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14. ABSTRACT

The majority of moderate and mild TBI (mTBI) patients report self-described visual and/or auditory (i.e. sensory) dysfunction and yet they often pass standard eye and hearing exams. Further, 80% of TBI patients are diagnosed as mTBI and appear normal on a standard CT or MRI scan. Due to the inherent variability of trauma, no single trauma case is exactly like another. This variability in combination with the lack of profound damage in mTBI patients in particular has made diagnosis of these patients challenging. The lack of an objective quantitative clinical metric for these changes in sensory function also prevents the initiation of clinical trials. Further, it highlights the lack of understanding of the underlying cause of the sensory dysfunction. Without an understanding of mechanism, rational therapies cannot be developed. The goals of this study are to identify sensitive, objective, quantitative tests to serve as diagnostics and outcome measures for sensory dysfunction in TBI patients and to better understand the physiological basis of sensory dysfunction. We hypothesize that combining objective structural and functional assessments in the same subjects is more likely to overcome the inherent variability of trauma and yield useful diagnostic metrics than would each test separately. Thus, we propose that a combination of assessments including a single metric that indexes integrative sensory abilities, and utilization of new, sensitive algorithms may be required for accurate diagnosis.

15. SUBJECT TERMS
mild traumatic brain injury (mTBI); visual dysfunction; auditory dysfunction; magnetic resonance imaging (MRI); electroencephalogram (EEG); visual evoked potential (VEP); auditory evoked potential (AEP); optical coherence tomography (OCT)

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INTRODUCTION

The majority of moderate and mild TBI (mTBI) patients report self-described visual and/or auditory (i.e. sensory) dysfunction and yet they often pass standard eye and hearing exams. Further, 80% of TBI patients are diagnosed as mTBI and appear normal on a standard CT or MRI scan. Due to the inherent variability of trauma, no single trauma case is exactly like another. This variability in combination with the lack of profound damage in mTBI patients in particular has made diagnosis of these patients challenging. The lack of an objective quantitative clinical metric for these changes in sensory function also prevents the initiation of clinical trials. Further, it highlights the lack of understanding of the underlying cause of the sensory dysfunction. Without an understanding of mechanism, rational therapies cannot be developed. The goals of this study are to identify sensitive, objective, quantitative tests to serve as diagnostics and outcome measures for sensory dysfunction in TBI patients and to better understand the physiological basis of sensory dysfunction. We hypothesize that combining objective structural and functional assessments in the same subjects is more likely to overcome the inherent variability of trauma and yield useful diagnostic metrics than would each test separately. Thus, we propose that a combination of assessments including a single metric that indexes integrative sensory abilities, and utilization of new, sensitive algorithms may be required for accurate diagnosis.

Keywords:
mild traumatic brain injury (mTBI); visual dysfunction; auditory dysfunction; magnetic resonance imaging (MRI); electroencephalogram (EEG); visual evoked potential (VEP); auditory evoked potential (AEP); optical coherence tomography (OCT)

BODY: Research Findings in alignment with SOW

Specific Aim 1: To derive a combination of objective and quantitative metrics to diagnose visual and/or auditory dysfunction after TBI.

Major Task 1: Obtain IRB approval.

We obtained full IRB and HRPO approval for all sites.

Major Task 2: Recruit, enroll, and screen potential subjects.

All subjects were recruited and assessed at VUMC. Sixty-five individuals consented to participate in this study. Inclusion criteria consisted of self-identified males and females from all racial and ethnic backgrounds who were at least 18 years of age or older and who experienced an mTBI (Glasgow coma score between 13 and 15; for the mTBI group) or with no history of mTBI (for the control group). Persistent auditory complaints were not required for inclusion in the mTBI group. Exclusion criteria included (i) a history of eye or ear disease, (ii) severe TBI (Glasgow coma scale <13), (iii) subjects with metallic implants, or exposure to metal fragments (i.e., MRI contraindication), (iv) children under the age of 18 years; and (v) pregnant females. Two participants (2 males; 1 with mTBI) were excluded prior to completing the study due to meeting 1 or more exclusion criteria defined above. Thus, the data from 63 participants were included in the analyses for this study. Participants were divided into two groups. The control group, including individuals with no reported or documented history of mTBI, consisted of 35 participants (26 females; 9 males) ranging in age from 23 to 71 years (mean: 39 years). Of the 10 control participants who reported their race and ethnicity, 9 identified as White and non-Hispanic

and 1 identified as Black and non-Hispanic. The mTBI group consisted of 28 participants (13 females; 15 males) ranging in age from 19 to 72 years (mean: 35 years). Of the 19 participants with mTBI who reported their race and ethnicity, 18 identified as White and non-Hispanic and 1 identified as White and Hispanic. The reported causes of mTBI included 10 participants involved in motor vehicle accidents, 6 fall-related injuries, 6 non-violent blunt-force trauma-related injuries, 3 sports-related injuries, 1 combat blast-related injury, 1 injury related to domestic violence, gun violence, or other form of assault, and 1 unspecified injury. Of the participants in the mTBI group, 19 participants reported a loss of consciousness at the time of their TBI.

All TBI subjects completed the neurobehavior symptom inventory (NSI). We are missing NSI responses from two subjects for a total of 26. Out of this total, 65% self-reported vision problems, sensitivity to light, and sensitivity to noise. 38% reported difficulty hearing. However, only 8% of subjects reported moderate to severe levels of vision problems or hearing difficulty and 15% reported moderate to severe levels of sensitivity to light or noise. Below we will indicate where we have looked to see if there was any correlation between these self-reports and findings on the assessments that were performed in the study.

Major Task 3: Measure retinal thickness, accommodation, convergence, acoustic reflex, and VEPs and AEPs in all subjects.

All subjects were measured at 20/20 BCVA with refraction and had a normal fundus exam. No group differences were detected in the Humphrey visual field (HVF) foveal sensitivity (**Fig. 1A**) or mean deviation (**Fig. 1B**) assessments. However, there were outliers in the TBI, but

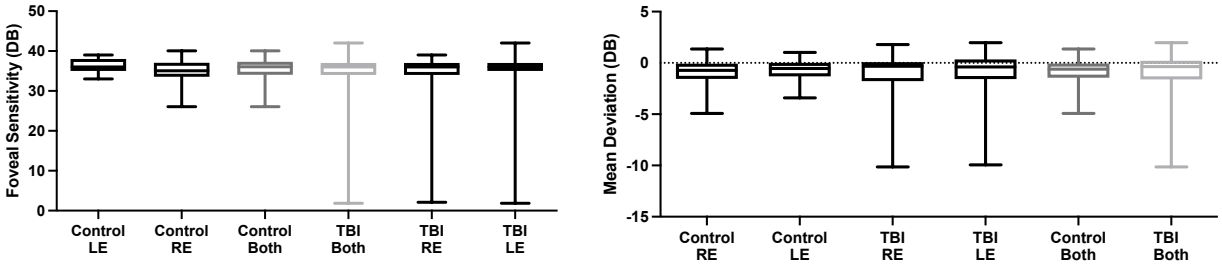

Figure 1. Quantification of foveal sensitivity (A) and mean deviation (B) by HVF in age-matched groups.

not the control, groups. We will follow up to see if the subjects that performed poorly on the visual fields also showed deficits in other assessments. MAJ Lucas Groves, MD, has completed the quality assessment of the peripapilary retinal nerve fiber layer (RNFL) thickness obtained by OCT and the VF images to assure they meet clinical threshold standards we only include data here that passed that threshold. The OCT data shows differences ($p<0.05$) between these groups. The RNFL thickness was similar in most retinal regions. However, we detected thickening of the superonasal region, $p<0.01$ (**Fig. 2A**). High individual variability is known to exist with OCT and demonstrates the strength of

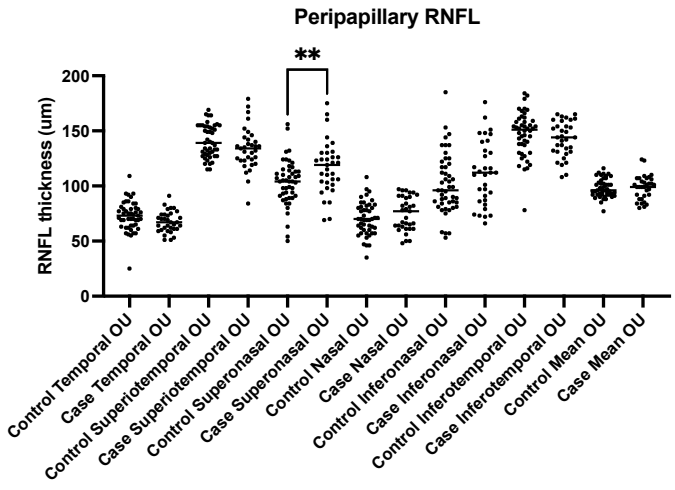

Figure 2. Quantification of OCT peripapillary RNFL thickness.

longitudinal OCT measurements whenever possible. However, the fact that we are detecting group differences is compelling and agrees with the few longitudinal OCT studies on TBI subjects that have been performed to date.

We detected differences in the visual evoked potential (VEP) in terms of amplitude and the binocular summation index (**Fig. 3**). The decrease in VEP amplitude suggests a loss of axons along the visual pathway. The increased binocular summation index could indicate loss of inhibitory signaling.

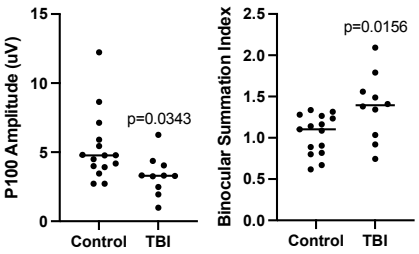

Figure 3. Quantification of VEP amplitude (A) and binocular summation index (B).

We also assessed accommodation and convergence since multiple publications have reported deficits in this population (for review see Merezhinskaya et al., 2019). We graphed the results in our subjects on the age-adjusted Hofstetter plot (**Fig. 4**). Some of our subjects were over the age of 50 and thus accurate assessments could not be obtained. Within those subjects under the age of 50, approximately 30% had deficits in the amplitude of accommodation (**Fig. 4**). We also detected a group difference in convergence function (**Fig. 4**). These results are being written up for publication. We will also be presenting on these results at the 8th Military Vision Symposium.

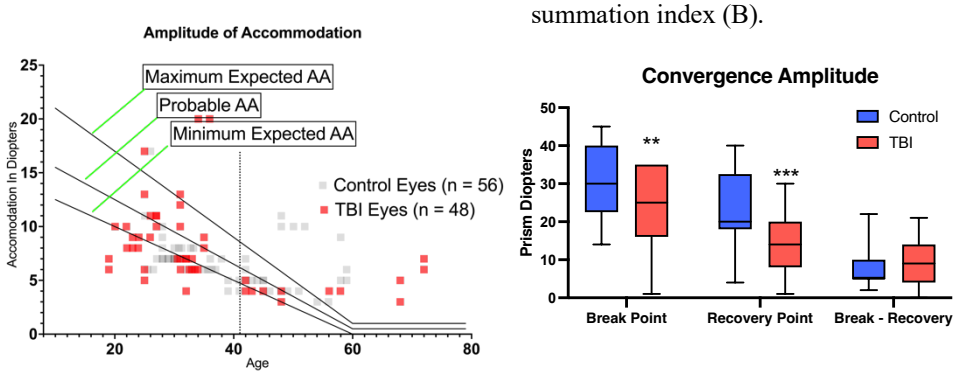

Figure 4. Effects of TBI on ocular motor function. Quantification of amplitude of accommodation overlaid on the Hofstetter plot of changes in accommodation over age (A). Quantification of convergence (B).

All participants completed ear-specific behavioral air- and bone-conducted pure-tone threshold testing using a Grason-Stadler Instruments (GSI) 61 audiometer coupled to Etymotic Research (ER) 3A insert earphones (air-conduction thresholds, standard audiometric frequencies), Sennheiser supra-aural headphones (air-conduction thresholds, extended high frequencies), or a bone oscillator (bone-conduction thresholds) (**Fig. 5**). Air-conducted pure-tone thresholds were measured at standard audiometric octave frequencies from 0.25 to 8 kHz, including the 3 and 6 kHz inter-octave frequencies, and at extended high-frequencies including 9, 10, 11, 12, 14, and 16 kHz. Bone-conducted thresholds were measured at 0.5, 1, 2, and/or 4 kHz only when air-conduction thresholds exceeded 20 dB HL at a given frequency.

Participants also completed tympanometry and MEMR threshold testing using the GSI Tympstar Pro coupled to rubber ear-tips. We required participants to have normal middle-ear function defined by a mobile tympanic membrane with compliance ³0.2 mmho and tympanometric peak pressure between -100 and +100 decaPascals. MEMRs were measured

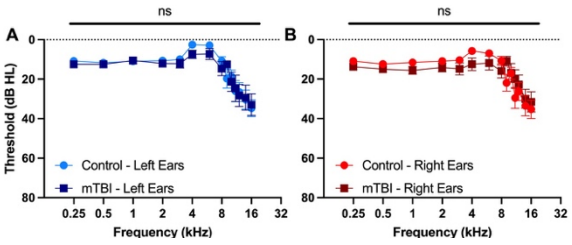

Figure 5. Quantification of audiograms in left (blue) and right (red) ears of control and mTBI subjects.

using a 0.226 kHz probe tone and ipsilateral and contralateral presentation of 0.5, 1, 2, and 4 kHz pure-tone and broadband noise (BBN) elicitors. The MEMR conditions measured in this study were: right ipsilateral (elicitor: right; probe: right), left ipsilateral (elicitor: left; probe: left), right contralateral (elicitor: left; probe: right), and left contralateral (elicitor: right; probe: left). We defined the MEMR threshold as the elicitor level (dB HL) that resulted in a change in tympanic membrane compliance of ³0.02 mmho. Additionally, we ensured growth of the MEMR by measuring responses 5 dB above and below the threshold level. This criterion represents the standard clinical protocol for measuring MEMR threshold; however, it may overestimate MEMR threshold level (e.g., Sun, 2008).

We measured participants' speech understanding in quiet by presenting recorded and calibrated NU6 monosyllabic word recognition lists that were ordered by difficulty (Hurley and Sells, 2003), using a custom software package routed through a GSI 61 audiometer coupled to ER 3A insert earphones. The presentation level for word recognition was 40 dB HL above the level of the participants' speech recognition threshold (SRT) for each ear, respectively. This level is often referred to as 40 dB sensation level (SL). If 40 dB SL exceeded the participant's loudness discomfort level, the presentation level that was used was recorded for reporting. A minimum of 20 dB SL was recommended. Each participant was presented with a full 25-word list despite the possibility that they may have reached the stopping criterion for a 10-word list (i.e., a score of 90% correct or greater based on responses to the first 10 words in the list). A percent correct score was calculated based on the subjective assessment of a licensed and certified audiologist with normal hearing or assisted-to-normal hearing. We converted NU6 percent correct scores to Rationalized Arcsine Units (RAU) due to ceiling or near-ceiling performance on this task. Speech understanding in background noise was measured using a recorded version of the QuickSIN (Killion et al., 2004) presented with multi-talker babble via insert earphones with the speech stimulus fixed at 70 dB HL. The QuickSIN provides an estimate of signal-to-noise ratio (SNR) loss based on the participant's ability to repeat key words from target sentences presented in SNRs ranging from 25 to 0 in 5 dB SNR steps. We presented 2 QuickSIN lists per ear and calculated the average SNR loss for each ear.

DPOAEs were measured for each ear at the cubic distortion frequency of 2f1-f2 with f2 primary tone frequencies ranging from 0.5 to 8 kHz at 4 points per octave and a frequency ratio of f2/f1=1.22. We measured DPOAEs using 2 different primary tone levels: (i) L1=65 dB SPL and L2=55 dB SPL (i.e., 65/55 dB condition) and (ii) L1=L2=70 dB SPL (i.e., 70/70 dB condition). All DPOAE testing was completed using the Mimosa Acoustics HearID hardware and software platforms coupled to an ER 10C probe with foam ear-tip. The DPOAE variables used for statistical analysis included the amplitude of the DPOAE for each frequency.

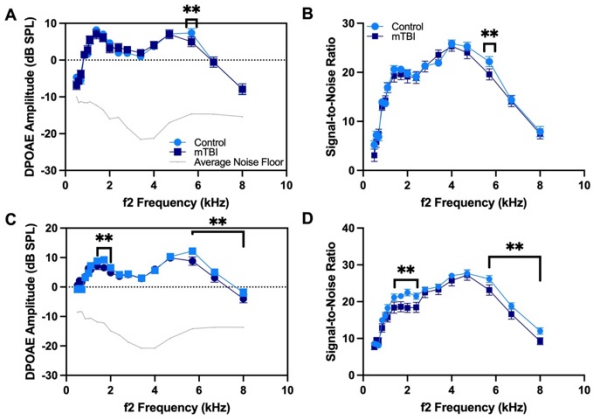

Figure 6. Quantification of DPOAE amplitude and signal to noise ratio in left and right ears of control and mTBI subjects.

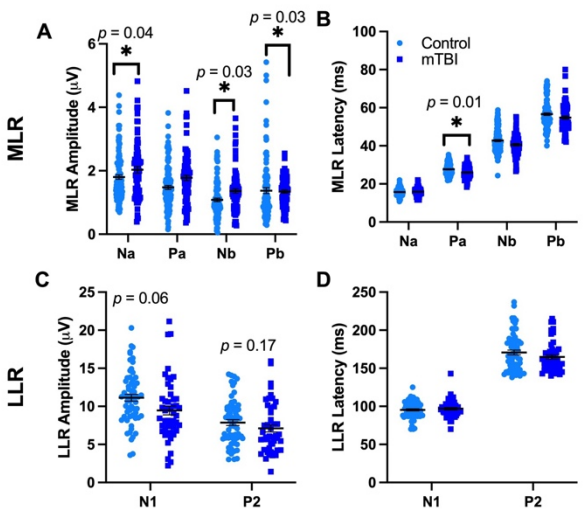

Figure 7. Quantification of MLR and LLR amplitude and latency in control and mTBI subjects.

We have applied linear mixed effect modeling to assess statistical significance of the results. The standard frequency range audiogram was normal in the mTBI subjects (**Fig. 5**). The ABR was similar between groups at all conditions tested (data not shown). In contrast, we detected frequency specific decreased function in the DPOAE amplitude and signal to noise ratio (**Fig. 6**). A group by age interaction was detected in the DPOAE amplitude that differed between the control and mTBI subjects. While not diagnostic, it does suggest a root cause for some of the self-reported auditory dysfunction.

The middle ear muscle reflex (MEMR) is a response to loud noises to protect the auditory system. We did not detect a difference between groups at low frequencies (0.5-4kHz). However, when we applied linear mixed effect modeling to the data we detected a group by frequency interaction, p=0.056 (data not shown).

Statistically significant differences were also detected in the amplitude of aspects of the MLR (**Fig. 7**). We neared significance in the LLR amplitude between groups.

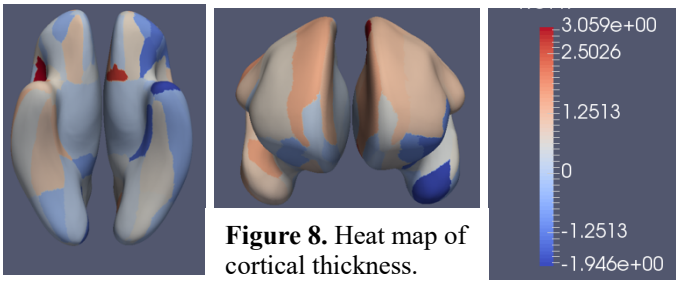

Figure 8. Heat map of cortical thickness.

Specific Aim 2: To identify and track alterations in the brain that underlies self-reported sensory deficits after TBI.

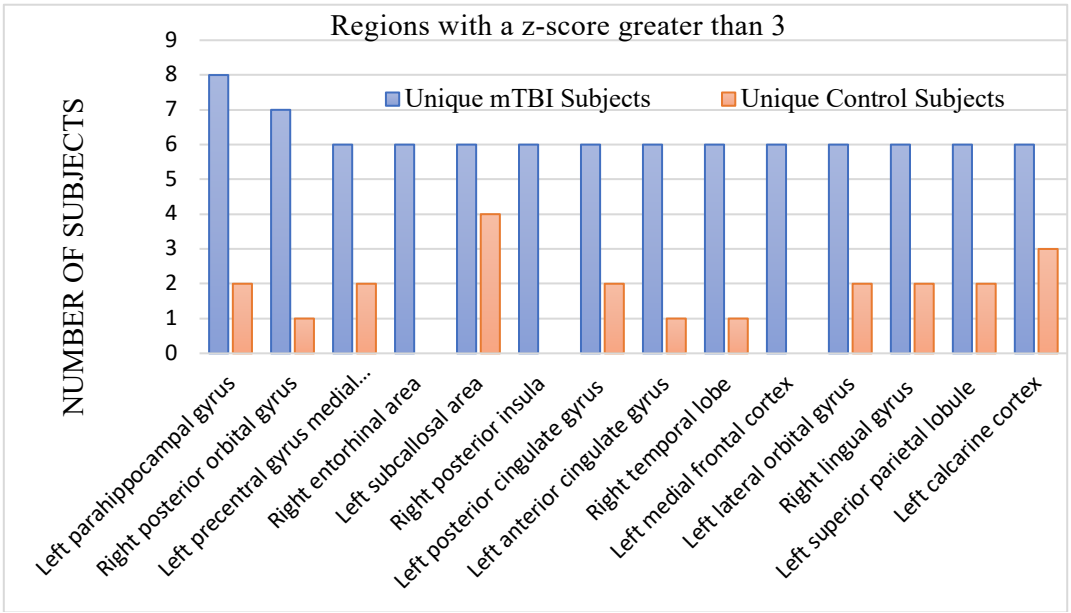

Figure 9. Differences in brain region thickness between control and mTBI subjects.

We have identified brain regions that differ in their size/shape from controls by a z-score of 3 or higher. **Fig. 8** shows a representative z-score heat map of a TBI subject brain. **Fig. 9** shows the number of control and TBI subjects with a z score of greater than 3 in terms of the difference in size from the control average. While a lot of variability is present in the left subcallosal area, most of the areas have very few normals in this range outside of normal average values. Multiple areas differed significantly in size in TBI subjects only including the right entorhinal area, right posterior insula, and left medial frontal cortex. Several other areas were different in many TBI subjects but only 1-2 control subjects: left parahippocampul gyrus, right posterior orbital gyrus, left precentral gyrus medial segment, left posterior and left anterior cingulate gyri, right temporal lobe, left lateral orbital gyrus, right lingual gyrus, and left superior parietal lobe. Descriptions of the functions of each of these brain regions are listed in **Table 1**.

Table 1

Region	Function
Left Parahippocampal Gyrus	Spatial memory and navigation
Right Posterior Orbital Gyrus	Odor perception
Left Precentral Gyrus Medial Segment	Voluntary motor movement
Right Entorhinal Area	Higher-order processing and memory
Left Subcallosal Area	Emotion and fear response
Right Posterior Insula	Thermosensory function and pain perception
Left Posterior Cingulate Gyrus	Cognition
Left Anterior Cingulate Gyrus	Emotion and decision making [21]
Right Temporal Lobe	Sensory processing, language, memory [22] – [23]
Left Medial Frontal Cortex	Attention, organizing motor response, evaluating risk [24]-[26]
Left Lateral Orbital Gyrus	Odor perception [15]
Right Lingual Gyrus	Visual processing, specifically familiar scenes and faces [27]
Left Superior Parietal Lobe	Visuospatial perception and attention [28]
Left Calcarine Cortex	Visual processing, specifically color processing and orientation [28]

Not surprisingly, several areas are associated with cognition, memory, and emotion – all functions known to be altered by TBI. Particularly interesting for our study is the detection of size differences in three visual areas: the right lingual gyrus, left superior parietal lobe, and the left calcarine cortex (i.e. visual cortex). We then looked for correlations between these three visual areas and self-reported visual symptoms from the NBSI as shown in **Table 2.** Surprisingly there was no clear correlation between self-reported systems and the size differences detected by MRI for the TBI subjects reporting mild to moderate symptoms. In contrast, the two subjects who reported very severe vision problems and severe light sensitivity also had significant size differences in all three visual areas.

Table 2

	TBI… [VKY]	TBI… [EPV]	TBI… [DE0]	TBI… [PV9]	TBI… [ZXA]	TBI… [DF3]	TBI… [GKQ]	TBI… [HZW]	TBI… [BZP]	TBI… [YX6]	TBI… [VK3]	TBI… [VVV]	TBI… [HJG]	
NBSI Self-Reported Vision Problems	Mild	Mild	None	Moderate	Moderate	None	Very Severe	None	None	None	None	Very Severe	Mild	Mild

NBSI Self-Reported Light Sensitivity	Moderate	Severe	None	Mild	Moderate	None	Severe	None	None	None	Mild	Severe	Moderate	Severe
Right Lingual Gyrus z-score greater than 3	No	No	No	Yes	No	Yes	Yes	No	Yes	No	No	Yes	Yes	No
Left Superior Parietal Lobe z-score greater than 3	No	No	Yes	No	No	No	Yes	Yes	No	Yes	Yes	Yes	No	No
Left Calcarine Cortex z-score greater than 3	Yes	Yes	No	No	Yes	No	No	Yes	Yes	No	No	No	No	Yes

Specific Aim 3: To identify deficits in multi-sensory integration and the cortical correlates of these deficits in complex TBI patients.

We have analyzed the behavioral aspect of the sensory integration tasks. In the stimulus reaction time task results we did not detect a different between the control and TBI groups in the visual, auditory, or audio-visual stimuli assessments. In the simultaneity judgement task there was also no difference in some of parameters, however, we are starting to possibly pull out differences in the number of correct responses and possibly a shift in the overall binding window for the TBI group. We need to add results from the subjects added in 2022 and analyze the corresponding EEG recordings.

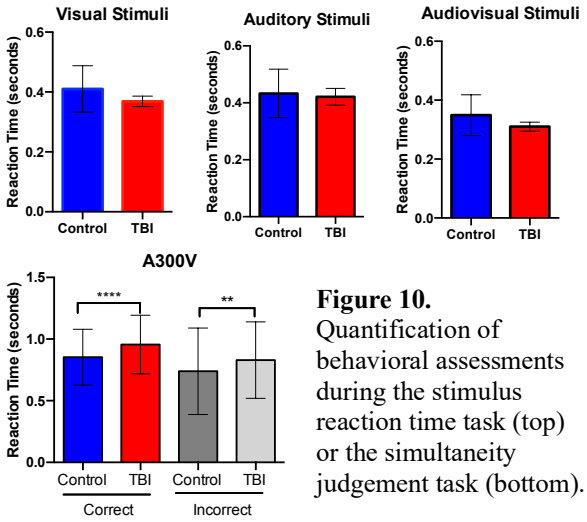

Figure 10. Quantification of behavioral assessments during the stimulus reaction time task (top) or the simultaneity judgement task (bottom).

Major Activities:

We have presented results from this project at conferences, published four manuscripts, submitted an additional manuscript, and have at least one more in preparation. We also have identified colleagues to analyze the resting state EEG data for a possible future publication. Finally, we received a good score on a follow-on NEI R01 application and have resubmitted it. The study would continue the MRI and visual assessments and would utilize data in the FITBIR database in order to obtain sufficient subjects for machine learning approaches. It is being reviewed in March.

REPORTABLE OUTCOMES

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

We have contributed to change in practice for TBI patients seen in optomotry or ophthalmology clinics in the DoD. Using our MRI dataset we have demonstrated the potential power of machine learning to pull out differences between TBI and control subjects and have used data from this project as preliminary data for an R01 grant that would not only continue the prospective study but also mine relevant data from the FITBIR database in order to obtain the numbers needed for a machine learning approach.

We have submitted an additional paper (on Audiological findings) and have another in preparation (on Ophthalmological findings).

Publications:

Kerley CI, Schilling KG, Blaber J, Miller B, Newton A, Anderson AW, Landman BA, **Rex TS**. (2020) MRI correlates of chronic symptoms in mild traumatic brain injury. *SPIE Medical Imaging*, International Society for Optics and Photonics. 11313:113132Q.

Schilling KG, Blaber J, Hansen C, Rogers B, Anderson AW, Smith S, **Rex TS**, Kanakaraj P, Resnick SM, Cutting L, Woodward N, Zald D, Landman BA. (2020) Distortion correction of diffusion weighted MRI without reverse phase-encoding scans or field-maps. *PLoS One* 15:e0236418

Elenberger J, Kim B, de Castro-Abeger A, **Rex TS.** (2020) Potential role for intrinsically photosensitive retinal ganglion cell dysfunction in TBI symptomology. *Neurology* 95: 826-833.

Kerley CI, Cai L, Yu C, Crawford LM, Schilling KG, Landman BA, **Rex TS.** (2021) Joint analysis of structural connectivity and cortical surface features: correlates with mild traumatic brain injury. *SPIE Medical Imaging*. 11596:115960R.

Stahl A, Racca JM, Dwyer RT, Berg KA, Holder JT, Hood LJ, Giffort RH, Rex TS. (submitted) Audiological deficits detected in individuals with chronic mild TBI. *Frontiers in Neurology*

Conference papers and presentations:

Kerley C, Schilling KG, Blaber J, Miller B, Newton A, Anderson AW, Landman BA, **Rex TS.** (2020) MRI correlates of chronic symptoms in mild traumatic brain injury. SPIE IP:MI. Houston, TX

Elenberger J, Crawford L, Singh E, Kerley C, Chen Q, Lavin P, Landman B, Anderson A, Colyer M, **Rex TS.** (2020) Ophthalmological findings from a pilot study of chronic mTBI subjects. Southeastern Vision Conference

Elenberger J, Crawford L, Singh E, Diethelm C, Lavin P, Kerley C, Anderson A, Landman B, **Rex TS**. (2020) Preliminary visual findings in mild TBI patients. Southeastern Vision Research Conference. poster.

Kerley CI, Cai L, Yu C, Crawford LM, Elenberger JM, Singh ES, Schilling KG, Aboud K, Landman BA, **Rex TS.** (2021) Joint analysis of structural connectivity and cortical surface features: correlates with mild traumatic brain injury. *SPIE Medical Imaging*: *Image Processing*. San Diego, CA. Oral Presentation

Singh E, Kerley CI, Crawford L, Elenberger J, Longmuir R, Anderson A, Landman B, **Rex TS**. (2021) Structural changes in visual areas detected by MRI in chronic mild TBI subjects. *Military Health Services Research Symposium* Cancelled due to COVID-19. Oral Presentation

Al Hussein Al Awamlh S, Crawford L, Elenberger J, Singh E, Diethelm C, Chen Q, Lavin P, Longmuir R, **Rex TS**. (2021) Few ophthalmological deficits in mild TBI subjects compared to age-matched controls. *Military Health Services Research Symposium* Cancelled due to COVID-19

Singh E, Kerley CI, Crawford L, Elenberger J, Longmuir R, Anderson A, Landman B, **Rex TS**. (2021) Structural changes in visual areas detected by MRI in chronic mild TBI subjects. *National Neurotrauma Symposium* virtual due to COVID-19

Al Hussein Al Awamlh S, Crawford L, Elenberger J, Singh E, Diethelm C, Chen Q, Lavin P, Longmuir R, **Rex TS**. (2021) Few ophthalmological deficits in mild TBI subjects compared to age-matched controls. *National Neurotrauma Symposium* virtual due to COVID-19

Rex TS, Al Hussein Al Awamlh S, Crawford L, Elenberger J, Singh E, Diethelm C, Chen Q, Groves L, Lavin P, Longmuir R. (2023) Few ophthalmological deficits in mild TBI subjects compared to age-matched controls. *6th Military Ocular Trauma Symposium* Boston, MA

CONCLUSIONS

We did not meet enrollment goals due to situations outside of our control including regulatory delays and COVID. As a result, we were unable to apply the analyses that we had originally planned. Despite this setback, we identified differences between controls and TBI subjects. It is notable that we chose the TBI group that is easiest to recruit – mild and chronic – but has the fewest and most subtle findings. The presumption is that if we can detect differences in this group then the same assays should result in even more robust differences in moderate and/or acute/subacute TBI subjects.

We detected group level differences in multiple assays despite our lower than desired recruitment numbers. In terms of visual dysfunction, we detected group differences in both ocular motor function and visual evoked potentials (VEP). Notably, there was not a clear correlation between measured deficits and self-reported symptoms. We detected decreased amplitude of accommodation as expected. We also detected decreased VEP amplitude and increased binocular summation index suggestion alterations in intermediate neuron signaling in the brain. We also detected a thinner temporal RNFL in TBI subjects as compared to controls, Notably, our data agrees with findings from other TBI studies showing decreased amplitude of accommodation, decreased VEP amplitude, and decreased temporal thinning of the RNFL. The finding of increased binocular summation index is a new finding from this study.

In terms of auditory dysfunction, we detected group differences in the middle ear muscle reflex (MEMR) and in the DPOAE. Again, there was no clear correlation with self-report of symptoms.

We did not pull out any clear differences in response times to the sensory integration tasks. We also have not had a chance to analyze the resting state EEG. However, we have reached out to colleagues on campus with expertise in this area to perform analyses. We detected structural differences in the cortex by MRI. We have published some of these findings. We have submitted an R01 grant application to continue the MRI and vision-related aspects of this study with the goal of applying machine learning to a larger cohort through another prospective study as well as data mining in the FITBIR database.

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APPENDICES

See attached updated Quad Chart and enrollment data.

REPORT OF INVENTIONS AND SUBCONTRACTS

(Pursuant to "Patent Rights" Contract Clause) (See Instructions on back)

Form Approved
OMB No. 9000-0095
Expires Jan 31, 2008

PLEASE DO NOT RETURN YOUR COMPLETED FORM TO THE ABOVE ORGANIZATION. RETURN COMPLETED FORM TO THE CONTRACTING OFFICER.

1.a. NAME OF CONTRACTOR/SUBCONTRACTOR	c. CONTRACT NUMBER	2.a. NAME OF GOVERNMENT PRIME CONTRACTOR	c. CONTRACT NUMBER	3. TYPE OF REPORT *(X one)*
VUMC				a. INTERIM [ ] b. FINAL [X]
b. ADDRESS *(Include ZIP Code)*	**d. AWARD DATE** *(YYYYMMDD)*	**b. ADDRESS** *(Include ZIP Code)*	**d. AWARD DATE** *(YYYYMMDD)*	**4. REPORTING PERIOD** *(YYYYMMDD)*
Office of Sponsored Programs 3319 West End Ave, Nashville TN 37203	20170915			a. FROM 20170915 b. TO 20220914

SECTION I - SUBJECT INVENTIONS

5. "SUBJECT INVENTIONS" REQUIRED TO BE REPORTED BY CONTRACTOR/SUBCONTRACTOR *(If "None," so state)*

NAME(S) OF INVENTOR(S) *(Last, First, Middle Initial)* a.	TITLE OF INVENTION(S) b.	DISCLOSURE NUMBER, PATENT APPLICATION SERIAL NUMBER OR PATENT NUMBER c.	ELECTION TO FILE PATENT APPLICATIONS *(X)* d.				CONFIRMATORY INSTRUMENT OR ASSIGNMENT FORWARDED TO CONTRACTING OFFICER *(X)* e.	
			(1) UNITED STATES		(2) FOREIGN			
			(a) YES	(b) NO	(a) YES	(b) NO	(a) YES	(b) NO
None	None	None						

f. EMPLOYER OF INVENTOR(S) NOT EMPLOYED BY CONTRACTOR/SUBCONTRACTOR		g. ELECTED FOREIGN COUNTRIES IN WHICH A PATENT APPLICATION WILL BE FILED	
(1) (a) NAME OF INVENTOR *(Last, First, Middle Initial)*	(2) (a) NAME OF INVENTOR *(Last, First, Middle Initial)*	(1) TITLE OF INVENTION	(2) FOREIGN COUNTRIES OF PATENT APPLICATION
(b) NAME OF EMPLOYER	(b) NAME OF EMPLOYER		
(c) ADDRESS OF EMPLOYER *(Include ZIP Code)*	(c) ADDRESS OF EMPLOYER *(Include ZIP Code)*		

SECTION II - SUBCONTRACTS *(Containing a "Patent Rights" clause)*

6. SUBCONTRACTS AWARDED BY CONTRACTOR/SUBCONTRACTOR *(If "None," so state)*

NAME OF SUBCONTRACTOR(S) a.	ADDRESS *(Include ZIP Code)* b.	SUBCONTRACT NUMBER(S) c.	FAR "PATENT RIGHTS" d.		DESCRIPTION OF WORK TO BE PERFORMED UNDER SUBCONTRACT(S) e.	SUBCONTRACT DATES *(YYYYMMDD)* f.	
			(1) CLAUSE NUMBER	(2) DATE *(YYYYMM)*		(1) AWARD	(2) ESTIMATED COMPLETION
None	None	None					

SECTION III - CERTIFICATION

7. CERTIFICATION OF REPORT BY CONTRACTOR/SUBCONTRACTOR *(Not required if: (X as appropriate))* [ ] **SMALL BUSINESS or** [ ] **NONPROFIT ORGANIZATION**

I certify that the reporting party has procedures for prompt identification and timely disclosure of "Subject Inventions," that such procedures have been followed and that all "Subject Inventions" have been reported.

a. NAME OF AUTHORIZED CONTRACTOR/SUBCONTRACTOR OFFICIAL *(Last, First, Middle Initial)*	b. TITLE	c. SIGNATURE	d. DATE SIGNED
Rex, Tonia, S	Professor	Tonia Rex	01/15/2023

DD FORM 882 INSTRUCTIONS

GENERAL

This form is for use in submitting INTERIM and FINAL invention reports to the Contracting Officer and for use in reporting the award of subcontracts containing a "Patent Rights" clause. If the form does not afford sufficient space, multiple forms may be used or plain sheets of paper with proper identification of information by item number may be attached.

An INTERIM report is due at least every 12 months from the date of contract award and shall include (a) a listing of "Subject Inventions" during the reporting period, (b) a certification of compliance with required invention identification and disclosure procedures together with a certification of reporting of all "Subject Inventions," and (c) any required information not previously reported on subcontracts containing a "Patent Rights" clause.

A FINAL report is due within 6 months if contractor is a small business firm or domestic nonprofit organization and within 3 months for all others after completion of the contract work and shall include (a) a listing of all "Subject Inventions" required by the contract to be reported, and (b) any required information not previously reported on subcontracts awarded during the course of or under the contract and containing a "Patent Rights" clause.

While the form may be used for simultaneously reporting inventions and subcontracts, it may also be used for reporting, promptly after award, subcontracts containing a "Patent Rights" clause.

Dates shall be entered where indicated in certain items on this form and shall be entered in six or eight digit numbers in the order of year and month (YYYYMM) or year, month and day (YYYYMMDD). Example: April 2005 should be entered as 200504 and April 15, 2005 should be entered as 20050415.

1.a. Self-explanatory.

1.b. Self-explanatory.

1.c. If "same" as Item 2.c., so state.

1.d. Self-explanatory.

2.a. If "same" as Item 1.a., so state.

2.b. Self-explanatory.

2.c. Procurement Instrument Identification (PII) number of contract (DFARS 204.7003).

2.d. through 5.e. Self-explanatory.

5.f. The name and address of the employer of each inventor not employed by the contractor or subcontractor is needed because the Government's rights in a reported invention may not be determined solely by the terms of the "Patent Rights" clause in the contract.

Example 1: If an invention is made by a Government employee assigned to work with a contractor, the Government rights in such an invention will be determined under Executive Order 10096.

Example 2: If an invention is made under a contract by joint inventors and one of the inventors is a Government employee, the Government's rights in such an inventor's interest in the invention will also be determined under Executive Order 10096, except where the contractor is a small business or nonprofit organization, in which case the provisions of 35 U.S.C. 202(e) will apply.

5.g.(1) Self-explanatory.

5.g.(2) Self-explanatory with the exception that the contractor or subcontractor shall indicate, if known at the time of this report, whether applications will be filed under either the Patent Cooperation Treaty (PCT) or the European Patent Convention (EPC). If such is known, the letters PCT or EPC shall be entered after each listed country.

6.a. Self-explanatory.

6.b. Self-explanatory.

6.c. Self-explanatory.

6.d. Patent Rights Clauses are located in FAR 52.227.

6.e. Self-explanatory.

6.f. Self-explanatory.

7. Certification not required by small business firms and domestic nonprofit organizations.

7.a. through 7.d. Self-explanatory.

Quantitative evaluation of visual and auditory dysfunction and multi-sensory integration in complex TBI patients

PI: Tonia S. Rex **Org:** Vanderbilt University Medical Center **Award Amount:** $2 million

Study/Product Aim(s)

Using a multi-site and multi-disciplinary approach, we will assess the physiological basis of sensory dysfunction in TBI patients, determine causal relationships between sensory dysfunction and mechanism of injury, and derive sensitive, objective, quantitative diagnostic metrics for TBI-induced sensory dysfunction.

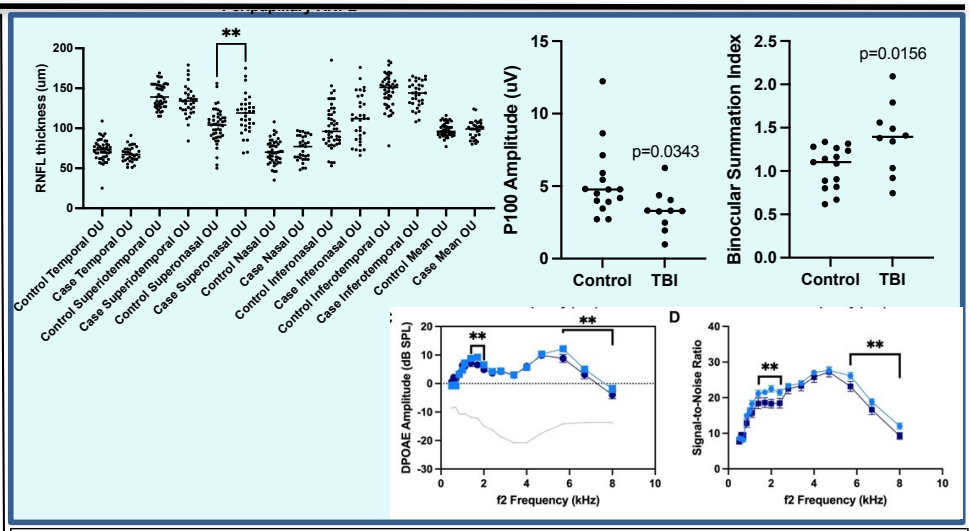
•SA 1: To derive a combination of objective and quantitative metrics to diagnose visual and/or auditory dysfunction after TBI.

• SA 2: To identify and track alterations in the brain that underlies self-reported sensory deficits after TBI.

• SA 3: To identify deficits in multi-sensory integration and the cortical correlates of these deficits in complex TBI patients.

Approach

To achieve our goals while addressing the complexity of trauma we will: 1) test the efficacy of a combination of measurements used together; 2) utilize novel, sensitive assays and analysis tools to identify subtle, but functionally important damage/deficits; and 3) quantify alterations in sensory integration using psychophysiological tools within an EEG framework.



Altered retinal nerve fiber layer thickness, visual evoked potentials, and distortion otoacoustic emission amplitudes in chronic mTBI subjects as compared to controls.

Timeline and Cost

Activities	CY	17	18	19	20
Specific Aim 1					
Specific Aim 2					
Specific Aim 3					
Estimated Budget ($K)		**$250**	**$500**	**$500**	**$750**

Updated: 01/19/2023

Goals/Milestones

CY17 Goal – Obtain IRB approval and recruit and screen subjects

☑ Obtain IRB approval at TVHCS and VUMC

☑ Advertise for normal controls and TBI subjects

CY18 Goal – Screen and Assess TBI and control subjects

☑Obtain IRB approval at Fort Campbell

☑Perform examinations, analyze results and upload data into FITBIR

☑Meet regularly with team members

CY19 Goal – Continue assessments and compile/analyze data

☑ Perform examinations, analyze results and upload data into FITBIR.

☑ Perform data analysis and submit results for publication

CY20 Goal – Finish assessments and compile/analyze data

☑ Perform examinations, analyze results and upload data into FITBIR.

☑ Perform data analysis and submit results for publication

Budget Expenditure to Date

Projected Expenditure: $2 million

Actual Expenditure: $2 million