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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) for improved clinical management of mTBI. Not having access to ANAM application programming interface (API), and identification of ANAM timing irregularities required adapting proposed eye movement metrics. Following transition to a new co-investigator (Co-I) proximal to the end of year 1, a matching-to-sample (M2S) analog 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. Given the delays in statement of work (SOW) related to transitioning Co-Is, the decision was made to focus on developing a single ANAM analog subtest sensitive to mTBI and integrated with eye-movement data. Multiple builds (9) of the analog M2S + eye-movement data have been completed during pilot testing.

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, 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 mTBI. Not having access to ANAM application programming interface (API), and identification of ANAM timing irregularities required adapting proposed eye movement metrics. It was previously attempted to retrospectively (or following completion of the testing) integrate data obtained from the eye-tracking software (e.g., area of interest) and ANAM software that ran in parallel utilizing Pulover's macro creator. Pilot testing of the macros was never completed by the original co-investigator's (Co-I) lab owhen supplied with two unpaid graduate student runs from the PI, just prior to transitioning Co-Is. Following transition to a new Co-I, Dr. Aaron Seitz, proximal to the end of year 1, a matching-to-sample (M2S) analog was created within the Co-I's lab using the Unity game engine. The Unity game engine is the preferred development platform used in the Co-I's lab, and the M2S analog subtest was incorporated into the previously developed computerized cognitive battery by Dr. Seitz and colleagues, specifically the Portable Automated Rapid Testing (PART). 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 two different data sets from different software suites 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. Given the delays in statement of work (SOW) related to transitioning Co-Is 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. Multiple builds (9) of the analog M2S + eye-movement data have been completed during pilot testing. The PART 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). 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 quite amenable to integration with an eye-tracking system/task design.

As Gazepoint is not compatible with the Unity game engine, upon transitioning to collaboration 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 used to collect eye-movements during the ANAM M2S task, which as aforementioned was then attempted to be integrated retrospectively with a macro. The Tobii analysis software was not utilized as precluded by eye-movement and cognitive data being collected simultaneously within the same PART application built in Unity. Eye-movement data cleaning and processing is completed using the MATLAB platform. MATLAB® combines a desktop environment tuned for iterative analysis and design processes with a programming language that expresses matrix and array mathematics directly. It includes the Live Editor for creating scripts that combine code, output, and formatted text in an executable notebook.

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, mTBI, headache, pain, sleep disturbance, insomnia, sleepiness, multimodal data

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Specific Aim 1: The 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 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.

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 hardware configuration and calibration of Tobii eye-tracker, CPU specifications, and desktop screen
- Subtask 2: Establish eye-tracking metrics: sampling rate, head box, fixation, saccadic, scan path, and pupillometry operationalization using eye-tracker SDK, ANAM xml output, timestamps, etc.

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.

- 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*

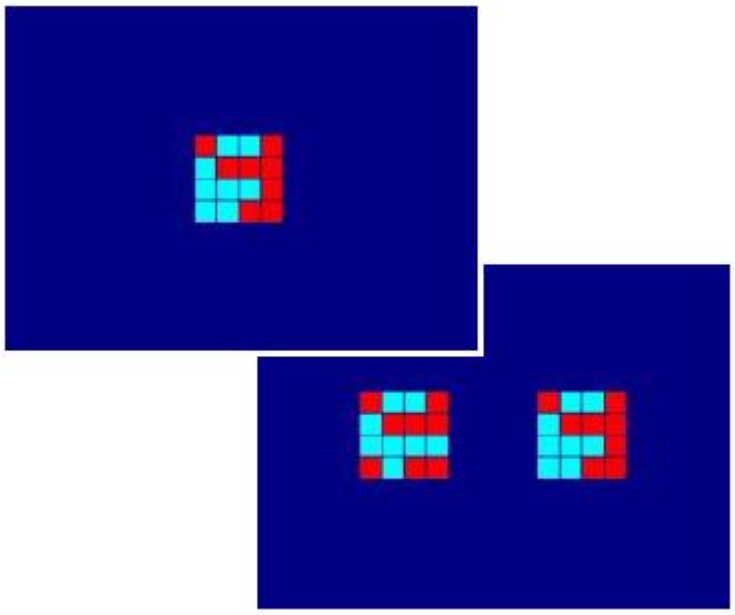
- *Milestone #6: Write and submit for publication results from iANAM versus ANAM comparison pilot testing*

What was accomplished under these goals?

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
            1. Co-I Change Letter attached
        ii. New subaward agreement, including revised SOW and revised budget, with Dr. Aaron Seitz at the University of California (UCR), approved 9-26-2022
            1. See attached AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT - W81XWH2110200
        iii. OHSU IRB modification, including the change of Co-I, approved 8/4/2022
            1. See attached approval letter
        iv. OHRO concurrence approval obtained 9-13-2022
            1. See attached concurrence approval correspondence
        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 – this remains the current build
    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. Link to the current PART M2S analog: https://drive.google.com/file/d/1CEdXBdh7WOMAgvVB1EfZZF2XDgDwAOOt/view?usp=sharing
    g. As of the writing of this report, data has recently been collected for 20 participants, including 3 clinical and several control participants with reported vision abnormalities (e.g., visuoperceptual neurodevelopmental condition which one control participant

received accommodations regarding throughout her academic tenure, including completion of their licensing examination). 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. The PART M2S analog pilot build is considered complete.

h. Screenshot of Matching to Sample (M2S) test format/structure and example trial/stimuli content:



i.

i. Data cleaning and processing is time intensive and completed on individual participant task performances/data prior to batch processing capabilities in the future. Currently creation and testing of cleaning and processing scripts is 75% complete. A graduate student with eye-tracking and MatLab expertise in Dr. Seitz's lab has been developing data cleaning and eye-movement processing scripts within MatLab in conjunction with Dr. Seitz. 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
```

```
o
o   % Stimulus displayed
o   count_stim = 0;
o   for i = 3:4:length(Data)
o       checkfield = string(fieldnames(Data(i).data));
o       str_check_stim = strfind(checkfield,'CorrectOptionDisplayed');
o       if str_check_stim{2,1} == 1
o           count_stim = count_stim + 1;
o           susp_counter=0;
o           for j = 2:length(Data(i).data.EyetrackerInfo)
o               if size(Data(i).data.EyetrackerInfo(j-
    1).EyetrackerInfo.RightEye.GazePointOnDisplayArea.x,2) == 1
o                   Stimdis(count_stim).Rx(j-1,1) = (1920 * Data(i).data.EyetrackerInfo(j-
    1).EyetrackerInfo.RightEye.GazePointOnDisplayArea.x)/pix_deg;
o                   Stimdis(count_stim).Ry(j-1,1) = (1080 * Data(i).data.EyetrackerInfo(j-
    1).EyetrackerInfo.RightEye.GazePointOnDisplayArea.y)/pix_deg_vert;
o   %                   Stimdis(count_stim).Rx(j-1,1) =
o               else
o                   Stimdis(count_stim).Rx(j-1,1) = NaN;
o                   Stimdis(count_stim).Ry(j-1,1) = NaN;
o               end
o               t1 = Data(i).data.EyetrackerInfo(j-1).t;
o               t2 = Data(i).data.EyetrackerInfo(j).t;
o               Stimdis(count_stim).T(j-1,1) = t2 - t1;
o
o               if Stimdis(count_stim).T(j-1,1)>5
o                   susp_counter=susp_counter+1;
o                   suspicious_value(count_stim,susp_counter)=t2 - t1;
o                   suspicious_value_one(count_stim,susp_counter)=t1;
o                   suspicious_value_two(count_stim,susp_counter)=t2;
o               end
o           end
o       end
o   end
o
o   %% Calculating distance and speed
o   for i = 1:length(Stimdis)
o       Stimdis(i).cumT(1,1) = Stimdis(i).T(1,1);
o       for j = 2:length(Stimdis(i).Rx)
o   %       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);
o   %       Stimdis(i).s(j,1) = Stimdis(i).d(j)/(Stimdis(i).T(j)/1000);
o           Stimdis(i).cumT(j,1) = Stimdis(i).cumT(j-1,1) + Stimdis(i).T(j,1);
o       end
o   end
o
```

```
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

%% 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;
```

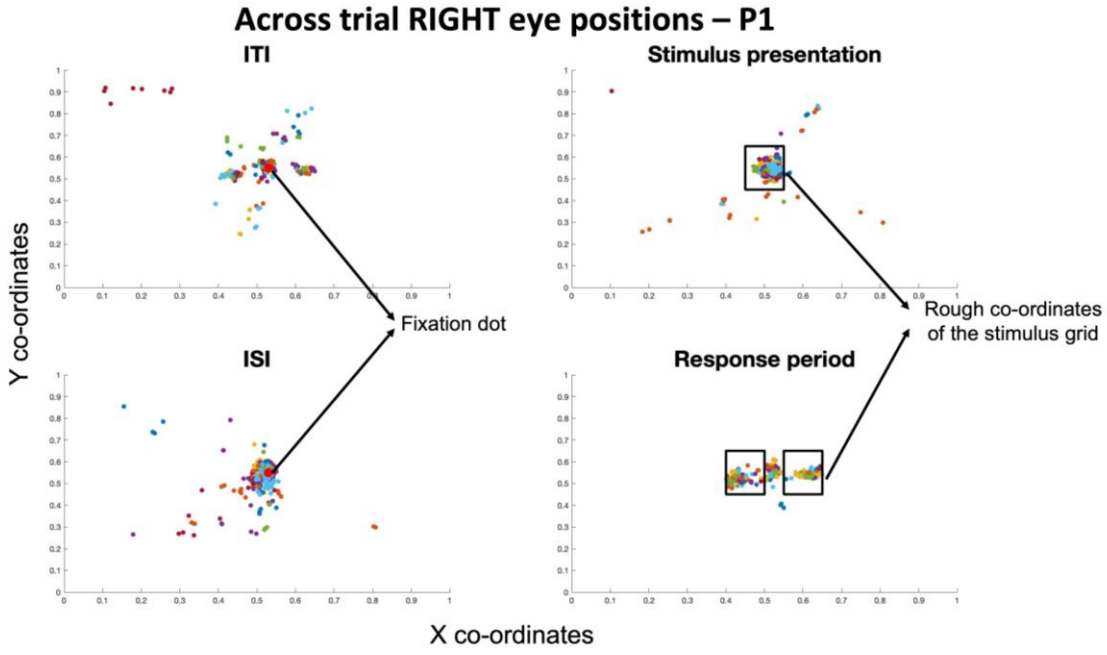
```
            Respdis(i).fix{cell,1}(count_fix,1) = Respdis(i).Rx(j);
            Respdis(i).fix{cell,1}(count_fix,2) = Respdis(i).Ry(j);
        end
    end
end

%% 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')
```

j.

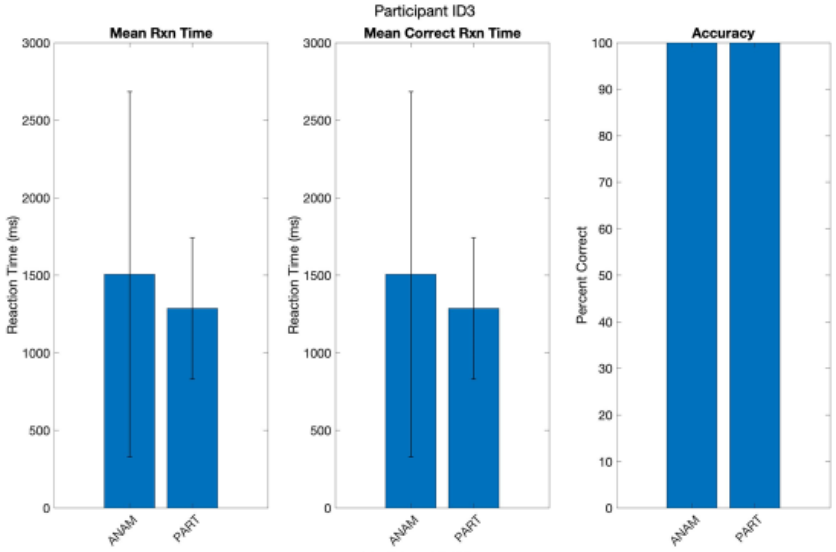


k.

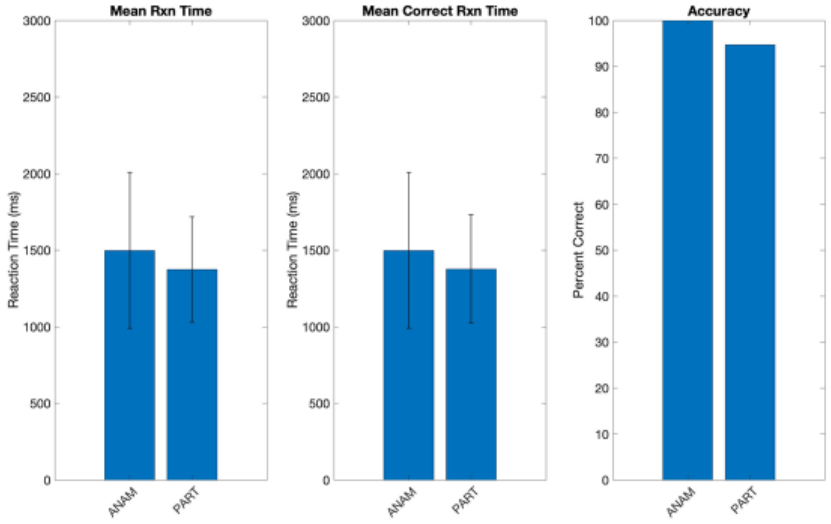
i. Above figure was examining individual eye (right) positions for the inter-stimulus intervals (ISI), inter-trial intervals (ITI), presentation of sample grid to be remembered (or "stimulus presentation"); and the "response period" where the sample grid and a foil grid are presented where the participant 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).

l. 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.

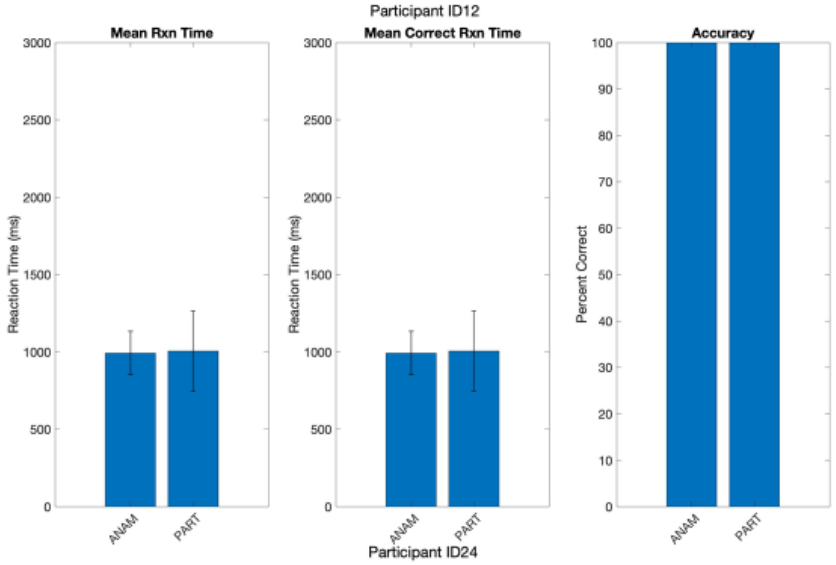
i.



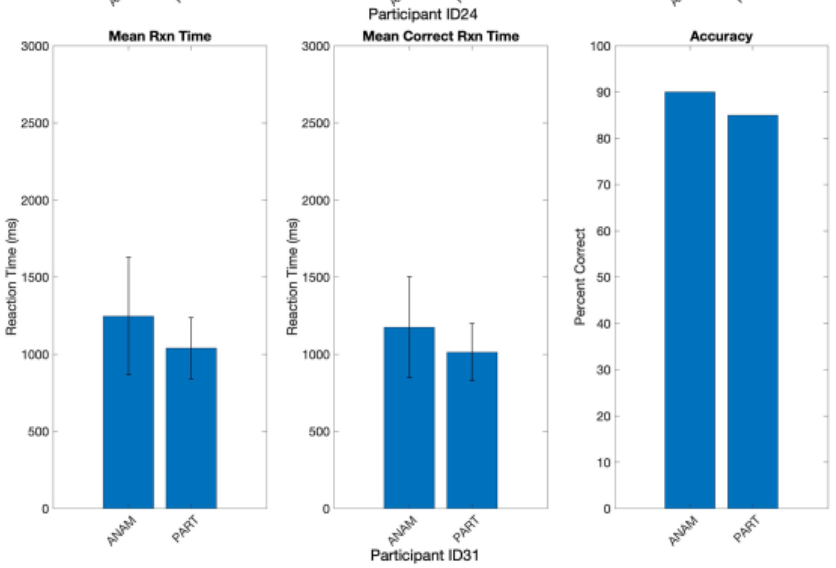
ii.



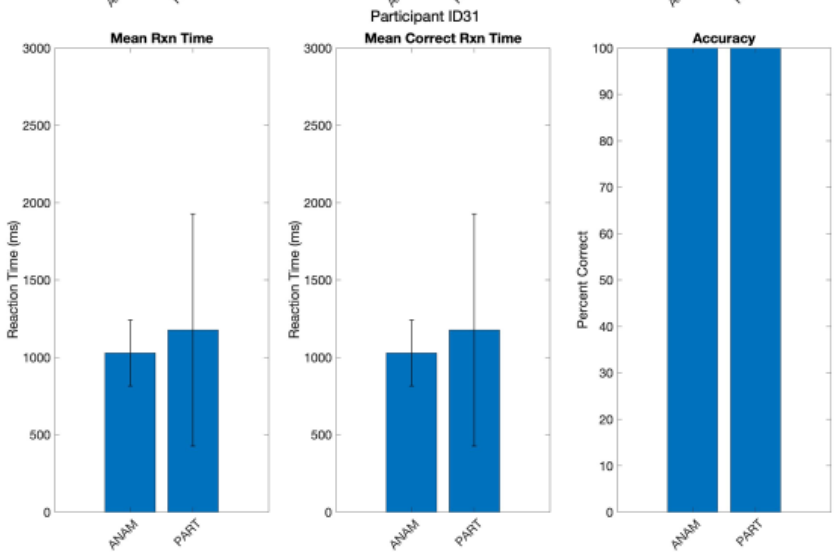
iii.


Participant ID12
Mean Rxn Time
Mean Correct Rxn Time
Accuracy
Reaction Time (ms)
Percent Correct
ANAM
PART

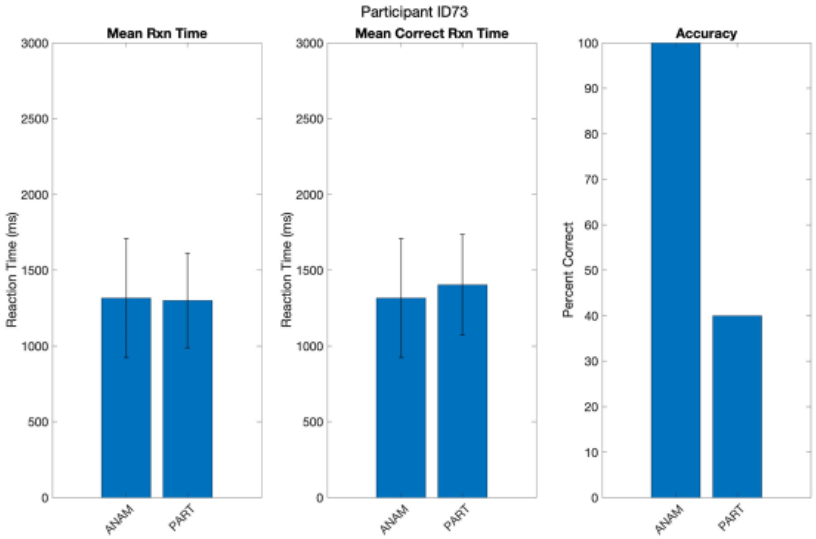
iv.


Participant ID24
Mean Rxn Time
Mean Correct Rxn Time
Accuracy
Reaction Time (ms)
Percent Correct
ANAM
PART

v.

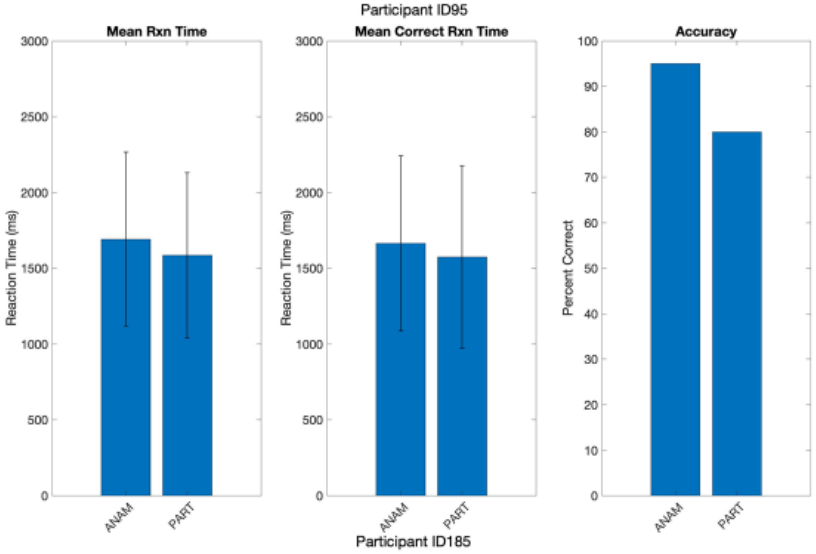

Participant ID31
Mean Rxn Time
Mean Correct Rxn Time
Accuracy
Reaction Time (ms)
Percent Correct
ANAM
PART

vi.

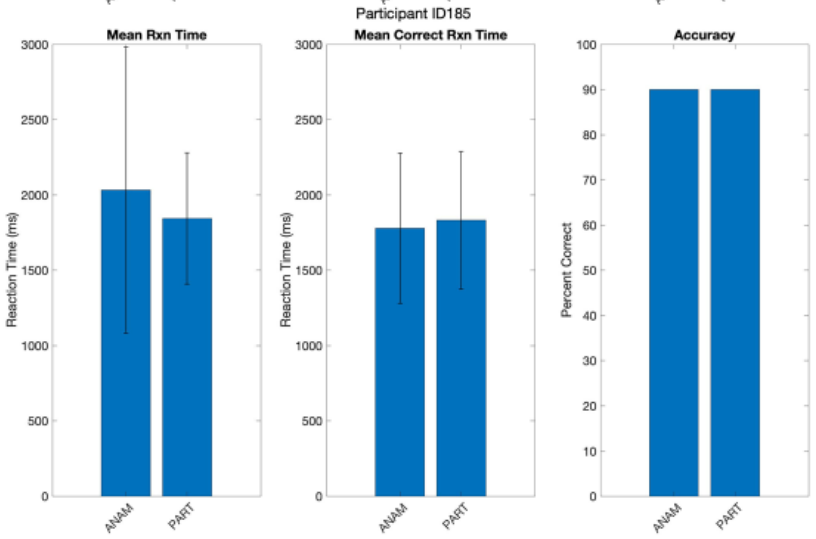


1. Participant noted misunderstanding of consistent task instructions as administration sequence for this participant was PART 1st and ANAM 2nd. This has been an isolated incident.

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. Previously approved recruitment fliers placed in several locations at the PI's medical clinic and the lobby TV screen continues as a recruitment strategy
   b. PI coordinated with Epic (name of electronic medical record) research team to build a batch control recruitment MyChart message (messaging application with electronic medical record), based upon study inclusion/exclusion criteria, for patients who have not opted out of research recruitment via MyChart. The Epic team loaded the patient list into the Epic Reporting Workbench and assisted study team with a one-time message send.
   c. PI coordinated with Epic research team to also build a silent best practice advisory (BPA) for recruitment of potential clinical participants, based upon study inclusion/exclusion criteria, for patients who have not opted out of research recruitment via MyChart. "Silent" meaning a MyChart alert is triggered within Epic to the PI when a family medicine appointment diagnosis associated with the clinical note includes any concussion related diagnoses, and does not involve the diagnosing physician during the clinical appointment to reduce/eliminate interference of the clinical visit due to study eligibility. Real time alerts will potentially allow the study team to recruit these patients in that time sensitive timeframe as proximal to injury as possible to capture recovery processes/status. The PI regularly monitors the recruitment alert tab in Epic interface and then pushes approved the MyChart recruitment message to eligible patients. Provider then selects silent BPA not trigger again for patient. Approximately daily alert frequency for eligible patients to participate in iANAM.
      i. See attached letter of MyChart recruitment message
   d. Continued use of Clincard for participant research incentive payments has not resulted in any participant issues/complaints.
   e. Annual no cost extension (NCE) approved.
   f. iANAM research team meetings interval modified to biweekly following NCE approval and progression through Major 2 and 3 tasks. Variable weekly or biweekly MATLAB data cleaning and processing script development with PI and Co-I lab members.
   g. Clinical comparison study ready to begin as eligible patients for research participation are recruited. To be completed during NCE year.
      i. All of the PI's remaining grant funds will be for participant research completion incentives. Following recent completion of 20 pilot participants, funds for 26 additional participants remains. Thus, original recruitment goal of 70 participants (35 clinical and 35 control) will not be met.
   h. As eye-movement cleaning and processing scripts continue to develop, consideration of the following behavioral/eye-tracking measures to understand differences between those with mTBI and controls have been proposed:
      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 during response periods
9. Number of switches between targets and distractors in patients vs controls
10. Corrective Saccades on the target vs distractor during response period

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
    c. Use a cut off of 30 degrees or 60 degrees to count it as an eye movement else count it as a fixation
2. If not an eye-movement, likely characterized as fixation measure

4) Specific objectives:
    a. Institutional IRB approval and HRPO approval following Co-I transition
    b. Establish new research team teleconference meetings of all key personnel to review study protocols and technical build/development metrics/ideas
    c. Purchase Tobii Nano Pro upon transition to new Co-I
    d. Include additional iANAM recruitment strategies during Co-I transition and pause in development
    e. Begin iANAM pilot testing upon completion of initial functional PART M2S analog task build and ongoing refinement of development pipeline
    f. Establish eye-tracking/software metrics: sampling rate, fixation, movements/saccades, scan path, switches operationalization using eye-tracker SDK (PART), ANAM xml output, timestamps, and review of eye-tracking cleaning/processing scripts, etc.
5) Significant results or key outcomes:
    a. See Major Activity documentation above for detailed discussion of iterative results/outcomes.
    b. Established research collaboration with Dr. Aaron Seitz as a co-investigator for iANAM and purchased new eye-tracking hardware (i.e., Tobii Nano Pro).
    c. Final PART M2S analog build (or fully integrated eye-tracking and computerized cognitive task) with time stamping of eye-movement data ready for use for clinical comparison study.
    d. Pilot data collection recently completed.
    e. NCE for Year 3 approved.
6) Other achievements:
    a. Approval from the OHSU family medicine department research program in addition to oversight approval obtained for MyChart message research recruitment (i.e., the silent BPAs discussed above) and informed PI first investigator to utilize recruitment strategy

within the department. Department interested/excited in utility of research strategy for other researchers in the department

b. Pursuit of ongoing collaboration opportunities with the new research team.

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?

1) Finish recruiting and collecting data for 26 paid participants for the clinical comparison study.
2) Finish developing/programming eye-movement cleaning/processing scripts. Then finalize behavioral/eye-tracking measures and develop/program analysis scripts.
3) Submit pilot data to FITBIR.
4) Fully process all pilot data for data analysis.
5) Run statistical analyses.
6) Write manuscript detailing results.
7) Submit manuscript for publication.
8) Submit a second manuscript for the clinical comparison study depending on progression of remaining cleaning/processing/analysis script development and programming, and timeline of remaining 26 paid participants recruitment/data collection, or consider submitting a two-part manuscript related to #6-7.

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 in Year 3 annual report.

What was the impact on other disciplines?

Nothing to report. Will be able to address in Year 3 annual report.

What was the impact on technology transfer?

Nothing to report. Will be able to address in Year 3 annual report.

What was the impact on society beyond science and technology?

Nothing to report. Will be able to address in Year 3 annual report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

- Focus on development of a single analog ANAM task (i.e., M2S) given complexity of development (i.e., identifying compatible eye-tracking system and programming platform, programming task, establishing task parameters, programming/developing cleaning and processing scripts, developing behavioral and eye-tracking measures, programming behavioral and eye-tracking measure analysis scripts, etc.) and time constraints related to transitioning co-investigators. Further basis for changes described above.

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

- U.S. Army Medical Research and Development Command administrative approval delays in new subcontract resulted in a delay in coordinated development activities.
- The reliability of pupillometry during sequential and dynamic stimulus presentation (i.e., a computerized cognitive task) is a concern generally, but likely research team will not have time to address within NCE Year 3 (as reflected in proposed eye-measures to potentially be examined noted above). Not considered needing resolved per se as numerous eye-tracking measures will be utilized with behavioral data.
- Funds available for only 26 instead of originally proposed 70 participants for clinical comparison study sample. Proposed resolution would be seeking oversight approval for clinical comparison study recruitment of additional unpaid research participants if data-analyses indicate insufficient power.
- Facilities & Administrative (F&A) costs (reduction or) waiver request was denied by OHSU school of medicine for initiating a subcontract with UCR and Dr. Seitz. This was a duplicative charge for the iANAM budget as previously incurred with initial co-investigator subcontract at UNT. OHSU Family Medicine Research Core graciously provided financial assistance to the PI to purchase the Tobii Nano Pro to avoid being over budget when initiated subcontract with Dr. Seitz at UCR and duplicative F&A charge was incurred. This also avoided the budget solution of losing PI FTE or eliminating research participant incentives to complete study activities to purchase the Tobii Nano Pro.
    - See attached FA waiver GFAMP0226A 20220726 and attached FM Research Funding Request_Duffield-3

Changes that had a significant impact on expenditures

See above and attached letters regarding duplicative F&A charge for initiating subcontract with UCR and Dr. Seitz, as well as purchase of new eye-tracker to complete study activities.

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. Will be able to address in Year 3 annual report.

  Journal publications.

  Nothing to report. Will be able to address in Year 3 annual report.

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

  Nothing to report.

  Other publications, conference papers and presentations

  Nothing to report. Will be able to address in Year 3 annual report.

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

  Nothing to report.

- **Technologies or techniques**

  PART 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).

Name:	Tyler Duffield
Project Role:	PI
Nearest person month worked:	2.41
Contribution to Project:	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:	0.9 (for 10 month Year 2 budget)
Contribution to Project:	Programmed within Unity the PART M2S analog task.
Name:	Samyukta Jayakumar
Project Role:	Graduate student – MATLAB expertise
Nearest person month worked:	3.7 (for 10 month Year 2 budget)
Contribution to Project:	Programming PART M2S data cleaning and data processing scripts within MATLAB. Assisting with eye-measure development and future programing 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?

Dr. Seitz (Co-I, key personnel) did not take salary (in-kind) as part of the UCR iANAM subcontract to allow limited remaining available funds to be dedicated to development/development personnel.

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.