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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. 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 propose to assess TBI patients from a Level 1 Trauma Center, two Veterans Administration Hospitals, and a military base that houses a satellite of the National Intrepid Center of Excellence. 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); sensory integration

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1. 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 propose that by assessing TBI patients in a Level 1 Trauma Center, two Veterans Administration Hospitals, and a military base that houses a satellite of the National Intrepid Center of Excellence. We will recruit sufficient numbers of subjects to definitively identify assessments that are sensitive and specific enough to diagnose sensory dysfunction in complex TBI patients. 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.

2. KEYWORDS:
mild traumatic brain injury (mTBI); visual dysfunction; auditory dysfunction; magnetic resonance imaging (MRI); electroencephalogram (EEG); sensory integration

3. ACCOMPLISHMENTS:
Major goals of the project:
Specific Aim 1: **To derive a combination of objective and quantitative metrics to diagnose visual and/or auditory dysfunction after TBI.** We will test the working hypothesis that our newly derived diagnostic battery is more sensitive and accurate than any single assessment alone.

Specific Aim 2: **To identify and track alterations in the brain that underlies self-reported sensory deficits after TBI.** We will test the working hypothesis that visual and auditory dysfunction after TBI is due to brain-level damage that is detectable with our sensitive, newly developed algorithms.

Specific Aim 3: To identify deficits in multi-sensory integration and the cortical correlates of these deficits in complex TBI patients. We will test the working hypothesis that alterations within each sensory modality result in combinatorial changes in multisensory integration that can be indexed to yield a sensitive, quantitative diagnostic of complex TBI due to sensory dysfunction.

Major Tasks:
1. Obtained IRB and HRPO approvals at all sites.
2. Coordinate study staff.

3. Recruit, enroll and screen potential subjects.
4. Perform ophthalmic exams.
5. Perform audiological exams.
6. Perform EEGs, including evoked potentials and sensory integration tasks.
7. Perform MRIs.
8. Analyze data

What was accomplished under these goals?
1) Major Activities:

A) We presented findings at the annual conference for the international society for optics and photonics -SPIE- in Houston, TX, February, 2020. We have been invited to give an oral presentation at the 2021 SPIE conference. We will also be presenting at the virtual Southeastern Vision Research Conference in December, 2020.

B) We have published three primary manuscripts and one review article. We have another manuscript that is currently under review in a TBI special issue of the journal, Vision Research.

2) Specific Objectives:
A. Recruitment: We have data on 50 subjects to date. All recruitment and assessments have occurred at VUMC. Due to COVID-19 this will continue to be the case.

B. Regulatory approvals and recruitment at Fort Campbell and TVHSC: We have obtained regulatory approvals for Fort Campbell, have set-up and tested the EEG system, and have provided advertising materials to our collaborators at Blanchfield Hospital and the Intrepid Spirit Center. Unfortunately, due to COVID-19 this site completely closed to clinical research in early March 2020 and remains closed for the foreseeable future. The same is true for TVHSC.

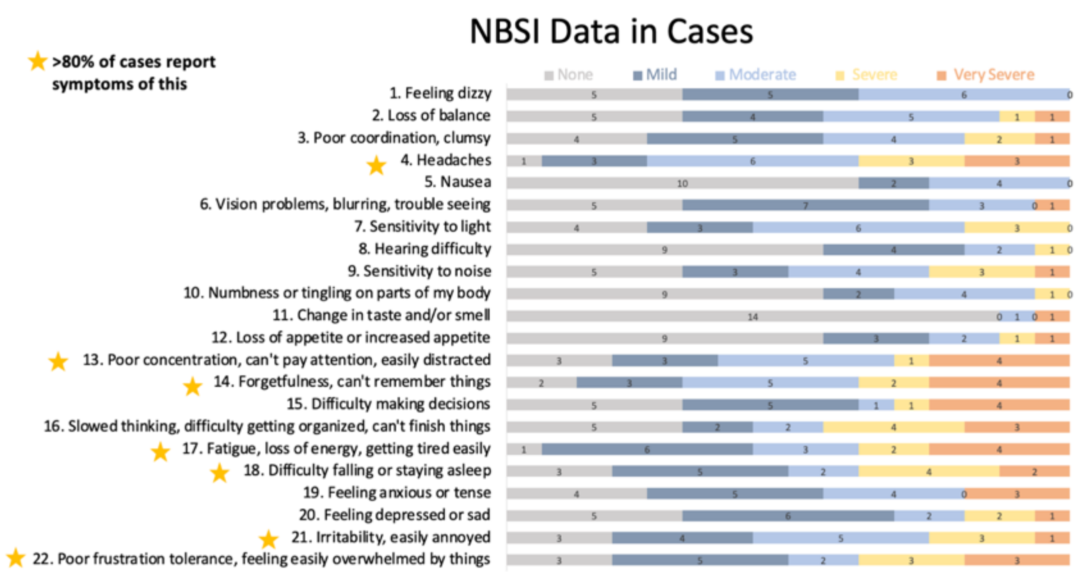

Figure 1. Summary of NBSI data. Colors indicate severity level. The numbers in the bars indicate the number of mTBI subjects who report that level of severity for that symptom. Stars indicate that 80% of mTBI subjects reported some level of severity for that symptom.

C. Study demographics: We have more control subjects (31 vs. 19) and they are older than the TBI subjects. The average age in our control group is 39 ± 10 years and the average age in our TBI group is 32 ± 10 years, $p<0.02$.

D. Self-reported symptoms on NBSI: Many subjects self-report symptoms not directly related to vision or hearing (**Figure 1**).

E. Ophthalmology: All subjects were measured at 20/20 BCVA with refraction and had a normal fundus exam. As previously reported, we continue to detect differences in accommodation amplitude in the TBI subjects compared to controls. After adjusting for differences in age between our cohorts there were no group differences in visual fields or OCT. Individual differences were noted and these are compared across assessments in **Table 1**. Outside normal limits (ONL) refers to values two standard deviations away from the control average.

Table 1. Summary of Assessment Results for Each Subject

Subject	OCT: RNFL, GCL	Optic Nerve MRI	Accommodative Amplitude	HVF Mean Deviation	Convergence	Self-report Vision
TBI 1	[1,2]WNL, -	WNL	[3]ONL	WNL	ONL	[4]None,[5]Mild
TBI 2	ONL (2), WNL	WNL	ONL	WNL	WNL	None, None
TBI 3	ONL (1), ONL (5)	WNL	WNL	WNL	ONL	Mild, Mod
TBI 4	ONL (2), WNL	WNL	WNL	WNL	WNL	Mild, Mod
TBI 5	ONL (2), WNL	-	ONL	WNL	WNL	None, None
TBI 6	WNL, WNL	-	ONL	WNL	WNL	None, None
TBI 7	WNL, WNL	WNL	WNL	WNL	ONL	Mod, Mild
TBI 8	WNL, ONL (1)	ONL	ONL	WNL	WNL	Mild, Sev
TBI 9	ONL (1), ONL (1)	WNL	ONL	WNL	WNL	Mild, Sev
TBI 10	WNL, WNL	WNL	WNL	WNL	WNL	None, None
TBI 11	WNL, ONL (1)	WNL	ONL	WNL	WNL	Mild, Mod
TBI 12	WNL, WNL	WNL	WNL	WNL	-	Mod, Mod
TBI 13	WNL, ONL (3)	-	WNL	WNL	WNL	Mild, Mod
TBI 14	WNL, ONL (1)	ONL	ONL	ONL	WNL	v. Sev, Sev
TBI 15	WNL, WNL	WNL	WNL	WNL	ONL	Mod, Mild
TBI 16	ONL (5), ONL (1)	WNL	ONL	WNL	WNL	Mild, Mod
Control 1	WNL, WNL	WNL	WNL	WNL	WNL	N/A
Control 2	ONL (1), ONL (3)	WNL	WNL	WNL	WNL	N/A
Control 3	ONL (4), ONL (1)	WNL	ONL	ONL	WNL	N/A
Control 4	-, WNL	WNL	WNL	WNL	ONL	N/A
Control 5	ONL (3), ONL (3)	WNL	WNL	WNL	ONL	N/A
Control 6	-, ONL (1)	WNL	WNL	WNL	WNL	N/A
Control 7	WNL, WNL	ONL	ONL	WNL	WNL	N/A
Control 8	WNL, WNL	WNL	WNL	WNL	WNL	N/A
Control 9	-	WNL	WNL	WNL	WNL	N/A
Control 10	WNL, WNL	WNL	WNL	WNL	ONL	N/A
Control 11	WNL, WNL	WNL	WNL	WNL	WNL	N/A
Control 12	WNL, WNL	WNL	WNL	WNL	WNL	N/A
Control 13	WNL, WNL	WNL	WNL	WNL	WNL	N/A
Control 14	WNL, WNL	WNL	ONL	WNL	WNL	N/A
Control 15	ONL (2), WNL	WNL	ONL	WNL	WNL	N/A
Control 16	ONL (1), ONL (1)	ONL	WNL	WNL	WNL	N/A
Control 17	ONL (1), WNL	WNL	WNL	WNL	WNL	N/A
Control 18	WNL, WNL	WNL	WNL	WNL	WNL	N/A
Control 19	WNL, WNL	WNL	WNL	WNL	WNL	N/A
Control 20	WNL, ONL (1)	WNL	WNL	WNL	WNL	N/A
Control 21	WNL, WNL	WNL	WNL	WNL	WNL	N/A
Control 22	WNL, WNL	WNL	ONL	WNL	WNL	N/A
Control 23	WNL, ONL (1)	WNL	ONL	WNL	WNL	N/A
Control 24	ONL (5), WNL	WNL	WNL	WNL	WNL	N/A
Control 25	-	WNL	WNL	WNL	WNL	N/A
Control 26	WNL, ONL (1)	WNL	WNL	WNL	WNL	N/A

Control 27	-	WNL	WNL	WNL	ONL	N/A
Control 28	ONL (1), ONL (1)	WNL	WNL	WNL	WNL	N/A
Control 29	-	WNL	WNL	WNL	WNL	N/A
Control 30	WNL, WNL	WNL	WNL	WNL	WNL	N/A
Control 31	WNL, WNL	WNL	WNL	WNL	WNL	N/A

[1]WNL- within normal limits; [2]OCT shows results from GCL thickness and RNFL thickness, (number of regions ONL in at least one eye; -, no data); [3]ONL – outside normal limits, defined as 2sd from the control mean; [4]Vision problems – blurring, trouble seeing; [5]Sensitivity to light; Mod = moderate; Sev = severe; v. Sev = very severe.

F. Audiology: All subjects to date have normal pure tone test and sound in quiet results. Here we show the self-reported audiological findings combining the relevant portions of the NBSI with a history that we collected during the study visit (**Table 2**). Notably, one subject reported high-pitched ringing and buzzing but claimed no hearing difficulty on the NBSI. Three TBI subjects reported ear pain, while no controls reported this. Similarly, 4 TBI subjects reported sensation of ear fullness, but no control subjects reported this symptom. Only 4 TBI subjects reported no hearing symptoms.

Table 2. Self-Reported Hearing Symptoms

	Subject	Sensation of Ear Fullness	Ear Pain	High-Pitched Ringing	Buzzing	Dizzy, Lightheaded, Spinning	Hearing Difficulty	Sensitivity to Noise
TBI	**TBIAB915VK3**	Yes	Yes	No	No	No	Mild	None
TBI	**TBIAU283YX6**	No	No	No	No	No	None	Mild
TBI	**TBIEE646HJG**	No	No	No	No	Yes	None	Mild
TBI	**TBIFM805VKY**	No	No	No	No	No	Mild	Moderate
TBI	**TBIHM275FHP**	No	No	No	No	No	None	None
TBI	**TBIKZ985DE0**	No	No	No	No	N/A	None	None
TBI	**TBIMN248ZXA**	No	No	Yes	No	Yes	None	Moderate
TBI	**TBIMP976PV9**	Yes	Yes	Yes	No	Yes	Moderate	V. Severe
TBI	**TBINL936EPV**	No	No	Yes	Yes	Yes	Mild	Severe
TBI	**TBINT393WTG**	Yes	No	Yes	Yes	Yes	None	None
TBI	**TBINT629HZW**	No	No	No	No	No	None	None
TBI	**TBIRP424JZ7**	No	No	No	No	Yes	Moderate	Moderate
TBI	**TBITK276RNC**	Yes	No	No	No	Yes	Mild	Moderate
TBI	**TBIUP203FE6**	No	No	No	No	N/A	Severe	Severe
TBI	**TBIVE931VVV**	No	Yes	Yes	No	Yes	None	Mild
TBI	**TBIXK172PG4**	No	No	No	No	No	None	Severe
Control	**TBIYM715WL8**	No	No	Yes	No	Yes	N/A	N/A
Control	**TBIAA244BCN**	No	No	No	No	No	N/A	N/A
Control	**TBIBB348FU8**	No	No	No	No	N/A	N/A	N/A
Control	**TBIBH383AN3**	No	No	No	No	No	N/A	N/A
Control	**TBIBV917BUF**	No	No	No	No	No	N/A	N/A
Control	**TBIBX790JWJ**	No	No	No	No	No	N/A	N/A
Control	**TBICR906TYQ**	No	No	No	No	N/A	N/A	N/A
Control	**TBIEL833YPB**	No	No	No	No	No	N/A	N/A
Control	**TBIFZ501TY3**	No	No	No	No	N/A	N/A	N/A
Control	**TBIGB357XGZ**	No	No	No	No	N/A	N/A	N/A
Control	**TBIGE232GPB**	No	No	Yes	No	No	N/A	N/A
Control	**TBIHD747HNB**	No	No	No	No	N/A	N/A	N/A
Control	**TBIHK104YHQ**	No	No	No	No	No	N/A	N/A
Control	**TBIHN219EDX**	No	No	No	No	N/A	N/A	N/A
Control	**TBIJT602VME**	No	No	No	No	No	N/A	N/A
Control	**TBIKT267ZE9**	No	No	No	No	No	N/A	N/A
Control	**TBILH935ARB**	No	No	No	No	No	N/A	N/A
Control	**TBILK832DFX**	No	No	No	No	N/A	N/A	N/A
Control	**TBILW057EPN**	No	No	No	No	No	N/A	N/A
Control	**TBIMP109NZV**	No	No	No	No	No	N/A	N/A
Control	**TBINV624CCD**	No	No	No	No	No	N/A	N/A
Control	**TBIPF613YVE**	No	No	No	No	No	N/A	N/A
Control	**TBIPH183DE5**	No	No	No	No	No	N/A	N/A
Control	**TBIPR224JZE**	No	No	Yes	No	Yes	N/A	N/A
Control	**TBIWE750HDW**	No	No	No	No	No	N/A	N/A
Control	**TBIWH699EW6**	No	No	No	No	N/A	N/A	N/A
Control	**TBIXB540KJZ**	No	No	Yes	No	No	N/A	N/A

Control	**TBIXP330UD1**	No	No	No	No	No	N/A	N/A
Control	**TBIYB337CZA**	No	No	No	No	No	N/A	N/A
Control	**TBIYN995VW1**	No	No	No	No	No	N/A	N/A
Control	**TBIZK496WN3**	No	No	No	No	No	N/A	N/A
Control	**TBIZV246JJ7**	No	No	No	No	No	N/A	N/A

In **Figure 2** we show a typical auditory evoked potential (AEP) Wave 5 waveform. To begin, we first performed a careful analysis of the control subject AEPs. Sub-average latency variance and "Q50" half peak width are unique, advanced AEP analysis methods. These measures were used to investigate traditionally held principles that increased latency variance results in broader and lower amplitude peaks. The findings of this study contradicted traditional principles and demonstrated that increased latency variance resulted in lower amplitude, but not broader peaks in human listeners. Additionally, narrower peaks were not significantly correlated with higher amplitude peaks in humans. The findings of this study should be considered with regard for the poor repeatability of sub-average latency variance and peak width measures employed. The impact of residual noise on the repeatability of these measures and their relationships among each other has yet to be determined. So far we have not identified relationships between sub-cortical and cortical responses when analyzed using absolute latency, peak-to-peak amplitude, sub-average latency variance, or peak width. However, differences in the stimulus parameters used to elicit the responses and in participant state could contribute to the lack of observed effects. Further developing and understanding measures of AEP inter-trial variability are important for future investigations of auditory neural impairments.

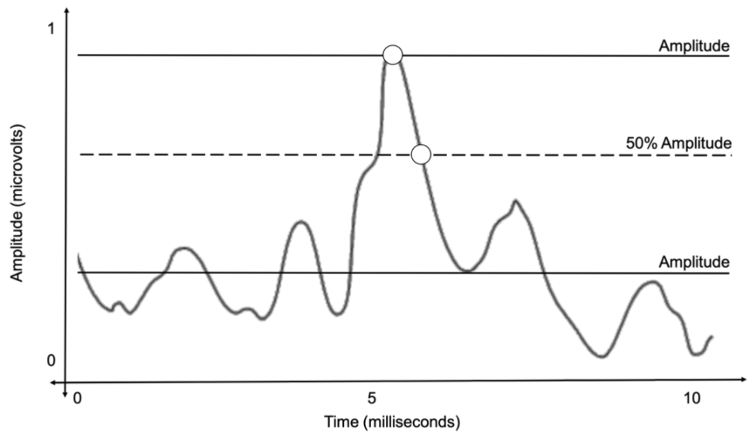

Figure 2. Representative ABR Wave V "Q50" half peak width calculation. The solid horizontal lines represent the peak-to-peak amplitude of ABR Wave V. The dashed horizontal line represents 50 percent of Wave V amplitude. Open circles represent Wave V absolute latency and the point at which the ABR waveform intersects the 50 percent amplitude line on the decelerating side of the peak. The "Q50" half peak width is the difference in latency (milliseconds) between the two open circles. Comparable calculations were completed for ABR Waves I and III and auditory LLR N1 and P2.

<u>G. MRI:</u> As previously reported, we continue to detect differences between controls and TBI subjects on whole brain MRI using machine learning and have since published one paper and just had another accepted for publication on this topic. Here we add the results of the optic nerve MRI. There were no group differences after correcting for age. However, there were a few TBI subjects who had larger sheath area and volume compared to the control average (2 sd larger), suggestive of swelling (**Figure 3**). This data is also in **Table 2.** Interestingly, the subjects who self-reported the most severe vision problems had a larger optic nerve sheath.

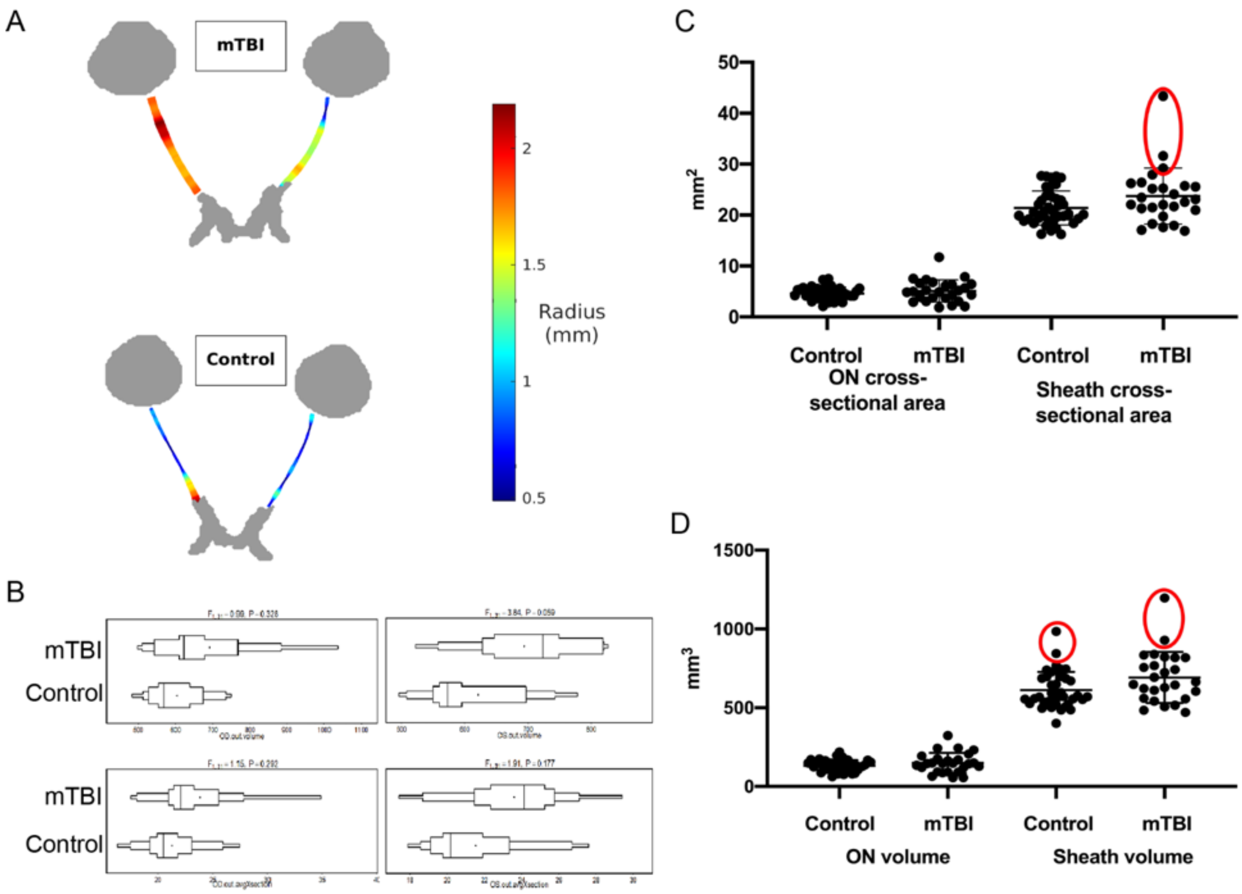

Figure 3. Increased Sheath cross-sectional area and volume in a subset of mTBI subjects. A. Representative images and heat maps of an average control and a mTBI subject with an enlarged optic nerve. B. The sheath cross-sectional area and volume measurements are similar for each eye within a subject. C. Quantification of the optic nerve (ON) and sheath cross-sectional areas for control and mTBI subjects. D. Quantification of the ON and sheath volume for control and mTBI subjects. Red circles indicate values 2 s.d. above the control mean.

H. We are using our newly developed Matlab tools to analyze the resting state EEG, VEP, and sensory integration EEG data.

4. IMPACT:

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

I participated in a VCE initiative to standardize a quantitative method for measuring the opto-motor system including convergence, accommodation, and saccadees in TBI patients. This document was recently finalized, and we expect to publish it shortly.

What was the impact on other disciplines?

We have published one paper in SPIE, with another recently accepted. These studies report on our MRI results and demonstrate the power of MRI and machine learning for detecting patterns not apparent by visual exam of MRI scans. These papers demonstrate that with machine learning, MRI might be useful in diagnosing mTBI subjects due to subtle, but consistent, differences in the MRIs of mTBI subjects compared to controls.

What was the impact on technology transfer?
None to date.

What was the impact on society beyond science and technology?
Nothing to Report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change:

COVID-19 resulted in closure of all clinical studies including recruitment efforts at all three sites beginning in early March, 2020. Both Fort Campbell and TVHSC are still closed to non-COVID-19 related clinical research. VUMC began re-opening non-COVID-19 related clinical research in late June, 2020. However, some of our assessments are performed in Vanderbilt University space, which did not reopen until August, 2020.

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

There is no clear indication as to when, or if, Fort Campbell and TVHSC will reopen for non-COVID-19 related clinical research. As we are now in a no-cost extension of this grant, we will focus our energies on recruiting and assessing subjects at VUMC only.

Changes that had a significant impact on expenditures:

We have had to provide percent effort to the VEI CTU in order to have an ophthalmic technician perform the necessary assessments.

Significant changes in use or care of human subjects:

Nothing to report.

6. PRODUCTS:

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, 2020.

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* Epub.

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

Elenberger J, Crawford L, Diethelm C, Singh E, Lavin P, Chen Q, Kerley C, Colyer MH, Anderson A, Landman B, **Rex TS.** (submitted). Ophthalmological findings from a pilot study of chronic mTBI subjects. Vis Res.; Special Issue on TBI.

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

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

Website or other internet site:
Nothing to report.

Technologies or techniques:
Nothing to Report

Inventions, patent applications, and/or licenses:
Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:
What individuals have worked on the project?

Name:	Tonia S. Rex
Project Role:	PI
Researcher Identifier (ORCID ID):	0000-0002-2566-8723
Nearest person month worked:	2.4
Contribution to Project:	Designed and organized study, hired personnel, navigated regulatory compliance and issues, supervised all activities, trained team members, published and presented research.
Funding Support:	NIH R01 EY022349; NIH U24 EY029893

Name:	Patrick Lavin/Reid Longmuir
Project Role:	Co-PI
Researcher Identifier (ORCID ID):	N/A
Nearest person month worked:	0.6
Contribution to Project:	Assisted with design of ophthalmic exam and performs the fundus exam on all subjects seen at VUMC. Note: Dr.

	Lavin retired this summer. So, Dr. Longmuir has taken over this role.
Funding Support:	N/A
Name:	Amy Chomsky
Project Role:	Co-PI (unpaid)
Researcher Identifier (ORCID ID):	N/A
Nearest person month worked:	0.6
Contribution to Project:	Assisted with design of ophthalmic exam and performs the fundus exam on all subjects seen at TVHCS, Nashville.
Funding Support:	N/A
Name:	Jennifer Lindsey
Project Role:	Co-PI
Researcher Identifier (ORCID ID):	N/A
Nearest person month worked:	0.36
Contribution to Project:	Assisted with design of ophthalmic exam and performs the fundus exam on all subjects seen at TVHCS, Murfreesboro.
Funding Support:	N/A
Name:	Martin Gallagher
Project Role:	Co-PI
Researcher Identifier (ORCID ID):	N/A
Nearest person month worked:	0.6
Contribution to Project:	Assisted with EEG troubleshooting and design of VEP protocol, trained team members on VEP analysis and quantification.
Funding Support:	NIH R21 NS096483
Name:	Mark Wallace
Project Role:	Co-PI
Researcher Identifier (ORCID ID):	N/A
Nearest person month worked:	0.6
Contribution to Project:	Designed sensory integration tasks, assisted with EEG trouble-shooting, trained team members on performing EEGs, and collecting and analyzing the resulting data.
Funding Support:	NIH R21 MH109225; NIH U54 HD083211
Name:	Linda Hood
Project Role:	Co-PI (unpaid)
Researcher Identifier (ORCID ID):	N/A
Nearest person month worked:	0.36
Contribution to Project:	Assisted with design of audiological exam, identified her own team members who assist with performance and analysis of audiological exam.
Funding Support:	

Name: Rene Gifford
Project Role: Co-PI (unpaid)
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 0.36
Contribution to Project: Assisted with design of audiological exam, identified her own team members who assist with performance and analysis of audiological exam.
Funding Support: NIH R01 DC009404; R01 DC013117

Name: Bennett Landman
Project Role: Co-PI
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 0.36
Contribution to Project: Assisted with design of MRI exam, training members of his laboratory to perform data analysis and quantification. Helped trouble-shoot MRI at both sites.
Funding Support: NIH R01 EB017230

Name: Adam Anderson
Project Role: Co-PI
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 0.36
Contribution to Project: Assisted with design and analysis of MRI exam, set-up the MRI protocol at Fort Campbell, and helped trouble-shoot MRI at both sites.
Funding Support: NIH R21 EB024311

Name: Bret Logan
Project Role: Co-PI
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 0.36
Contribution to Project: Provides access to the Fort Campbell Intrepid Center patients and Blanchfield Hospital Radiology Department for the MRI. Assisted with navigating IRB/HRPO.
Funding Support: N/A

Name: Marc Zola
Project Role: Co-PI
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 0.36
Contribution to Project: Provides access to the Fort Campbell Intrepid Center patients, assisted with navigating IRB/HRPO, performs the EEGs, and analyzes the resting-state EEGs.
Funding Support: N/A

Name: Kara Bean
Project Role: Co-PI
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 0.36
Contribution to Project: Assisted with design of audiological exam, and performs the audiological exam at Fort Campbell.
Funding Support: N/A

Name: Angelletta Payne
Project Role: Co-PI
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 0.36
Contribution to Project: Assisted with design of ophthalmic exam and performs the fundus exam on subjects seen at Fort Campbell.
Funding Support: N/A

Name: Lucas Groves
Project Role: Co-PI
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 0.36
Contribution to Project: Assisted with design of ophthalmic exam, helped obtain approval for study at Fort Campbell, and performs the fundus exam on subjects seen at Fort Campbell.
Funding Support: N/A

Name: Cindy Chen
Project Role: Co-PI
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 0.6
Contribution to Project: Assisted study design and assures proper study design and implementation from a statistical perspective.
Funding Support: N/A

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. Lavin has retired and Dr. Longmuir has taken over his role. Dr. Longmuir is a neuro-ophthalmologist at the Vanderbilt Eye Institute.

What other organizations were involved as partners?

No longer able to collaborate with TVHCS and Fort Campbell due to COVID-19 restrictions.

8. SPECIAL REPORTING REQUIREMENTS:

None.

9. APPENDICES:

See attached updated Quad Chart.

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.

Subject	OCT: RNFL, GCL	Optic Nerve MRI	Accommodative Amplitude	HVF Mean Deviation	Convergence	Self-report Vision
TBI 1	[1,2]WNL, -	WNL	[3]ONL	WNL	ONL	[4]None, [5]Mild
TBI 2	ONL (2), WNL	WNL	ONL	WNL	WNL	None, None
TBI 3	ONL (1), ONL (5)	WNL	WNL	WNL	ONL	Mild, Mod
TBI 4	ONL (2), WNL	WNL	WNL	WNL	WNL	Mild, Mod
TBI 5	ONL (2), WNL	-	ONL	WNL	WNL	None, None
TBI 6	WNL, WNL	-	ONL	WNL	WNL	None, None
TBI 7	WNL, WNL	WNL	WNL	WNL	ONL	Mod, Mild
TBI 8	WNL, ONL (1)	ONL	ONL	WNL	WNL	Mild, Sev
TBI 9	ONL (1), ONL (1)	WNL	ONL	WNL	WNL	Mild, Sev
TBI 10	WNL, WNL	WNL	WNL	WNL	WNL	None, None
TBI 11	WNL, ONL (1)	WNL	ONL	WNL	WNL	Mild, Mod
TBI 12	WNL, WNL	WNL	WNL	WNL	-	Mod, Mod
TBI 13	WNL, ONL (3)	-	WNL	WNL	WNL	Mild, Mod
TBI 14	WNL, ONL (1)	ONL	ONL	ONL	WNL	v. Sev, Sev
TBI 15	WNL, WNL	WNL	WNL	WNL	ONL	Mod, Mild
TBI 16	ONL (5), ONL (1)	WNL	ONL	WNL	WNL	Mild, Mod

Single subject cross assay analysis. ONL = outside normal limits, defined as 2 standard deviations higher or lower than the control average; WNL = within normal limits; Yellow highlight = Subjects with swollen optic nerve and self-reported severe photophobia. They were also deficient in accommodative amplitude and were ONL in GCL thickness in one region. The subject with the most severe vision complaints was also ONL in Humphrey Visual Field (HVF) Mean Deviation.

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: 10/20/2020

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: $1,227,751