturbance, insomnia, sleepiness, multimodal data			
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1. INTRODUCTION:

The purpose of this research was to integrate simultaneously collected eye movement data with computerized cognitive assessment data (ANAM) for improved clinical management of mild traumatic brain injury (mTBI). One limitation of the commercially available ANAM software is that it does not have the capability to interface with any other software program. Not having access to ANAM application programming interface (API) necessitated creating an analog ANAM task (matching-to-sample, or M2S), using stimulus parameters available in the ANAM technical manual (appendix 2) for comparability, to be able to simultaneously sample (collect) eye-movement data.

Specifically, the M2S analog subtest was incorporated into the previously developed computerized cognitive battery by Dr. Seitz and colleagues, known as the Portable Automated Rapid Testing (PART). PART is a free application for download that has a range of psychoacoustical tasks focusing on auditory function. Working with Dr. Seitz allowed for the possibility of eye-tracking data and computerized cognitive task data to be within the same platform, meaning fully integrated from development, versus trying to sample data from two different software suites in parallel, both of which require highly sensitive temporal resolution. M2S has been shown to be sensitive to concussion recovery (Meyers and Vincent, 2020). Therefore, the M2S subtest was selected for analog development and biometric (eye-movements) integration, which was the focus of Years 2-3 on this project. The Co-I, Dr. Seitz, was instrumental in achieving the goal of developing a fully integrated biometric + computerized cognitive task. This was an important goal as it related to findings of a recent structured review that examined the current methodologies for data collection, analysis, and interpretation of eye-tracking in individuals following mTBI (Stuart et al., 2020). Of 22 reviewed studies, the authors concluded that saccades, fixations, and nystagmus were generally impaired in mTBI compared to controls. However, the influence of mTBI on specific outcomes was inconsistent (e.g., mixed findings for anti-saccadic tasks) due to numerous methodological and reporting factors, fixations tended to be an overlooked eye-movement outcome, and only two studies assessed for cognitive function. The authors noted this is highly problematic for this research area as eye-movements are underpinned by cognitive processes and cognitive deficits related to mTBI have been shown to lead to abnormal performance on quantified eye-movement examinations. *They advocated for future eye-tracking research protocols that always collect cognitive performance data to better understand the relationship between eye-movements and cognitive function, as examined through mTBI-induced functional changes.* Lastly, only one study reported data on basic visual functions (i.e., visual acuity), which has been found to lead to abnormal eye-movement performances and was further recommended as a necessary data point for all future eye-tracking protocols (Stuart et al., 2020). The current research met both structured review authors recommendations (i.e., collecting both cognitive and eye-movement data and collecting basic visual acuity data).

Meyers JE, Vincent AS. Automated neuropsychological assessment metrics (v4) military battery: military normative data, 2020, *Military Medicine*, 185, 9/10:e1706.

Stuart S, Parrington L, Martini D, Peterka R, Chesnutt J, King L. The Measurement of Eye Movements in Mild Traumatic Brain Injury: A Structured Review of an Emerging Area. *Front*

Sports Act Living. 2020 Jan 28;2:5. doi: 10.3389/fspor.2020.00005. PMID: 33345000; PMCID: PMC7739790.

2. KEYWORDS:

Eye-tracking, eye-movements, fixations, saccades, Automated Neuropsychological Assessment Metrics (ANAM), Portable Automated Rapid Testing (PART), computerized cognitive task, matching-to-sample (M2S), MATLAB, mild traumatic brain injury (mTBI), headache, pain, sleep disturbance, insomnia, sleepiness, multimodal data

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Specific Aim 1: The (original) primary aim of the proposed project is to use the eye-tracking parameters of fixations, saccades, and scan path (combination of fixations and saccades to complete a specific task) fully integrated with the ANAM Military battery to improve the sensitivity of mTBI detection and resolution.

Specific Aim 2: The (original) secondary aim is to use the eye-tracking parameter of pupil dilation fully integrated with the ANAM Military battery to provide greater specificity (or differentiation from mTBI) of state dependent influences (i.e., sleep disturbance, headache, mood, engagement/effort) of impaired post-traumatic cognitive performances compared to current clinical decision making.

Overall, the following accomplishments were achieved:

Major Task 1: Finalize Protocols and Obtain IRB Approval

- Subtask 1: PI and Co-I create written protocol and obtain institutional IRB approval
- Subtask 2: Submit HRPO documentation
- Milestone #1: *HRPO approval obtained*
- Subtask 3: Two teleconference meetings of all key personnel to review study protocols and technical build metrics
- Milestone #2: *Initial build metrics finalized and establish regular meetings*

Major Task 2: Integration and Synchronization of ANAM & Eye-Tracking Modalities (iANAM)

- Subtask 1: Establish PART M2S analog configuration and calibration of Tobii eye-tracker, CPU specifications, and desktop screen – program/build M2S analog in Unity game engine
- Subtask 2: Establish eye-tracking metrics: sampling rate, head box, fixation, and saccadic operationalization using eye-tracker SDK, ANAM xml output, timestamps, etc. – program eye-movement cleaning and processing scripts in MATLAB

Major Task 3: iANAM Pilot Testing

- Subtask 1: Recruit pilot testing volunteers; [10 clinical + 10 control volunteers]
- Subtask 2: Assess calibration and data quality of iANAM; modify software and hardware as necessary
- Subtask 3: Assess pilot testing volunteers' reaction/satisfaction of iANAM
- Milestone #3: *iANAM ready to launch*
- Milestone #4: *Write and submit for publication results from iANAM pilot testing*

Major Task 4: Conduct Pilot Comparison Study of iANAM Military Battery and ANAM Military Battery regarding mTBI detection and resolution – adapted to just M2S subtest commercial versus analog comparison

- Subtask 1: Recruit study subjects
- Subtask 2: Conduct pilot comparison study; [35 mTBI subjects and 35 control subjects]
- Milestone #5: *Two meetings of all personnel to discuss database, analyses, and outcome interpretation*
- Milestone #6: *Write and submit for publication results from iANAM versus ANAM comparison pilot testing*

What was accomplished under these goals?

The following summary includes accomplishments throughout the course of this project. All major milestones have been reached. Given the delays in statement of work (SOW) related to terminating the contract with the original Co-I [Dr. Thomas Parsons] and contracting needs to establish a new contract with Dr. Seitz, the replacement Co-I, and the complexities and related time intensive nature of development activities, the decision was made to focus on developing a single ANAM analog subtest sensitive to mTBI and integrated with eye-movement data, which has been completed. Multiple builds (9) of the analog M2S + eye-movement data were developed during pilot testing. The M2S analog task has an embedded fixation point located at the center of the 4x4 cell sample grid with different configurations of red and blue cells (see below for example figure), which is a common saccadic experimental metric controlling for attention of gaze to start a task. The central fixation point remains following the sample stimulus leaving the screen (or grid to be remembered) and is spatially centered between the two response grids until the response grids appear on the screen, at which time the fixation point disappears from the screen. A central fixation point during the interval from sample stimuli to presentation of response stimuli ensures participants have the same initial focal point for recording eye-movements. Thus, M2S is a computerized cognitive task highly amenable to integration with an eye-tracking experimental design.

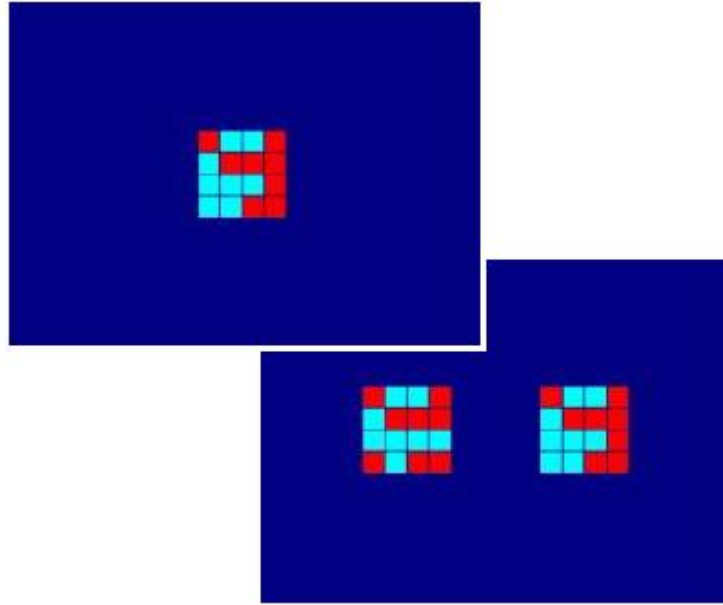
Because the Gazepoint eye-tracking system was not compatible with the Unity game engine, upon transitioning to collaborate with Dr. Seitz, the Tobii Pro Nano was purchased and replaced the Gazepoint eye-tracking system to complete the remainder of the SOW. The Gazepoint eye-tracking system was previously used to collect eye-movements during the ANAM M2S task, which as aforementioned (and delineated in previous annual reports) was then attempted to be integrated retrospectively with a macro. The Tobii analysis software is compatible with the Unity game engine and allowed eye-movement and cognitive data to be sampled/collected simultaneously within the same software platform designed for programming video games. All accomplishments throughout the grant period, some of which have been reported in previous annual reports, as well as recent accomplishments that have occurred in the no cost extension (NCE) period, are included below.

1) Major activities for Task 1:

- a. Institutional IRB modification approval and HRPO modification approval obtained following transition of co-investigator (Co-I).
 - i. Terminated research subaward agreement with initial Co-I, Dr. Thomas Parsons at the University of North Texas (UNT) effective 6/5/2022, due to lack of ability of Dr. Parsons to deliver what he committed to do for the project. This necessitated finding another collaborator with the knowledge, experience, and

availability to collaborate, which thankfully was found in the current Co-I, Dr. Seitz. Contracting was completed with his institution and IRB amendments were submitted and approved for this to go into effect.

1. Co-I Change Letter attached as part of Annual Report 2022
 - ii. New subaward agreement, including revised SOW and revised budget, with Dr. Aaron Seitz at the University of California (UCR), approved 9-26-2022
 - iii. OHSU IRB modification, including the change of Co-I, approved 8/4/2022
 - iv. OHRO concurrence approval obtained 9-13-2022
 - v. All subject recruitment remained exclusively at OHSU
 - vi. The major activities and roles for Dr. Seitz and his lab members (application programmer and MATLAB expert) were as follows:
 1. Assist with development of eye-tracking system
 2. Training project personnel on use of software systems
 3. Assisting with data analyses, interpretation, and dissemination
 - b. Tobii Pro Nano hardware and software (Eye Tracker Manager for eye-tracker calibration) obtained and configured for desktop computer
 - c. Weekly teleconference meetings established with Dr. Seitz and his team
- 2) Major activities for Task 2 and Task 3 – integrated as activities in each task are dependent upon the other during pilot testing, assessment of data quality, and subsequent development:
- a. PART build 1-6 for M2S analog occur in 11/2022
 - b. PART build 7 in 12/2022
 - c. PART build 8 in 1/2023
 - d. PART build 9 in 2/2023
 - e. Basis for rebuilds during pilot testing included: application failure prior to M2S task completion, application errors such as pauses in the application for delayed loading of subsequent stimuli, correcting coordinates of stimulus grids, modifying timing jitter of M2S analog to be consistent with ANAM M2S stimulus parameters, modifying eye-movement sampling rate for consistency with stimulus presentation parameters of the M2S task, and time-stamping eye-movement data.
 - f. Administration of the ANAM M2S (as well as the ANAM mTBI battery subjective questionnaires: sleepiness scale, mood scale, neurobehavioral symptom inventory (NSI), PTSD checklist for DSM-5 (PCL-5) and PART analog M2S tasks are counterbalanced across participants. The eye-tracker is calibrated prior to administration of both the ANAM M2S and PART M2S analog task, and the tester leaves the room for M2S task completion following calibration.
 - g. Screenshot of Matching to Sample (M2S) test format/structure and example trial/stimuli content:



- i.
- h. Data cleaning and processing is time intensive and has been completed on individual participant task performances/data prior to batch processing capabilities that are planned to occur in the future. Currently creation and testing of cleaning and processing scripts is 75% complete. To date, a major accomplishment is that Dr. Seitz and his team have reviewed and processed de-identified data via the below MATLAB script, which took months to write, and we are excited to report it is able to evaluate the eye-movement data. Future work is ongoing to identify the best way to process these data to accomplish the goals of this study. See below (% or %% explains subsequent script processes/sub-processes):
- %% EM Analysis for Single Participant
 -
 - clear all
 - close all
 - clc
 -
 - %% Reading the .json file
 - fname = '236_001_003_M2SHybridLogger_23_03_06_13_54_41.json';
 - val = jsondecode(fileread(fname));
 - Data = val.data;
 -
 - %% Define variables
 - v_d = 20 * 2.54;
 - screencm = [44.8 24.91];
 - wRect = [1920 1080];
 - pix_deg = 1./((2*atan((screencm(1)/wRect(1))./(2*v_d))).*(180/pi));
 - pix_deg_vert = pi * wRect(2) / atan(screencm(2)/v_d/2) / 360;
 -
 - % Display bounds during Stimulus presentation

- StimDisp = [Data(1).data.InitialDisplayBounds.LowerBoundX,
Data(1).data.InitialDisplayBounds.UpperBoundX,
Data(1).data.InitialDisplayBounds.UpperBoundX,
Data(1).data.InitialDisplayBounds.LowerBoundX,
Data(1).data.InitialDisplayBounds.LowerBoundX; ...
- Data(1).data.InitialDisplayBounds.LowerBoundY,
Data(1).data.InitialDisplayBounds.LowerBoundY,
Data(1).data.InitialDisplayBounds.UpperBoundY,
Data(1).data.InitialDisplayBounds.UpperBoundY,
Data(1).data.InitialDisplayBounds.LowerBoundY];
- StimDisp(1,:) = (1920 * StimDisp(1,:))./pix_deg;
- StimDisp(2,:) = (1080 * StimDisp(2,:))./pix_deg_vert;
-
- % Display bounds during response period
- RespDisp = [Data(1).data.IncorrectResponseBounds.LowerBoundX,
Data(1).data.IncorrectResponseBounds.UpperBoundX,
Data(1).data.IncorrectResponseBounds.UpperBoundX,
Data(1).data.IncorrectResponseBounds.LowerBoundX,
Data(1).data.IncorrectResponseBounds.LowerBoundX; ...
- Data(1).data.IncorrectResponseBounds.LowerBoundY,
Data(1).data.IncorrectResponseBounds.LowerBoundY,
Data(1).data.IncorrectResponseBounds.UpperBoundY,
Data(1).data.IncorrectResponseBounds.UpperBoundY,
Data(1).data.IncorrectResponseBounds.LowerBoundY; ...
- Data(1).data.CorrectResponseBounds.LowerBoundX,
Data(1).data.CorrectResponseBounds.UpperBoundX,
Data(1).data.CorrectResponseBounds.UpperBoundX,
Data(1).data.CorrectResponseBounds.LowerBoundX,
Data(1).data.CorrectResponseBounds.LowerBoundX; ...
- Data(1).data.CorrectResponseBounds.LowerBoundY,
Data(1).data.CorrectResponseBounds.LowerBoundY,
Data(1).data.CorrectResponseBounds.UpperBoundY,
Data(1).data.CorrectResponseBounds.UpperBoundY,
Data(1).data.CorrectResponseBounds.LowerBoundY];
- RespDisp(1,:) = pix_deg * screencm(1) * RespDisp(1,:);
- RespDisp(2,:) = pix_deg_vert * screencm(2) * RespDisp(2,:);
- RespDisp(3,:) = pix_deg * screencm(1) * RespDisp(3,:);
- RespDisp(4,:) = pix_deg_vert * screencm(2) * RespDisp(4,:);
-
- %% Duration of the Stimulus event
-
- % Stimulus displayed
- count_stim = 0;
- for i = 3:4:length(Data)
- checkfield = string(fieldnames(Data(i).data));
- str_check_stim = strfind(checkfield,'CorrectOptionDisplayed');

```

○   if str_check_stim{2,1} == 1
○       count_stim = count_stim + 1;
○       susp_counter=0;
○       for j = 2:length(Data(i).data.EyetrackerInfo)
○           if size(Data(i).data.EyetrackerInfo(j-
1).EyetrackerInfo.RightEye.GazePointOnDisplayArea.x,2) == 1
○               Stimdis(count_stim).Rx(j-1,1) = (1920 * Data(i).data.EyetrackerInfo(j-
1).EyetrackerInfo.RightEye.GazePointOnDisplayArea.x)/pix_deg;
○               Stimdis(count_stim).Ry(j-1,1) = (1080 * Data(i).data.EyetrackerInfo(j-
1).EyetrackerInfo.RightEye.GazePointOnDisplayArea.y)/pix_deg_vert;
○           %           Stimdis(count_stim).Rx(j-1,1) =
○           else
○               Stimdis(count_stim).Rx(j-1,1) = NaN;
○               Stimdis(count_stim).Ry(j-1,1) = NaN;
○           end
○           t1 = Data(i).data.EyetrackerInfo(j-1).t;
○           t2 = Data(i).data.EyetrackerInfo(j).t;
○           Stimdis(count_stim).T(j-1,1) = t2 - t1;
○
○           if Stimdis(count_stim).T(j-1,1)>5
○               susp_counter=susp_counter+1;
○               suspicious_value(count_stim,susp_counter)=t2 - t1;
○               suspicious_value_one(count_stim,susp_counter)=t1;
○               suspicious_value_two(count_stim,susp_counter)=t2;
○           end
○       end
○   end
○ end
○
○ %% Calculating distance and speed
○ for i = 1:length(Stimdis)
○     Stimdis(i).cumT(1,1) = Stimdis(i).T(1,1);
○     for j = 2:length(Stimdis(i).Rx)
○         %     Stimdis(i).d(j,1) = sqrt((Stimdis(i).Rx(j) - Stimdis(i).Rx(j-1)).^2 +
(Stimdis(i).Ry(j) - Stimdis(i).Ry(j-1)).^2);
○         %     Stimdis(i).s(j,1) = Stimdis(i).d(j)/(Stimdis(i).T(j)/1000);
○         Stimdis(i).cumT(j,1) = Stimdis(i).cumT(j-1,1) + Stimdis(i).T(j,1);
○     end
○ end
○
○ sampling = 0:100:3100;
○ for i = 1:length(Stimdis)
○     [minval, ci] = min(abs(Stimdis(i).cumT - sampling));
○     Stimdis(i).ci = ci';
○     em = 0;
○     for j = 2:length(Stimdis(i).ci)

```

```

○ x1 = Stimdis(i).Rx(Stimdis(i).ci(j-1)); y1 = Stimdis(i).Ry(Stimdis(i).ci(j-1));
○ x2 = Stimdis(i).Rx(Stimdis(i).ci(j)); y2 = Stimdis(i).Ry(Stimdis(i).ci(j));
○ Stimdis(i).d(j,1) = sqrt((x2-x1)^2 + (y2-y1)^2);
○ if Stimdis(i).d(j,1) > 0.5 % identifying EM within 100 ms using a spatial cutoff
of 0.5 degrees of visual angle
○ em = em + 1;
○ Stimdis(i).emi(em,1) = Stimdis(i).cumT(Stimdis(i).ci(j,1),1);
○ Stimdis(i).emx(em,1) = Stimdis(i).Rx(Stimdis(i).ci(j,1),1);
○ Stimdis(i).emy(em,1) = Stimdis(i).Ry(Stimdis(i).ci(j,1),1);
○ end
○ end
○ end
○
○ %% Finding fixation periods and EM periods
○
○ for i = 1:length(Stimdis)
○ count_em = 0;
○ cell = 1;
○ count_fix = 0;
○ for j = 2:length(Stimdis(i).s)
○ if Stimdis(i).Rx(j-1) ~= Stimdis(i).Rx(j)
○ cell = cell + 1;
○ count_fix = 0;
○ end
○ if Stimdis(i).d(j) > 0.5
○ Stimdis(i).Eyecode(j,1) = 1;
○ else
○ Stimdis(i).Eyecode(j,1) = 0;
○ end
○ if Stimdis(i).d(j) < 0.5 || isnan(Stimdis(i).d(j))
○ count_fix = count_fix + 1;
○ Stimdis(i).fix{cell,1}(count_fix,1) = Stimdis(i).Rx(j);
○ Stimdis(i).fix{cell,1}(count_fix,2) = Stimdis(i).Ry(j);
○ elseif Stimdis(i).d(j) > 0.5 %&& Stimdis(i).Rx(j) < 1920 && Stimdis(i).Ry(j) <
1080
○ count_em = count_em + 1;
○ Stimdis(i).em(count_em,1) = Stimdis(i).Rx(j);
○ Stimdis(i).em(count_em,2) = Stimdis(i).Ry(j);
○ end
○ end
○ end
○
○ %% Plotting EM and fixations
○ figure(1)
○ for i = 1:2 %length(Stimdis)
○ subplot(1,2,i)

```

```

○ % subplot(4,5,i)
○ plot(Stimdis(i).cumT,Stimdis(i).Ry,'-r','Linewidth',3)
○ hold on
○ plot(Stimdis(i).cumT, Stimdis(i).Rx,'-g','Linewidth',3)
○ hold on
○ % for j = 1:length(Stimdis(i).Eyecode)
○ %     if Stimdis(i).Eyecode(j) == 1
○ %         bar(Stimdis(i).cumT(j),Stimdis(i).Ry(j),0.1)
○ %         hold on
○ for j = 1:length(Stimdis(i).emi)
○     bar(Stimdis(i).emi(j),Stimdis(i).emx(j,1),0.2,'k')
○     hold on
○ end
○ %     end
○ % end
○ xlim([0 3100])
○ ylim([0 50])
○ xlabel('Time (ms)','fontsize',18)
○ ylabel('Location (dva)','fontsize',18)
○ legend('Y location','X location','EM','fontsize',18,'location','best')
○ title(['Trial - ' num2str(i)],'fontsize',20)
○ end
○
○ sgtitle('Participant ID 236','fontsize',22)
○ % hold on
○ % plot(StimDisp(1,:),StimDisp(2:),'-k','LineWidth',3)
○ % xlim([0 1920])
○ % ylim([0 1080])
○
○ %% Duration of the Response event
○
○ % Response Period
○ count_resp = 0;
○ count = 0;
○ for i = 5:4:length(Data)
○     count = count + 1;
○     checkfield = string(fieldnames(Data(i).data));
○     str_check_resp = strfind(checkfield,'OptionsDisplayed');
○     if str_check_resp{2,1} == 1
○         count_resp = count_resp + 1;
○         for j = 2:length(Data(i).data.EyetrackerInfo)
○             if size(Data(i).data.EyetrackerInfo(j-
1).EyetrackerInfo.RightEye.GazePointOnDisplayArea.x,2) == 1
○                 Respdis(count_resp).Rx(j-1,1) = (1920 * Data(i).data.EyetrackerInfo(j-
1).EyetrackerInfo.RightEye.GazePointOnDisplayArea.x)/pix_deg;

```

```

○           Respdis(count_resp).Ry(j-1,1) = (1080 * Data(i).data.EyetrackerInfo(j-
○ 1).EyetrackerInfo.RightEye.GazePointOnDisplayArea.y)/pix_deg_vert;
○ %           Respdis(count_stim).Rx(j-1,1) =
○           else
○           Respdis(count_resp).Rx(j-1,1) = NaN;
○           Respdis(count_resp).Ry(j-1,1) = NaN;
○           end
○           t1 = Data(i).data.EyetrackerInfo(j-1).t;
○           t2 = Data(i).data.EyetrackerInfo(j).t;
○           Respdis(count_resp).T(j-1,1) = t2 - t1;
○           end
○       end
○   end
○   end
○   %% Calculating distance and speed
○   for i = 1:length(Respdis)
○       for j = 2:length(Respdis(i).Rx)
○           Respdis(i).d(j,1) = sqrt((Respdis(i).Rx(j) - Respdis(i).Rx(j-1))^2 +
○ (Respdis(i).Ry(j) - Respdis(i).Ry(j-1))^2);
○           Respdis(i).s(j,1) = Respdis(i).d(j)/(Respdis(i).T(j)/1000);
○       end
○   end
○   %% Finding fixation periods and EM periods
○   for i = 1:length(Respdis)
○       count_em = 0;
○       cell = 1;
○       count_fix = 0;
○       for j = 2:length(Respdis(i).s)
○           if Respdis(i).Rx(j) ~= Respdis(i).Rx(j+1)
○               cell = cell + 1;
○               count_fix = 0;
○           end
○           if Respdis(i).s(j) > 60 %&& Respdis(i).Rx(j) < 1920 && Respdis(i).Ry(j) <
○ 1080
○               count_em = count_em + 1;
○               Respdis(i).em(count_em,1) = Respdis(i).Rx(j);
○               Respdis(i).em(count_em,2) = Respdis(i).Ry(j);
○           else
○               count_fix = count_fix + 1;
○               Respdis(i).fix{cell,1}(count_fix,1) = Respdis(i).Rx(j);
○               Respdis(i).fix{cell,1}(count_fix,2) = Respdis(i).Ry(j);
○           end
○       end
○   end
○   end

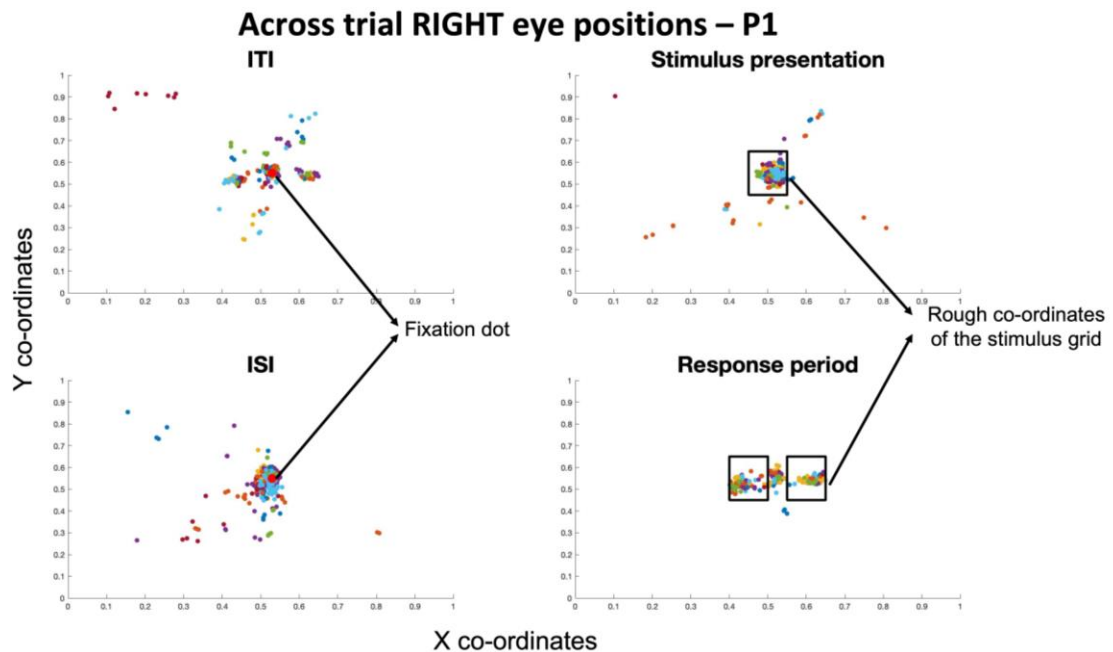
```

```

○
○ %% Plotting EM and fixations
○ figure(2)
○ for i = 1:length(Respdis)
○     subplot(4,5,i)
○     plot(Respdis(i).em(:,1),Respdis(i).em(:,2),'-','Markersize',25)
○     hold on
○     plot(RespDisp(1,:),RespDisp(2:),'-k','LineWidth',3)
○     hold on
○     plot(RespDisp(3,:),RespDisp(4:),'-k','LineWidth',3)
○     xlim([0 1920/pix_deg])
○     ylim([0 1080/pix_deg_vert])
○ end
○
○ figure(3)
○
○ plot(RespDisp(1,:),RespDisp(2:),'-k','LineWidth',3)
○ hold on
○ plot(RespDisp(3,:),RespDisp(4:),'-k','LineWidth',3)
○ xlim([0 1920])
○ ylim([0 1080])
○ axis('square')

```

i.

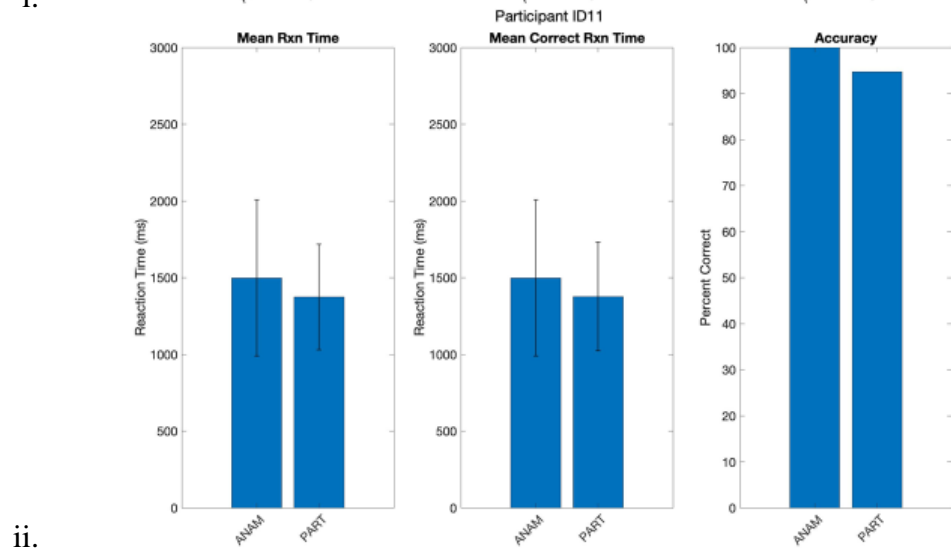
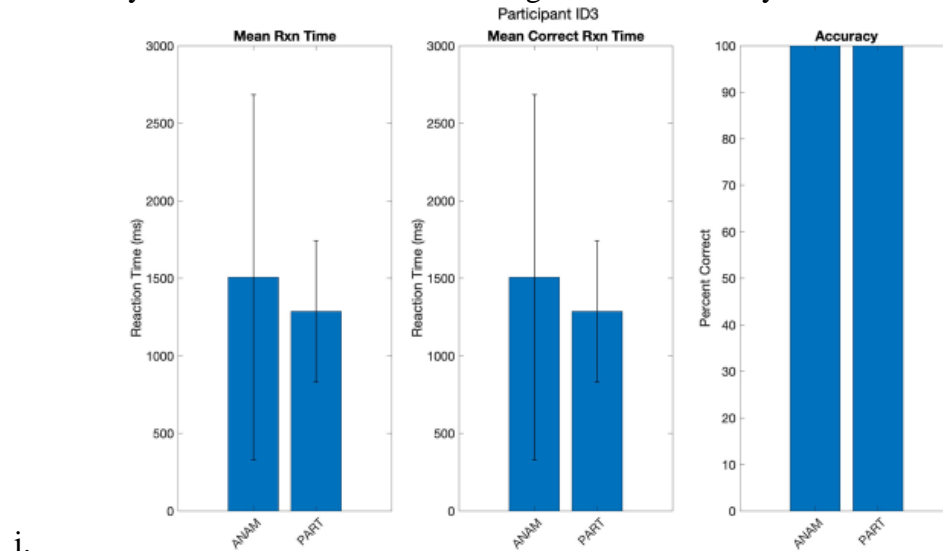


j.

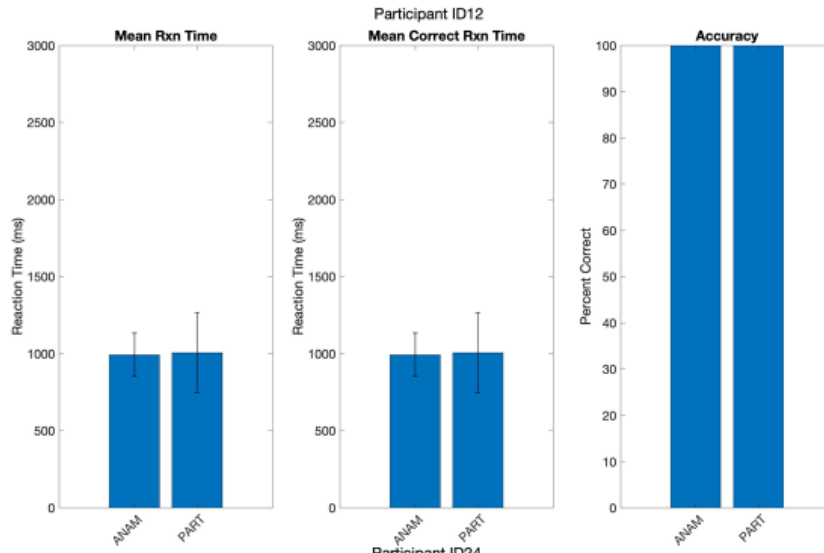
- i. Above figure was examining individual eye (right) positions for the inter-stimulus intervals (ISI), inter-trial intervals (ITI), presentation of sample grid to be remembered (or “stimulus presentation”); and the “response period” where the sample grid and a foil grid are presented where the participant identifies which grid was previously presented – this review informed cognitive task timing jitter (or event or stimulus presentation parameters/settings, e.g., duration

of time sample grid is on the screen) related to measuring eye-movements during stimulus presentation, interval between task stimuli, and during the response period (or fluctuations in the temporal position of fixation/eye-gaze during the M2S task events – including prior to and following stimuli and in between trials).

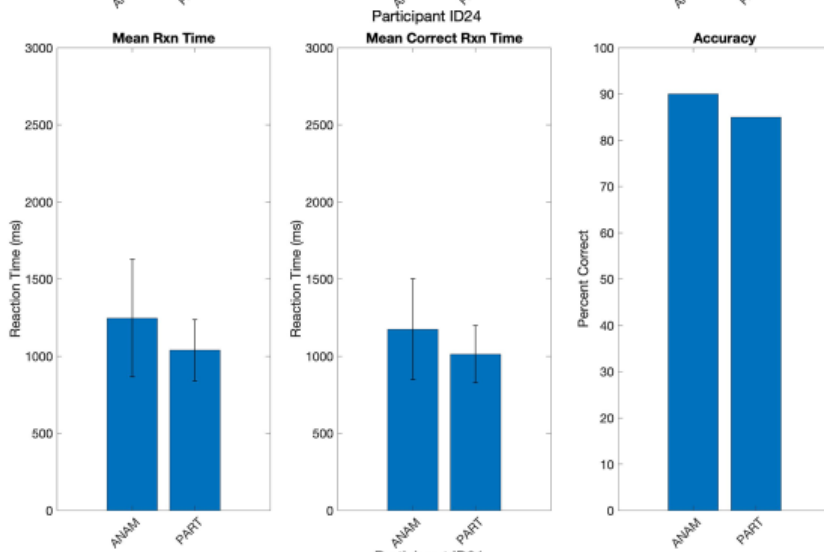
- k. Comparison of mean reaction time (both for correct and incorrect responses) as well as accuracy (total correct responses, 0-20 is possible based upon total presented trials) between the ANAM M2S and PART M2S analog task for 8 participants through build 7 approximately. The two tasks demonstrated general consistency.



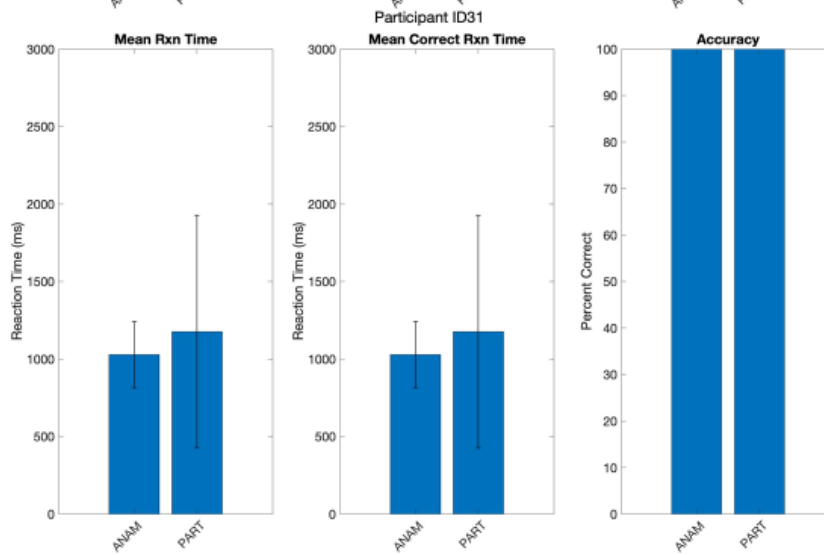
iii.



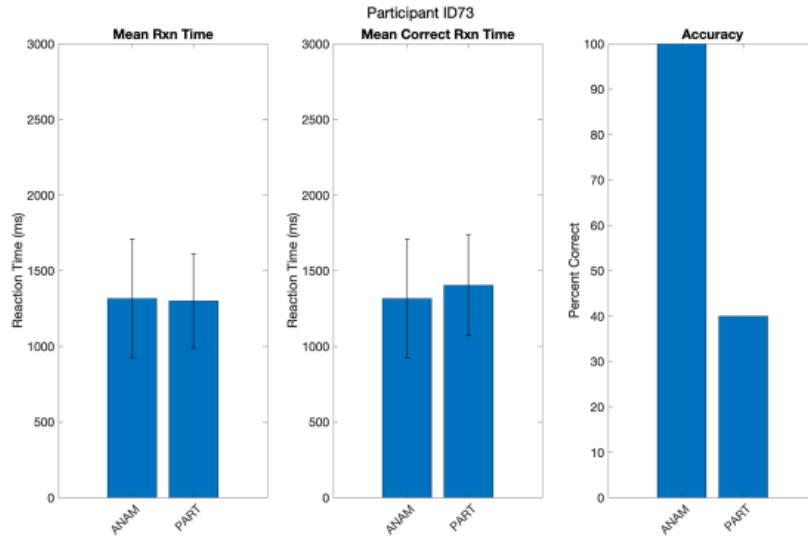
iv.



v.

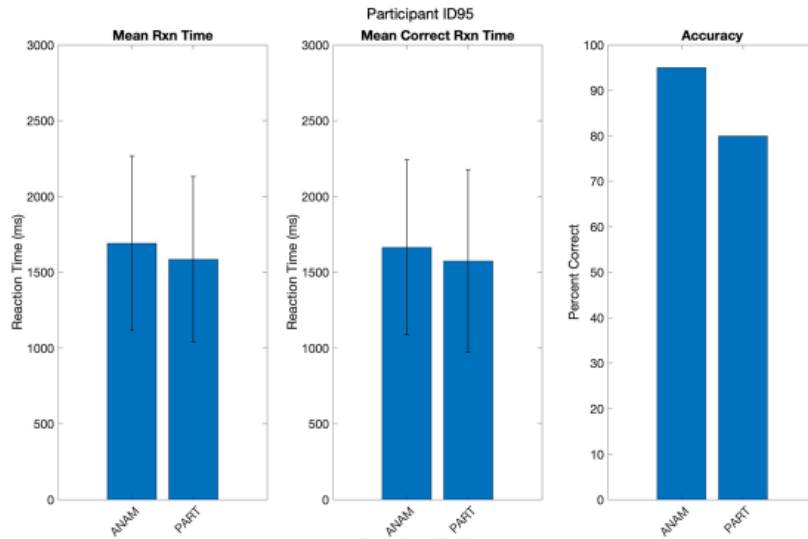


vi.

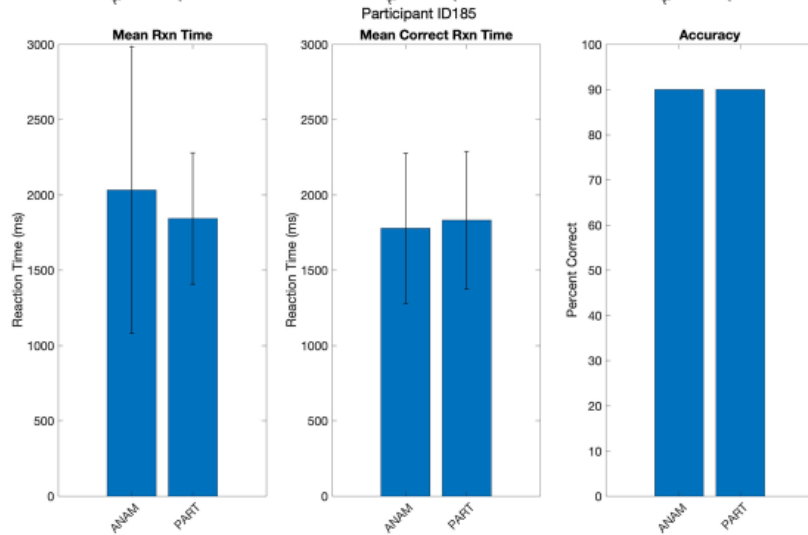


- Participant noted misunderstanding of consistent task instructions as administration sequence for this participant was PART 1st and ANAM 2nd. This has been an isolated incident.

vii.



viii.



- ix. Study participants' reaction/satisfaction to the M2S analog task has been positive to M2S analog, without noted change to task experience with inclusion of collection of eye-movements.
 - x. No presentation or publication to date given ongoing data cleaning/processing development and recent completion of pilot study.
- 3) Major activities for Task 4:
- a. PART build 10 in 2/2023 – this is the final build
 - b. Link to the final PART M2S analog (build 10):
 - i. <https://apps.apple.com/us/app/p-a-r-t/id1126512332>
 - c. Basis for final rebuild was modifying timing jitter of M2S analog to be consistent with ANAM M2S stimulus parameters, modifying eye-movement sampling rate for consistency with stimulus presentation parameters of the M2S task, time-stamping eye-movement data, and display resolution of computer.
 - d. Data has been collected for 31 participants in total, 17 participants completed the final PART build (10), including a small number of mTBI participants (all in the chronic recovery period, but one participant developed post-traumatic epilepsy) and many control participants with reported ocular, visuoperceptual, vestibular, psychiatric (e.g., Bipolar disorder), neurologic, and/or neurodevelopmental disorders (e.g., ADHD)
 - i. Although the original recruitment goal was 70 participants (35 clinical and 35 control), we are pleased to report that the initial setbacks in Years 1-2 did not prevent us from collecting data from participants. We were able to collect data on a large enough sample to accomplish the aims of the project.
 - ii. All of the PI's remaining grant funds in the NCE year went towards participant research completion incentives.
 - e. Collected eye-dominance data (right versus left), which is similar to hand dominance, as part of the final PART build. These data offer the future possibility of creating eye-movement processing (monocular versus binocular) scripts.
 - f. Collect visual (operating) distance data (physical distance of participants eyes from eye-tracker) that could also be used in future eye-movement processing scripts
 - g. Now that data collection is completed, the OHSU REDCap database has been transitioned out of production mode to only be used for data analysis purposes; see Transition Plan Questionnaire for details.
 - h. Regularly scheduled iANAM research team meetings resulted in the progression through Task 4, and included MATLAB data cleaning and processing script development and behavioral and eye-tracking measure development with PI and Co-I lab members.
 - i. Eye-movement cleaning and processing scripts continues to be developed after the writing of this Final Report. Future consideration related to data analysis will involve following behavioral/eye-tracking measures in participants with mTBI and/or visual dysfunction:
 - i. **Behavioral measures:** Accuracy (i.e. correct/incorrect response), reaction time (i.e., time required for trial response)
 - ii. **Eye tracking measures:**
 1. Distribution of latencies during stimulus and response periods
 2. Distribution of times before Eye Movements (EM) are made
 3. Latency of first EM

4. Distribution after first EM
5. Fixations during stimulus and response periods
6. Duration of fixations
7. Number of fixations on the target vs distractors
8. Switches (eye-movement from one response grid to the other response grid) during response periods script is almost complete – many iterations required
9. Number of switches between targets and distractors in clinical vs controls
10. Corrective Saccades on the target vs distractor during response period – this appears to be a relevant eye-tracking measure during response grid fixation periods with preliminary processing of initial build 10 participants

iii. **Potential Methods of Implementation**

1. **To calculate eye-movement:**
 - a. Convert the eye position data (x,y) into pixels or pixels per degree
 - b. Calculate the speed from distance and time – currently developing script to include/account for differences in individual participant visual distance
 - c. Currently using an eye velocity of 60 degrees/per second to count it as an eye movement
 2. If not an eye-movement, likely characterized as fixation measure
- 4) Specific objectives: All objectives have been completed and described in the previous section. Future work is planned to continue development of eye-movement data processing scripts, and eye-tracking and behavioral measures.
 - 5) Significant results or key outcomes:
 - a. See Major Activity documentation above for detailed discussion of iterative results/outcomes.
 - b. Continued research collaboration with Dr. Aaron Seitz as a co-investigator for iANAM (and lab/study team).
 - c. Final PART M2S analog build – build 10 - or fully integrated eye-tracking and computerized cognitive task with time stamping of eye-movement data used for clinical comparison study.
 - d. Data collection recently completed. This includes to this author's knowledge the first study to collect (simultaneous) integrated eye-movement and cognitive performance data, as well as visual acuity data for an mTBI sample.
 - e. NCE for Year 3 completed.
 - 6) Other achievements:
 - a. ANAM usage key provided by Vista Life Sciences free of charge upon consultation to allow completion of data collection in NCE Year 3 as there was no available budget for an ANAM subscription. Thank you VLS.
 - b. Dr. Tyler Duffield plans to continue this avenue of research by becoming an OHSU research volunteer. He has transferred the role of PI from an IRB regulatory standpoint to Dr. Theodoroff so that together with the rest of the study team, they will be able to conduct analytics and dissemination of results in the future. OHSU IRB transfer

approval has been obtained (see PI-transfer_CR-Check-in_Approval letter_MODCR00026666_iANAM document).

What opportunities for training and professional development has the project provided?

The project was not intended for training, but the PI has been engaged in foundational learning of the MATLAB platform with the Co-I lab member, and learning eye-tracking data cleaning/processing/analysis when using an SDK and not the GUI analysis software available through Tobii, as the Co-I lab member develops and tests scripts.

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

See Transition Plan Questionnaire

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report. Will be able to address during Transition period.

What was the impact on other disciplines?

Nothing to report. Will be able to address during Transition period.

What was the impact on technology transfer?

Nothing to report. Will be able to address during Transition period.

What was the impact on society beyond science and technology?

Nothing to report. Will be able to address during Transition period.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

- After attempting for a year to have the Co-I originally named in the grant [Dr. Parsons], assist with the work intended, the contract with his institution was terminated due to lack of follow-through with SOW activities. When pilot testing of the macros continued to not be completed, this was the final factor which necessitated finding a new Co-I to collaborate with. Following transition to the new Co-I, Dr. Aaron Seitz in Year 2, a matching-to-sample (M2S) analog was

created by Dr. Seitz and his team using the Unity game engine. The Unity game engine is the preferred development platform used by Dr. Seitz, and the M2S analog subtest was incorporated into the previously developed computerized cognitive battery by Dr. Seitz and his team, known as the Portable Automated Rapid Testing (PART) system. This allowed for the eye-tracking and computerized cognitive task to be within the same platform, or fully integrated from development, versus trying to integrate data from two different software suites running in parallel that both require highly sensitive temporal resolution. M2S is a subtest within the ANAM Military mTBI battery that is previously demonstrated to be sensitive to mTBI recovery.

- Dr. Duffield, (PI) is leaving employment at OHSU at the end of 12/2023. Due to this project being in a NCE year, it is not possible to transfer the award to another individual to be PI for the remainder of the NCE period (through 3/31/2024). What is possible and has been done is to transition from an OHSU IRB regulatory standpoint the PI on record to be Dr. Sarah Theodoroff so that work related to data analysis and processing as mentioned throughout this report can continue (see Transition Plan Questionnaire). OHSU IRB transfer approval obtained (see PI-transfer_CR-Check-in_Approval letter_MODCR00026666_iANAM document).

Actual or anticipated problems or delays and actions or plans to resolve them

See above related to change in Co-I and employment status of PI.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report.

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals

Nothing to report.

Significant changes in use of biohazards and/or select agents

Nothing to report.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Nothing to report.

Journal publications.

Nothing to report.

Books or other non-periodical, one-time publications.

Nothing to report.

Other publications, conference papers and presentations

Nothing to report.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

M2S analog task – an integrated eye-tracking and computerized cognitive task as described above.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

(a person month equals approximately 160 hours of effort).

<i>Name:</i>	Tyler Duffield
<i>Project Role:</i>	PI
<i>Nearest person month worked:</i>	Previously 2.41, 0.00 (Time worked on this grant is in-kind during NCE Year.)
<i>Contribution to Project:</i>	Grant writer, literature reviewer, iANAM variable development, iANAM hardware configuration development, IRB development and approval, ClinCard approval and activation, REDCap development and

activation, eye-movement measure development, pilot and clinical comparison study participant recruitment and data collection, will complete data analyses, interpretation, and dissemination.

Name: Aaron Seitz
Project Role: Co-I
Nearest person month worked: 0.00 (Time worked on this grant is in-kind.)
Contribution to Project: Oversight of development of eye-tracking systems, training project personnel on software systems, oversight of all eye-movement cleaning/processing scripts and eye-measure development, will assist with data analyses, interpretation, and dissemination

Name: Zachary Ruiz
Project Role: Application Programmer
Nearest person month worked: Previously 0.9 (for 10 month Year 2 budget), 0.00 (Time worked on this grant is in-kind during NCE Year.)

Contribution to Project: Programmed within Unity the PART M2S analog task.

Name: Samyukta Jayakumar
Project Role: Graduate student – MATLAB expertise
Nearest person month worked: Previously 3.7 (for 10 month Year 2 budget), 0.00 (Time worked on this grant is in-kind during NCE Year.)

Contribution to Project: Programming PART M2S data cleaning and data processing scripts within MATLAB. Assisting with eye-measure development and future programming of analysis scripts in MATLAB.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

All key personnel did not take salary (in-kind) as part of the UCR iANAM subcontract following execution of remaining budget for these activities.

What other organizations were involved as partners?

Organization Name: University of California, Riverside

Location of Organization: Riverside, California

Partner's contribution to the project:

- *In-kind support:* Primary site for eye-tracking and software development activities.

- *Facilities:* Undergraduate application programmer and graduate MATLAB expert were funded at UCR and work in Co-I's research laboratory.
- *Collaboration:* Collaborative development activities, collaborative analysis activities, and future collaborative production of scholarly materials from data generated from the grant. MATLAB expert also training PI on MATLAB platform and eye-movement cleaning/processing.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: Not applicable.

QUAD CHARTS: Not applicable.

- 9. APPENDICES:** Please see "Other" attachment for combined pdf of all referenced letters/documents created under this award.