Sleep, chronic pain, and sensory sensitivity in TBI: From observation to intervention

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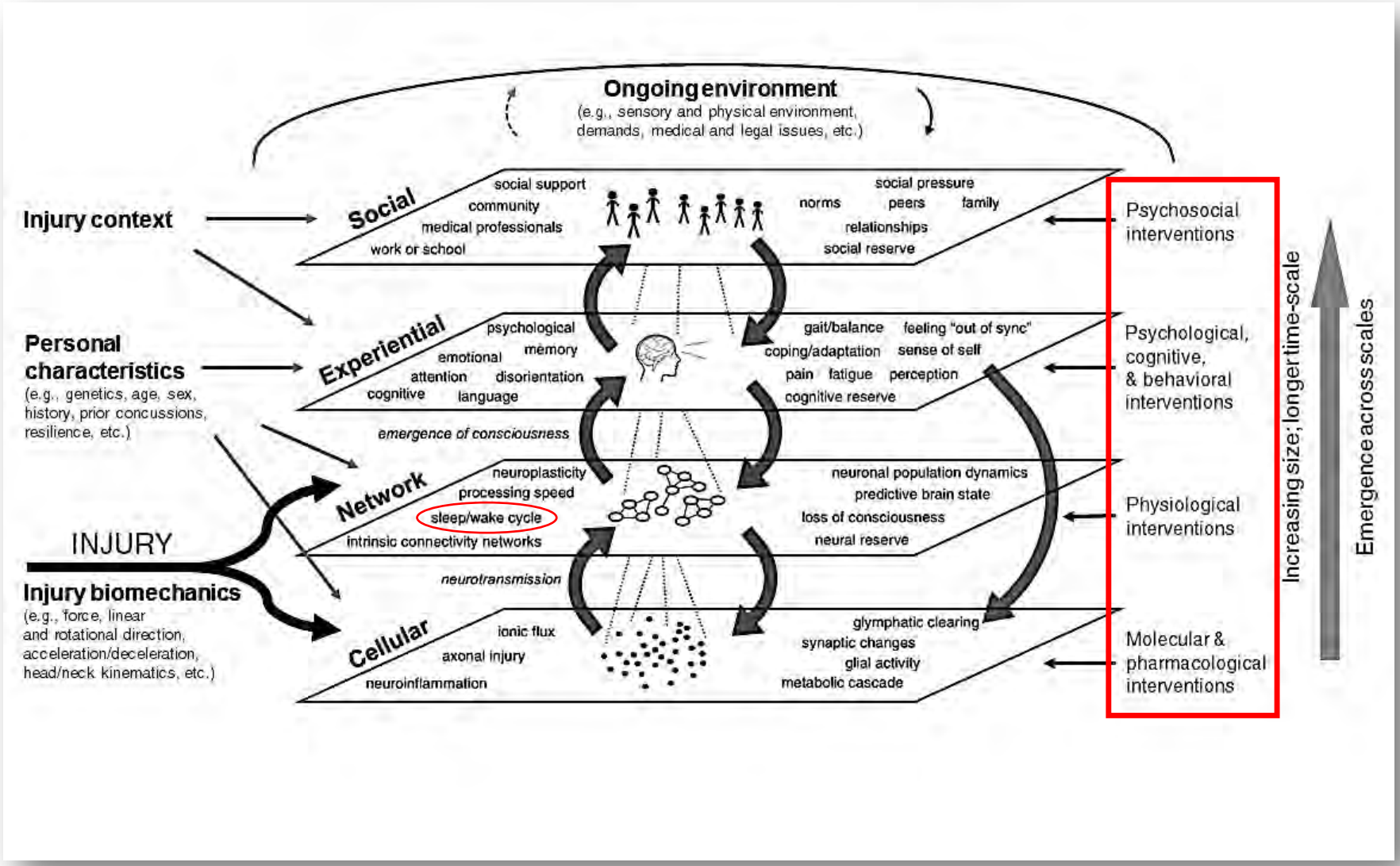
October 29, 2020

VA Portland Health Care System

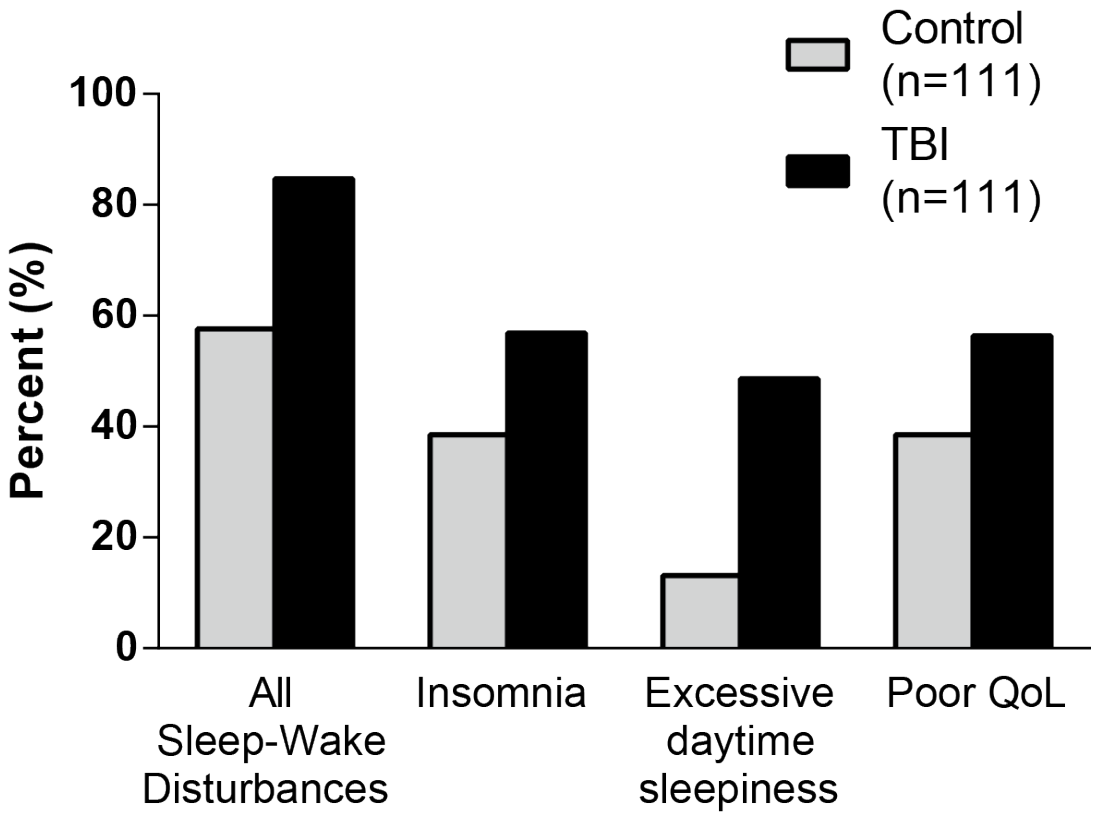
Oregon Health & Science University

Mild TBI as a multi-scale, complex system



Erin Kenzie, Elle Parks, Erin Bigler, Miranda Lim, Jim Chesnutt, Wayne Wakeland, 2017, *Front Neurol*

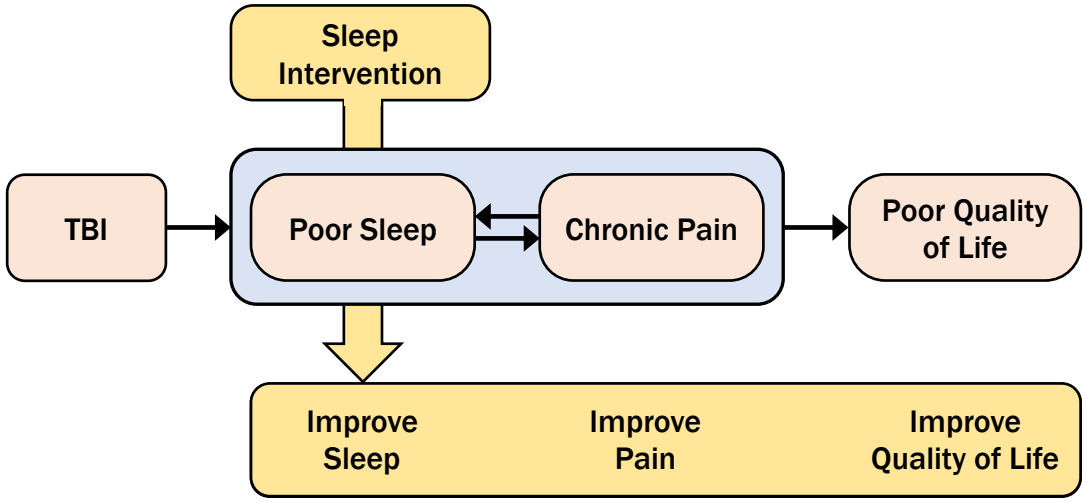
Sleep disturbances are common in mild TBI



Unpublished data, Portland VA Sleep Clinic

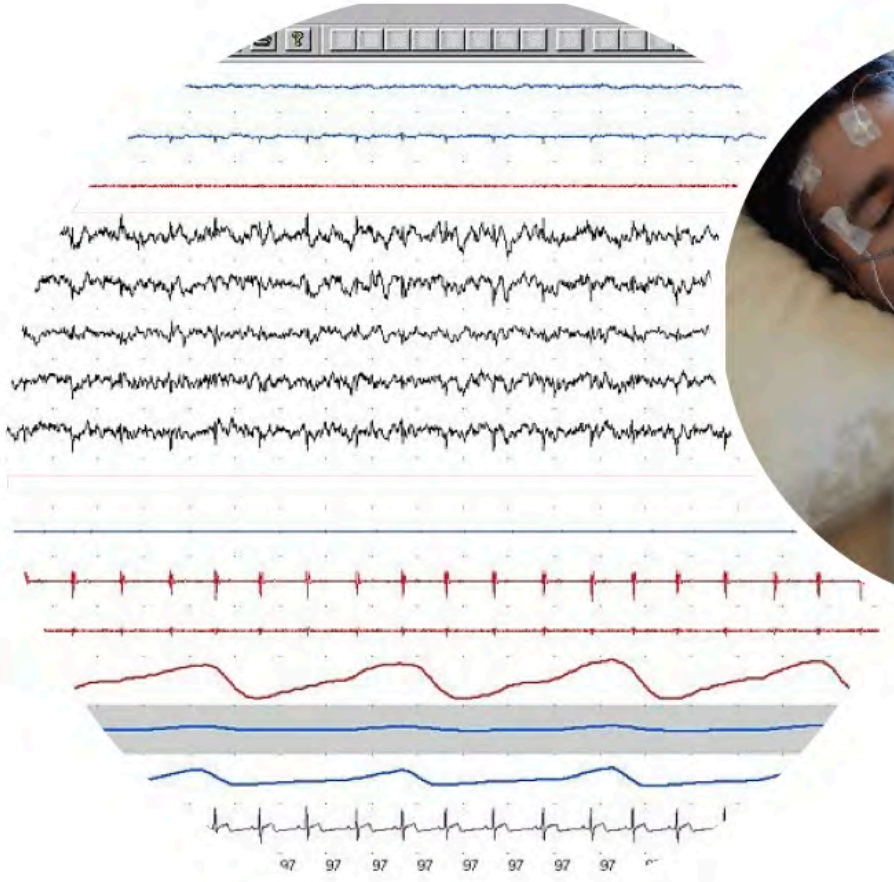
Symptom	ICD-10[33]	DSM-IV[23]
Headache	✓	✓
Dizziness	✓	✓
Fatigue	✓	✓
Irritability	✓	✓
Sleep problems	✓	✓
Concentration problems	✓	-
Memory problems	✓	-
Problems tolerating stress/emotion/alcohol	✓	-
Affect changes, anxiety, or depression	-	✓
Changes in personality	-	✓
Apathy	-	✓

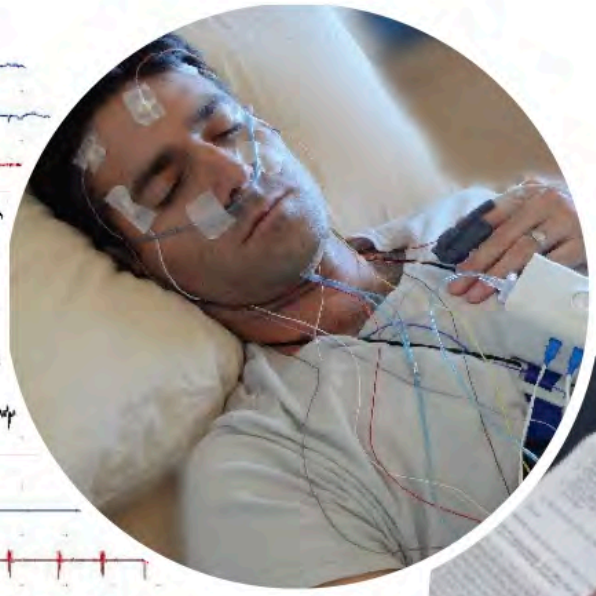
TBI affects sleep and chronic pain

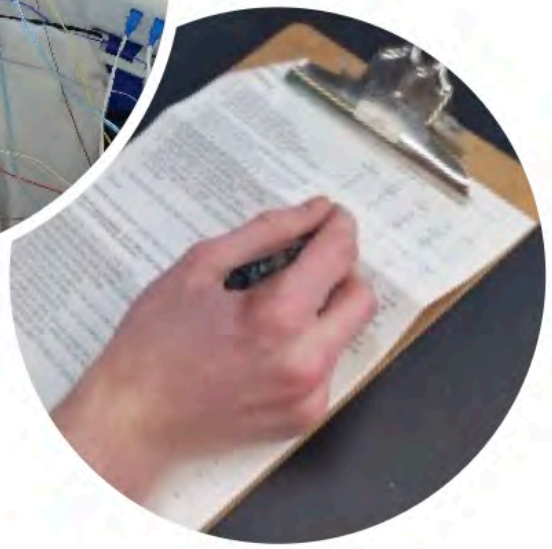


TBI, sleep, and chronic pain

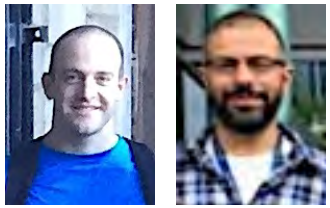
Veterans (n=670) recruited from the
Portland VA Sleep Disorders Clinic

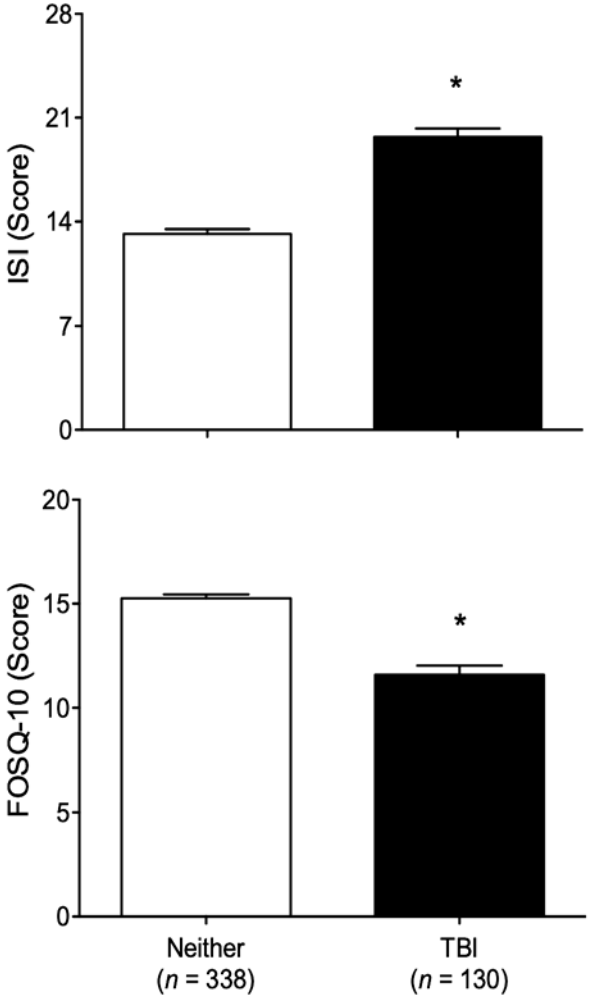




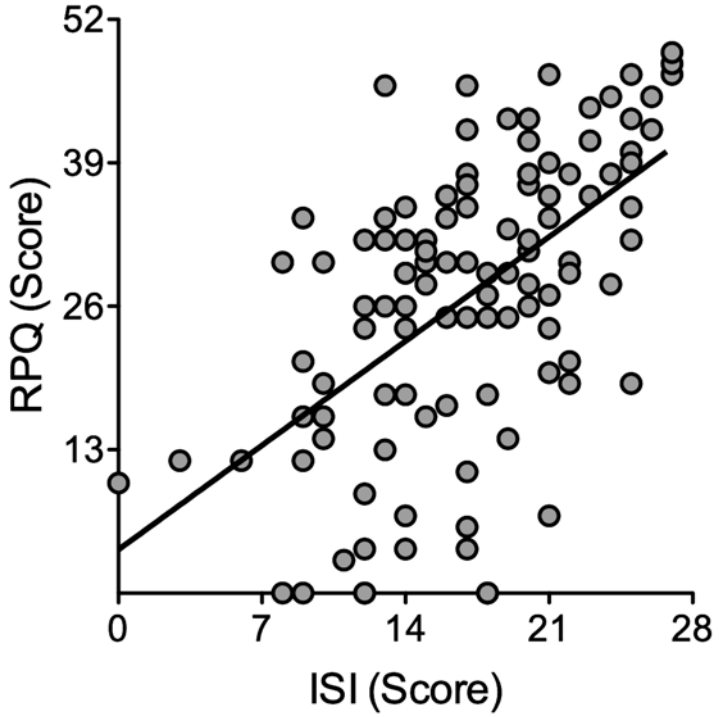


TBI, sleep, and chronic pain



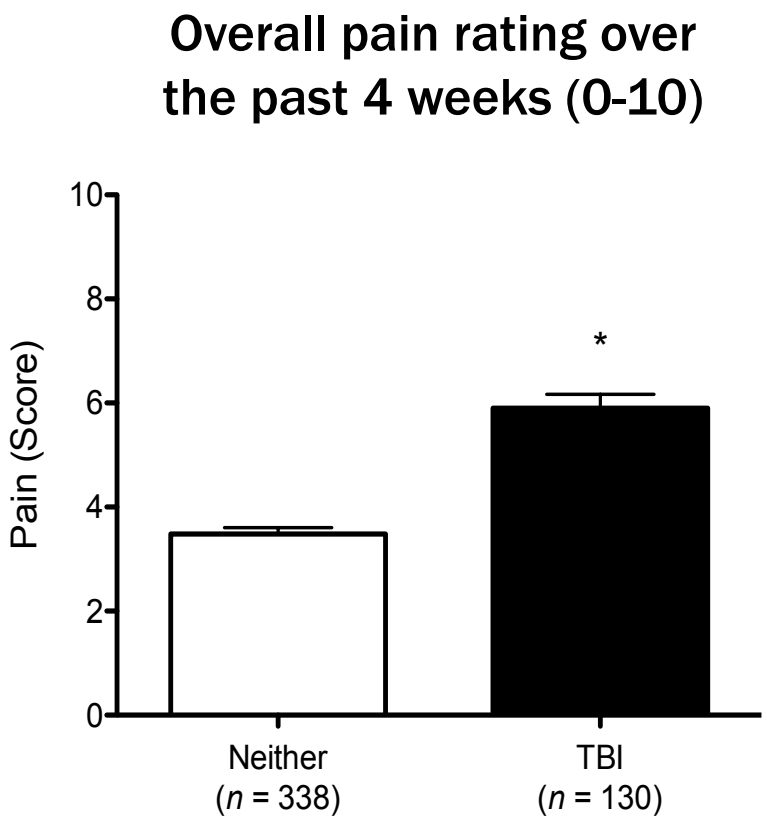


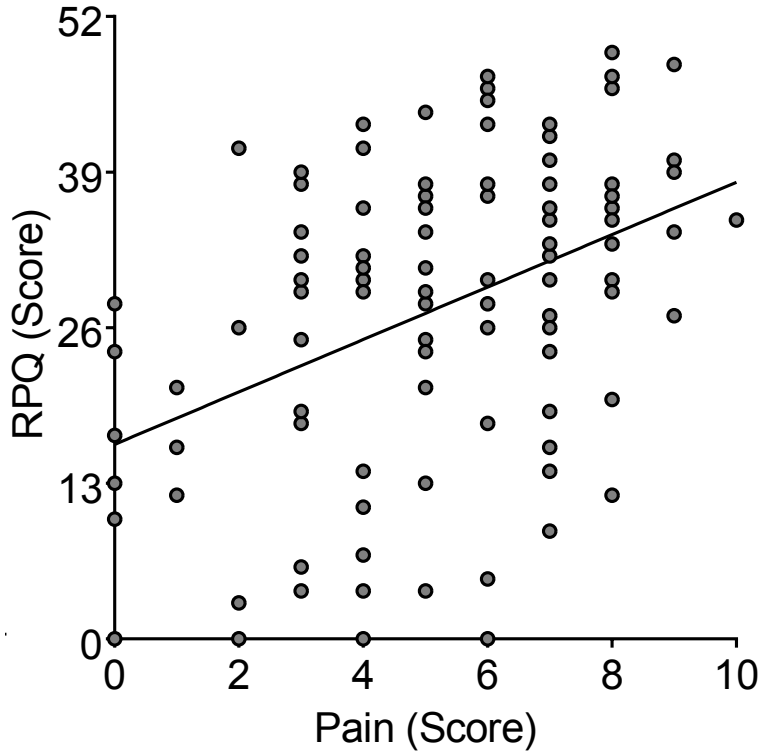
Rivermead Postconcussive Questionnaire correlates with Insomnia Severity Index



Balba & Elliott *et al*. *Journal of Clinical Sleep Medicine*, 2018

TBI, sleep, and chronic pain





Balba & Elliott *et al*. *Journal of Clinical Sleep Medicine*, 2018




Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Increased Sleep Disturbances and Pain in Veterans With Comorbid Traumatic Brain Injury and Posttraumatic Stress Disorder

Nadir M. Balba, MA[1,2*]; Jonathan E. Elliott, PhD[1,3*]; Kris B. Weymann, PhD, RN[1,4]; Ryan A. Opel, BSc[5]; Benjamin J. Morasco, PhD[6,7]; Mary M. Heinricher, PhD[1,2,8]; Miranda M. Lim, MD, PhD[1,2,3,8,9]

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Study Objectives: Veterans are at an increased risk for traumatic brain injury (TBI) and posttraumatic stress disorder (PTSD). Both TBI and PTSD are associated with sleep disturbances and increased pain. Furthermore, sleep disturbances and pain are reciprocally related. Although both TBI and PTSD are independently linked to sleep disturbances and pain, it remains unclear how these symptoms show worse sleep disturbances and pain compared to those with only TBI or PTSD. We hypothesized that Veterans with comorbid TBI+PTSD compared to Veterans with only TBI or PTSD.

Methods: Veterans (n = 639) from the VA Portland Health Care System completed overnight polysomnography and questionnaires. Primary outcome variables were self-reported sleep disturbances and current pain intensity. Participants were categorized into four groups: (1) neither: without TBI or PTSD (n = 383); (2) TBI: only TBI (n = 67); (3) PTSD: only PTSD (n = 126); and (4) TBI+PTSD: with both TBI and PTSD (n = 63).

Results: The PTSD and TBI+PTSD groups reported worse sleep compared to the TBI and neither groups. Pain was worst in the TBI+PTSD group in intensity compared to the other groups.

Conclusions: These data suggest sleep and pain are worst in Veterans with TBI and PTSD, and that Veterans with TBI only may be despite not having as much pain. Thus, although this is a complex relationship, these data suggest that the presence of PTSD in the comorbid group may be driving pain in this population.

Keywords: sleep-wake disturbances, concussion, polytrauma clinical triad, insomnia, headaches, sensory sensitivity

Citation: Balba NM, Elliott JE, Weymann KB, Opel RA, Duke JW, Olsen BS, Morasco BJ, Heinricher MM, Lim MM. Sleep disturbances in Veterans with comorbid traumatic brain injury and posttraumatic stress disorder. *J Clin Sleep Med.* 2

BRIEF SUMMARY

Current Knowledge/Study Rationale: Traumatic brain injury (TBI) and posttraumatic stress disorder (PTSD) are independently associated with sleep disturbances and pain, both of which can exacerbate the other. The relationship between TBI, PTSD, sleep, and pain will help improve treatment and rehabilitation

Study Impact: This study demonstrates that Veterans with PTSD and with both PTSD and TBI report significantly greater current pain intensity. These data help in the limited understanding of how TBI and PTSD differ from Veterans with only TBI or PTSD and contribute to the development of impairment in this vulnerable population.

INTRODUCTION

Traumatic brain injury (TBI) is defined as a disruption in brain function, or other brain pathology, resulting from an external force.[1] The most recent estimate from the Centers for Disease Control and Prevention found that approximately 2.5 million people in the United States sustain a TBI each year,[2] with a significantly higher incidence of TBI among Veterans. Although TBI severity can be mild, moderate, or severe, ~80% are classified as mild,[3] and are associated with a variety of sequelae as well as an increased risk of the development of posttraumatic stress disorder and debilitating

Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Sleep Disturbances in Traumatic Brain Injury: Associations With Sensory Sensitivity

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Study Objectives: Sleep disturbances following traumatic brain injury (TBI) in Veterans are very common and often persist as chronic sequelae. In addition, sensory sensitivity, ie, discomfort upon exposure to light and noise, is common after TBI. However, the relationship between sleep disturbances and sensory sensitivity in Veterans following TBI has not yet been examined, yet both are established early markers of neurodegeneration.

Methods: Veterans (n = 95) in the chronic phase of recovery from TBI at the VA Portland Health Care System completed an overnight polysomnography and provided self-report data on sensory (eg, light and noise) sensitivity, and sleep disturbances. Participants were categorized into four sensory sensitivity groups: (1) "neither," neither light nor noise sensitivity (n = 36); (2) "light," only light sensitivity (n = 12); (3) "noise," only noise sensitivity (n = 24); and (4) "both," light and noise sensitivity (n = 23).

Results: Veterans with TBI reported sleep disturbances that were significantly correlated with the severity of their sensory sensitivity and associated with posttraumatic stress disorder (PTSD). Multiple linear regression revealed insomnia severity to be the strongest predictor of the relationship between sleep disturbances and sensory sensitivity. Furthermore, sensory sensitivity was associated with a higher mean heart rate during sleep, even after controlling for PTSD status.

Conclusions: These data are the first to report the prevalence and association between sensory sensitivity and sleep disturbances in Veterans with TBI. These data also suggest that the underlying mechanism of the sleep-sensory relationship could be due in part to comorbid PTSD and autonomic nervous system hyperarousal.

Keywords: autonomic hyperarousal, light sensitivity, neurodegeneration, noise sensitivity, PTSD, Veterans

Citation: Elliott JE, Opel RA, Weymann KB, Chau AQ, Papesh MA, Callahan ML, Storzbach D, Lim MM. Sleep disturbances in traumatic brain injury: associations with sensory sensitivity. *J Clin Sleep Med.* 2018;14(7):1177–1186.

BRIEF SUMMARY

Current Knowledge/Study Rationale: Traumatic brain injury (TBI) is common in Veterans and is often independently associated with persistent sleep disturbances as well as sensory (ie, light and noise) sensitivity. The current study sought to correlate sensory sensitivity with sleep disturbances in Veterans with TBI who have undergone in-laboratory polysomnography.

Study Impact: In Veterans with TBI, sensory sensitivity was strongly correlated with sleep disturbances and posttraumatic stress disorder symptom severity, and insomnia severity was the strongest predictor of this relationship. Furthermore, sensory sensitivity was associated with an increased mean heart rate during sleep, even after controlling for posttraumatic stress disorder status. These data suggest the underlying mechanism of the sleep-sensory relationship could be due in part to comorbid posttraumatic stress disorder and autonomic hyperarousal.

INTRODUCTION

Each year approximately 2.5 million Americans sustain a traumatic brain injury (TBI),[1,2] with a significantly higher incidence among military personnel. Although TBI severity can range from mild, moderate, to severe, ~80% are classified as mild,[3] and can be associated with persistent and debilitating sequelae that prevent the return to normal physical, cognitive, and emotional functioning. Among the most prevalent and persistent symptoms of TBI are sleep disturbances.[4–6] The pathophysiology underlying sleep disturbances following TBI remains unclear, although recent work has implicated a neuroanatomical mechanism based on an impaired orexin/hypocretin system.[7–15] Additionally, sleep disturbances have been implicated in the pathogenesis of neurodegenerative disorders such as Alzheimer disease, a process that may be accelerated by TBI.[16]

Light and noise sensitivity are also frequently associated sequelae of TBI.[17] Although the association between light/noise sensitivity and acute TBI was established in 1967 by Jonnson et al.,[18] it was objectively demonstrated in 1984 through seminal work by Waddell and Gronwall in patients with TBI at

Balba & Elliott *et al.*, 2018
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Elliott *et al.*, 2018
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Rivermead Postconcussive Questionnaire (13Q)

Compared with **before** the accident, do you **now** (i.e., over the last 24 hours) suffer from:

	not experienced	no more of a problem	mild problem	moderate problem	severe problem
Headaches	0	1	2	3	4
Feelings of dizziness	0	1	2	3	4
Nausea and/or vomiting	0	1	2	3	4
Noise sensitivity (easily upset by loud noise)	0	1	2	3	4
Sleep disturbance	0	1	2	3	4
Fatigue, tiring more easily	0	1	2	3	4
Being irritable, easily angered	0	1	2	3	4
Feeling depressed or tearful	0	1	2	3	4
Feeling frustrated or impatient	0	1	2	3	4
Forgetfulness, poor memory	0	1	2	3	4
Poor concentration	0	1	2	3	4
Taking longer to think	0	1	2	3	4
Blurred vision	0	1	2	3	4
Light sensitivity (easily upset by bright light)	0	1	2	3	4
Double vision	0	1	2	3	4
Restlessness	0	1	2	3	4

TBI, sleep, and sensory sensitivity

Veterans (n=95) with TBI

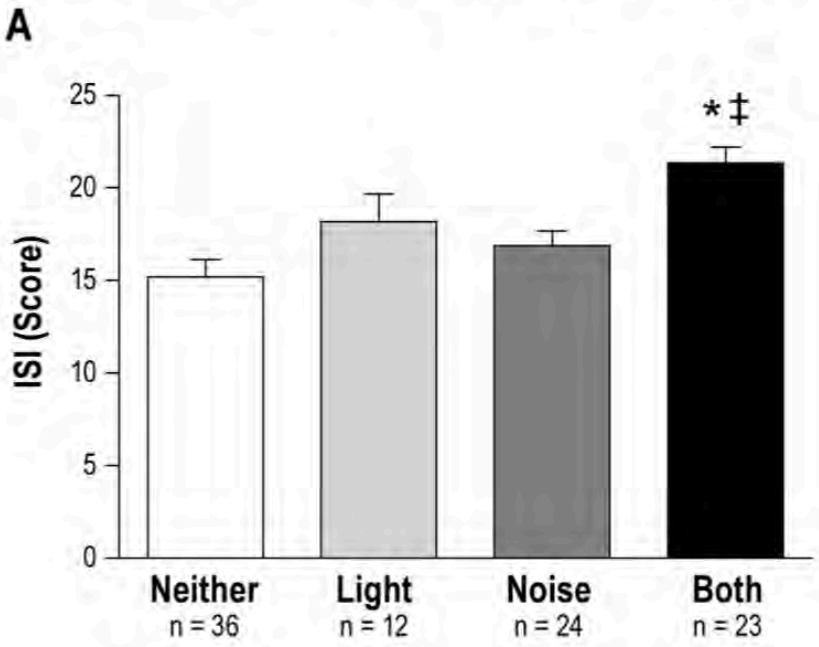
Table 1—Demographic and general health parameters in Veterans with and without sensory sensitivity.

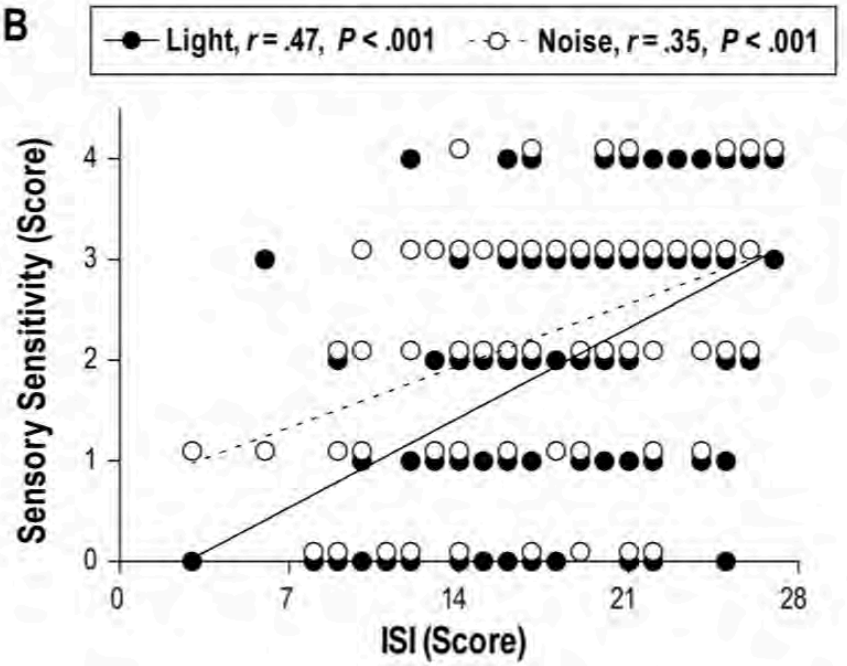
	Neither (n = 36)	Light (n = 12)	Noise (n = 24)	Both (n = 23)	Statistic	*P*
Age, years, mean ± SD	49.4 ± 15.9	42.0 ± 13.9	41.4 ± 17.0	40.6 ± 13.9	2.138	.101
BMI, kg/m^2, mean ± SD	32.1 ± 6.0	34.3 ± 9.2	31.4 ± 6.2	31.0 ± 6.2	0.760	.519
Sex male	34 (94%)	9 (75%)	22 (92%)	21 (91%)	4.070	.254
Race Caucasian	34 (94%)	9 (75%)	20 (83%)	18 (78%)	4.390	.222
Education ≥ some college	29 (83%)	10 (83%)	20 (83%)	19 (83%)	0.006	1.000
Exercise > 90 min/wk	25 (69%)	7 (58%)	18 (75%)	13 (57%)	2.300	.513
Anxiety	8 (22%)	2 (17%)	7 (29%)	1 (4%)	5.116	.163
Diabetes	4 (11%)	1 (8%)	0 (0%)	2 (9%)	2.724	.436
Hypertension	14 (39%)	2 (17%)	8 (33%)	9 (39%)	2.219	.528
Heart disease	5 (14%)	1 (8%)	5 (21%)	2 (9%)	1.815	.612
Lung disease	3 (8%)	0 (0%)	4 (17%)	3 (13%)	2.711	.438
Headaches	20 (56%)	10 (83%)	18 (75%)	15 (65%)	4.244	.236
Sleep apnea	9 (25%)	4 (33%)	7 (29%)	7 (30%)	0.402	.940

Age and BMI were tested using one-way ANOVA, all other variables were tested using chi square. ANOVA = analysis of variance, BMI = body mass index, SD = standard deviation.

Elliott *et al.*, 2018, *Journal of Clinical Sleep Medicine*

Multisensory sensitivity is associated with worse insomnia





Elliott *et al*., 2018, *Journal of Clinical Sleep Medicine*

Multisensory sensitivity is also associated with factors: Higher #TBI, tinnitus, and PTSD

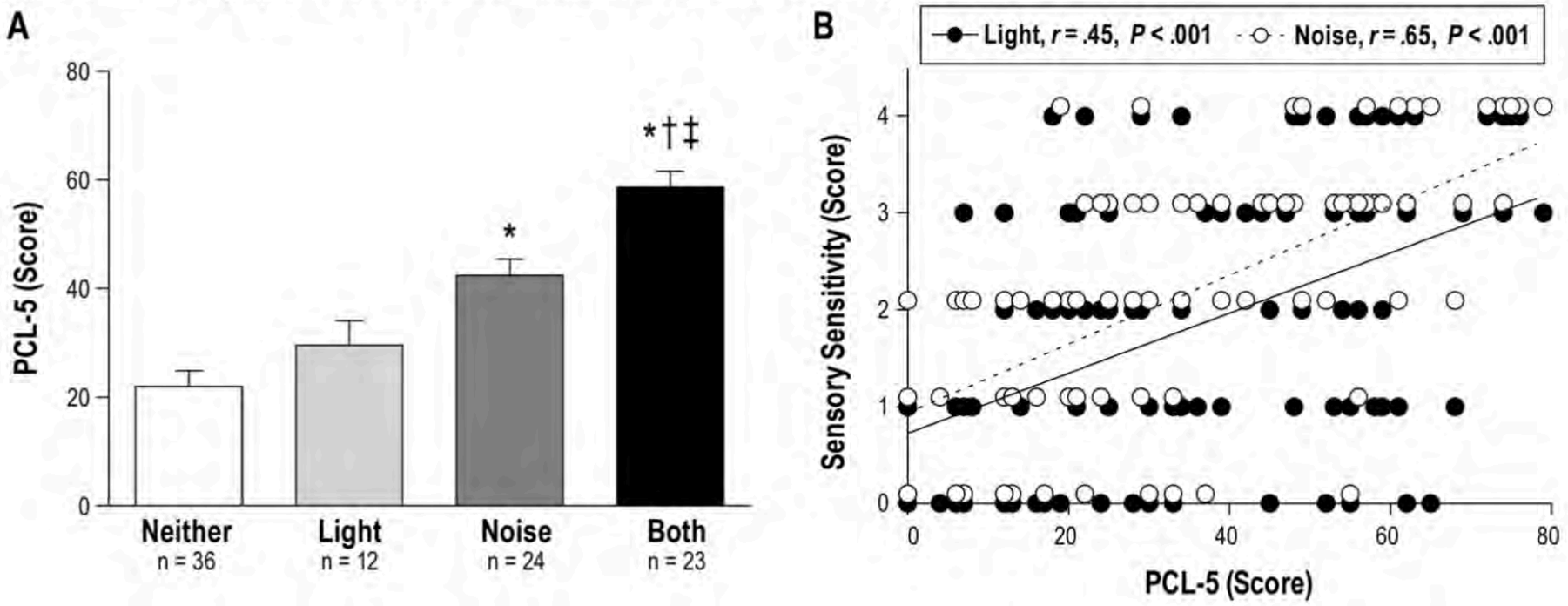
Table 2—TBI characteristics and PTSD status in Veterans with and without sensory sensitivity.

	Neither (n = 36)	Light (n = 12)	Noise (n = 24)	Both (n = 23)	Statistic	*P*
Number of TBIs, mean ± SD	1.9 ± 1.0	1.7 ± 1.3	2.5 ± 1.7	3.7 ± 4.3*	2.966	.036
Years since TBI, mean ± SD	21.9 ± 18.8	20.1 ± 18.8	17.1 ± 15.6	18.1 ± 15.4	0.442	.724
PCS	13 (36%)	8 (67%)	16 (67%)	13 (57%)	6.925	.074
LOC	16 (44%)	5 (42%)	16 (67%)	10 (44%)	3.826	.281
Confusion	10 (28%)	4 (33%)	14 (58%)	13 (57%)	7.871	.049
PTA	6 (17%)	3 (25%)	4 (17%)	5 (22%)	6.925	.074
Blunt injury	8 (22%)	2 (17%)	8 (33%)	7 (30%)	1.698	.637
Blast injury	10 (28%)	3 (25%)	9 (38%)	13 (57%)	5.827	.120
Hearing loss	10 (28%)	3 (25%)	10 (42%)	13 (57%)	5.950	.114
Tinnitus	19 (53%)	4 (33%)	18 (75%)	22 (96%)* †	18.470	< .001
OEF/OIF	14 (39%)	4 (33%)	11 (46%)	15 (65%)	4.919	.178
PTSD	8 (22%)	4 (33%)	15 (63%)*	22 (96%)* †	33.060	< .001

Number of TBIs and TBI Recency were tested using one-way ANOVA; all other variables were tested using chi square. * = $P < .05$ versus Neither; † = $P < .05$ versus Light. LOC = loss of conscious, OEF/OIF = Operation Enduring Freedom/Operation Iraqi Freedom, PCS = postconcussive syndrome, PTA = posttraumatic amnesia, PTSD = posttraumatic stress disorder, SD = standard deviation, TBI = traumatic brain injury.

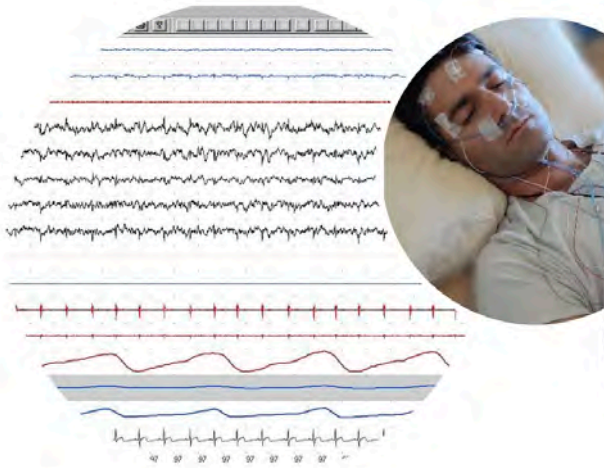
Elliott *et al.*, 2018, *Journal of Clinical Sleep Medicine*

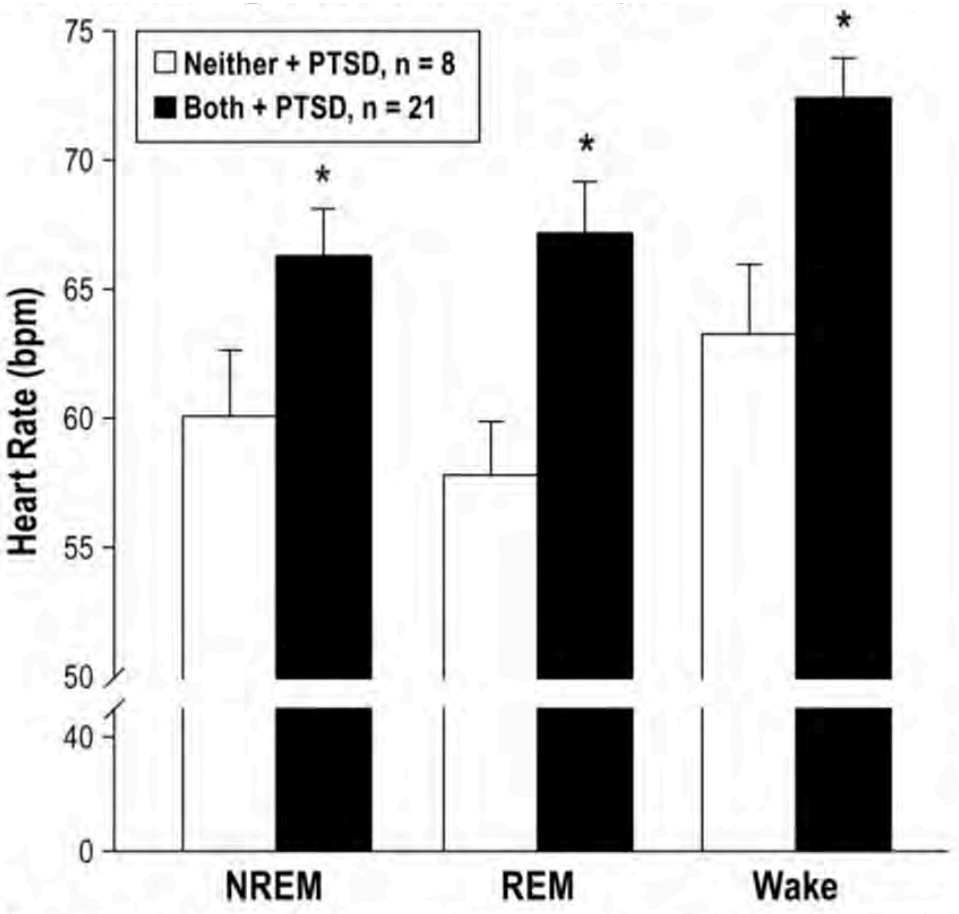
Sensory sensitivity is associated with worse PTSD



Elliott *et al*., 2018, *Journal of Clinical Sleep Medicine*

Sensory sensitivity in PTSD is associated with increased HR, both awake and asleep





Elliott *et al*., 2018, *Journal of Clinical Sleep Medicine*

Summary

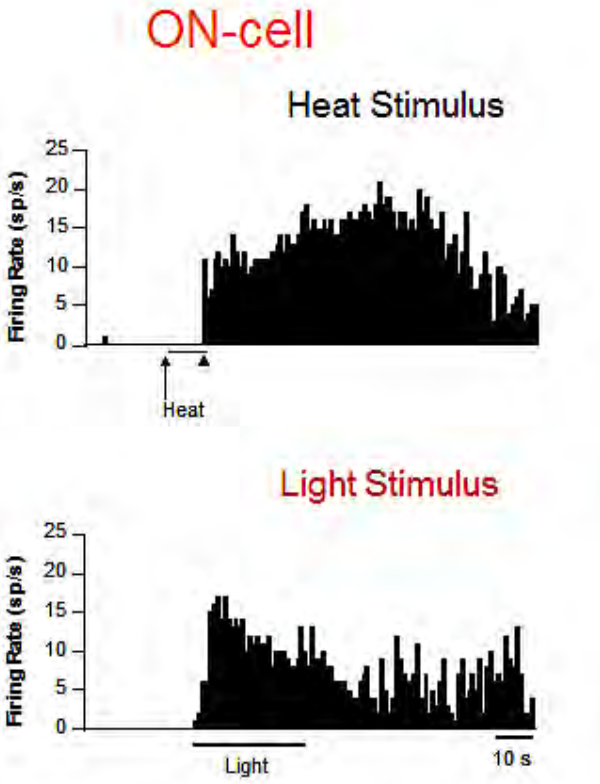
- TBI is associated with sleep disturbances and chronic pain.
- TBI is associated with phono- and photosensitivity.
- Multisensory sensitivity is associated with higher #TBI, tinnitus, and PTSD.
- Veterans with PTSD and multisensory sensitivity have increased HR.

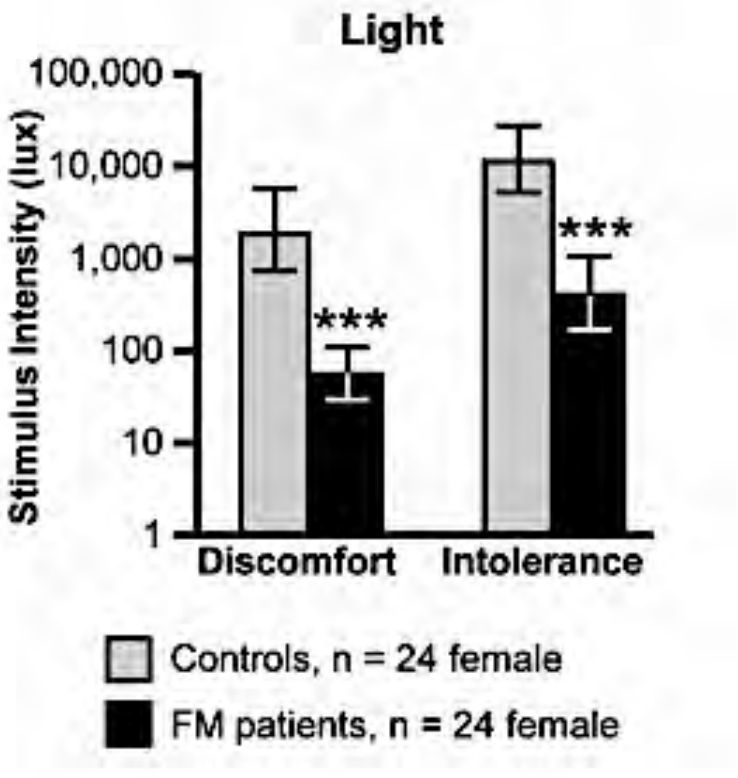
Our funded TBI/Sleep studies

Sponsor	Title	Co-Investigators	Ins s
VA CSRD	SmART-TBI: BCAA in TBI	Akiva Cohen, PhD	CHOP
VA RRD	Sleep-EEG predictors of functional outcome after TBI	Risa Richardson, PhD Mo Modarres, PhD	VA Tampa
DoD PH/TBI	Photosensitivity and Pain in Complex TBI	Mary Heinricher, PhD	OHSU
DoD CNRM	Light therapy to improve sleep and biomarkers in TBI	Jessica Gill, PhD, RN	NIH/USUHS
NIH NIA	REM Sleep Behavior Disorder (RBD) NAPS Consortium	Yo-El Ju, M Brad Boev	
NIH NCCIH	IMMINENT: Internet Mindfulness Meditation to improve sleep and pain in TBI	Barry Oke	

Photosensitivity as a window into CNS pain

- Light activates pain neurons in the brainstem.
- Patients with fibromyalgia report photosensitivity.

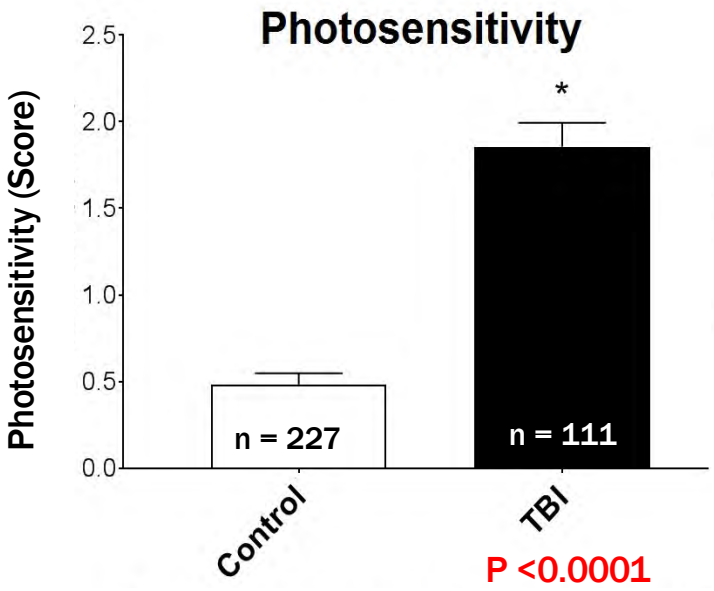


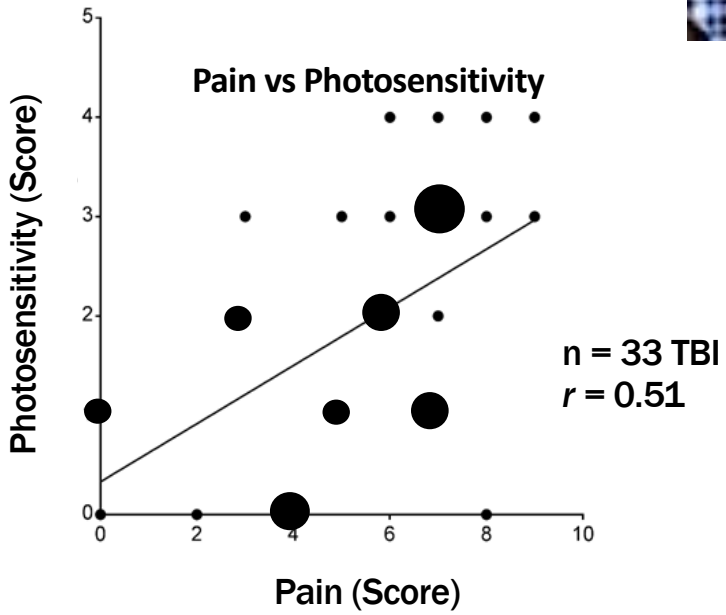


Martenson et al., 2016

Photosensitivity as a window into CNS pain

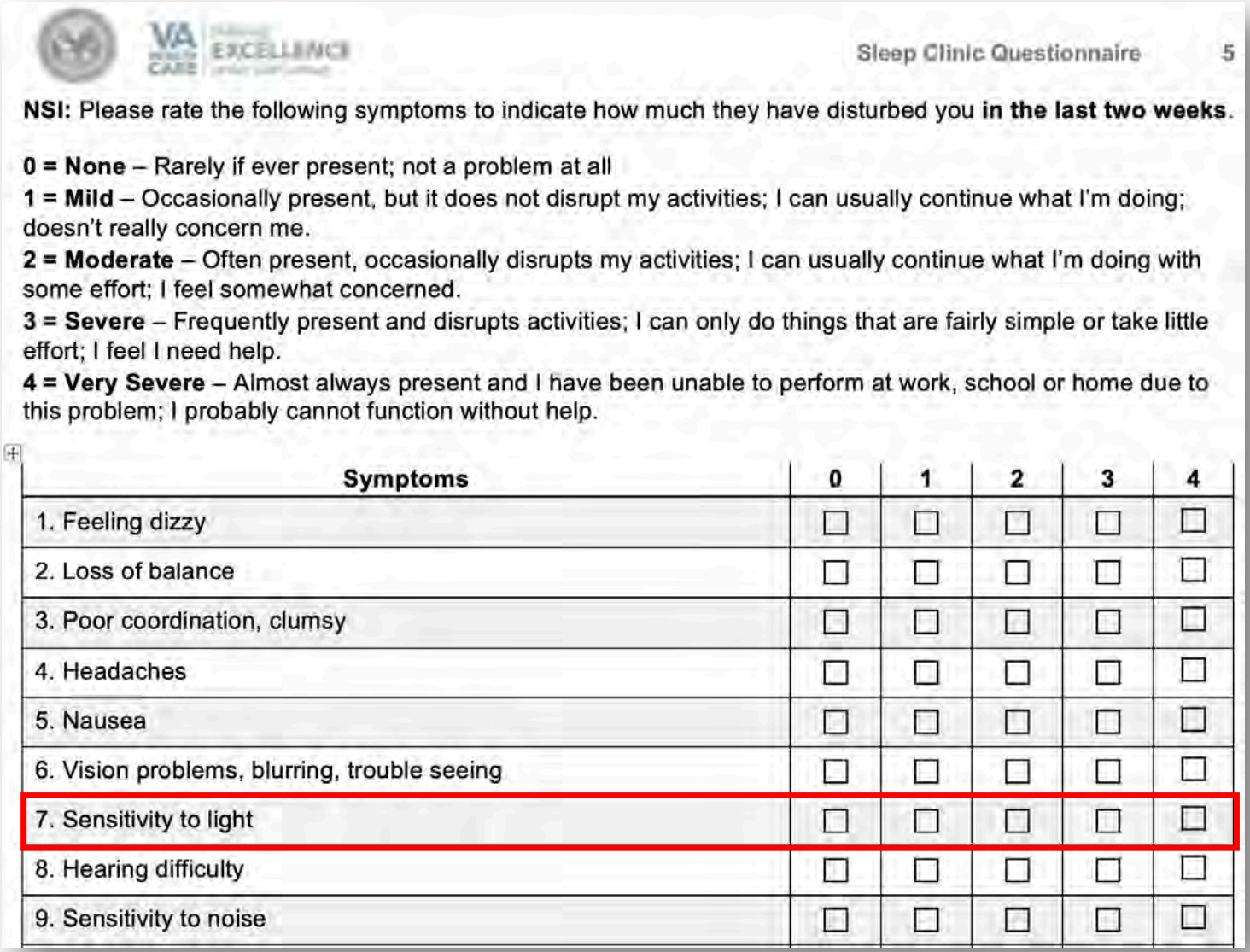
What about Veterans with TBI??





Adapted from: Balba & Elliott *et al.*, 2018, *Journal of Clinical Sleep Medicine*

Quantifying photosensitivity: NSI



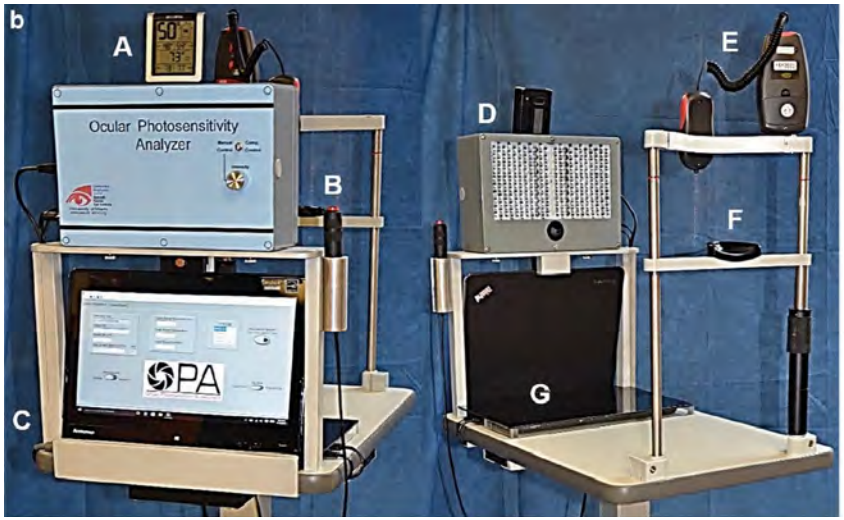
Sleep Clinic Questionnaire 5

NSI: Please rate the following symptoms to indicate how much they have disturbed you **in the last two weeks**.

0 = None – Rarely if ever present; not a problem at all
1 = Mild – Occasionally present, but it does not disrupt my activities; I can usually continue what I'm doing; doesn't really concern me.
2 = Moderate – Often present, occasionally disrupts my activities; I can usually continue what I'm doing with some effort; I feel somewhat concerned.
3 = Severe – Frequently present and disrupts activities; I can only do things that are fairly simple or take little effort; I feel I need help.
4 = Very Severe – Almost always present and I have been unable to perform at work, school or home due to this problem; I probably cannot function without help.

Symptoms	0	1	2	3	4
1. Feeling dizzy	☐	☐	☐	☐	☐
2. Loss of balance	☐	☐	☐	☐	☐
3. Poor coordination, clumsy	☐	☐	☐	☐	☐
4. Headaches	☐	☐	☐	☐	☐
5. Nausea	☐	☐	☐	☐	☐
6. Vision problems, blurring, trouble seeing	☐	☐	☐	☐	☐
7. Sensitivity to light	☐	☐	☐	☐	☐
8. Hearing difficulty	☐	☐	☐	☐	☐
9. Sensitivity to noise	☐	☐	☐	☐	☐

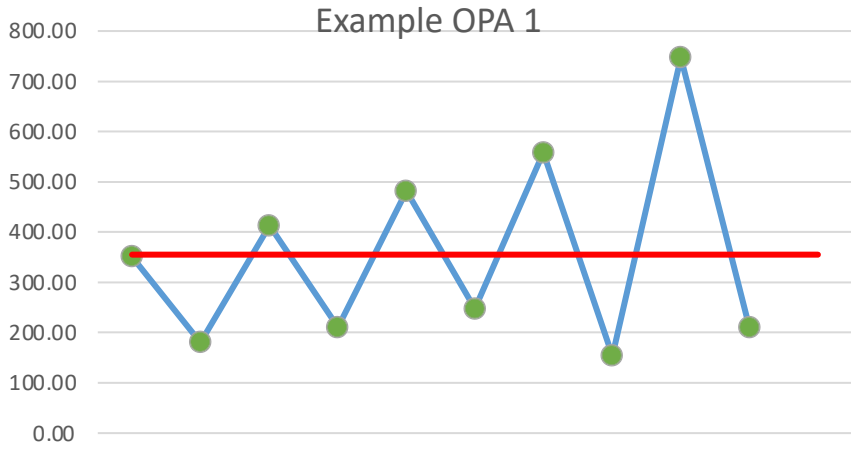
Quantifying photosensitivity: Ocular Photosensitivity Analyzer (OPA)

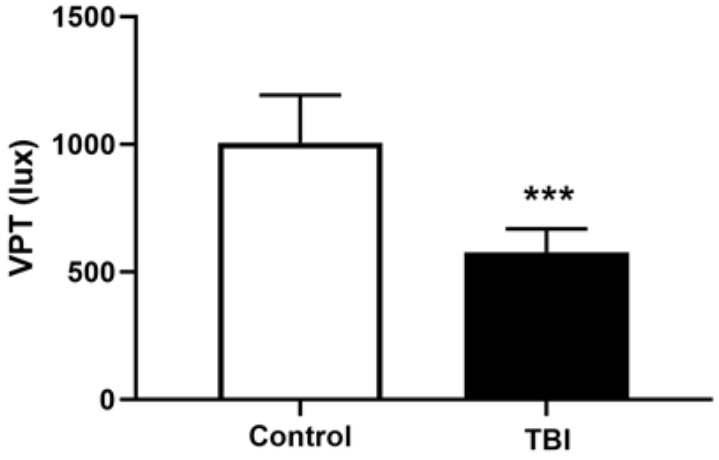


Light dose examples (lux)

Direct sunlight: up to 100,000 lux
Full daylight (indirect): ~10,000 lux
Overcast day: ~1,000 lux
Office lighting: ~500 lux
Full moon on a clear night: 1 lux

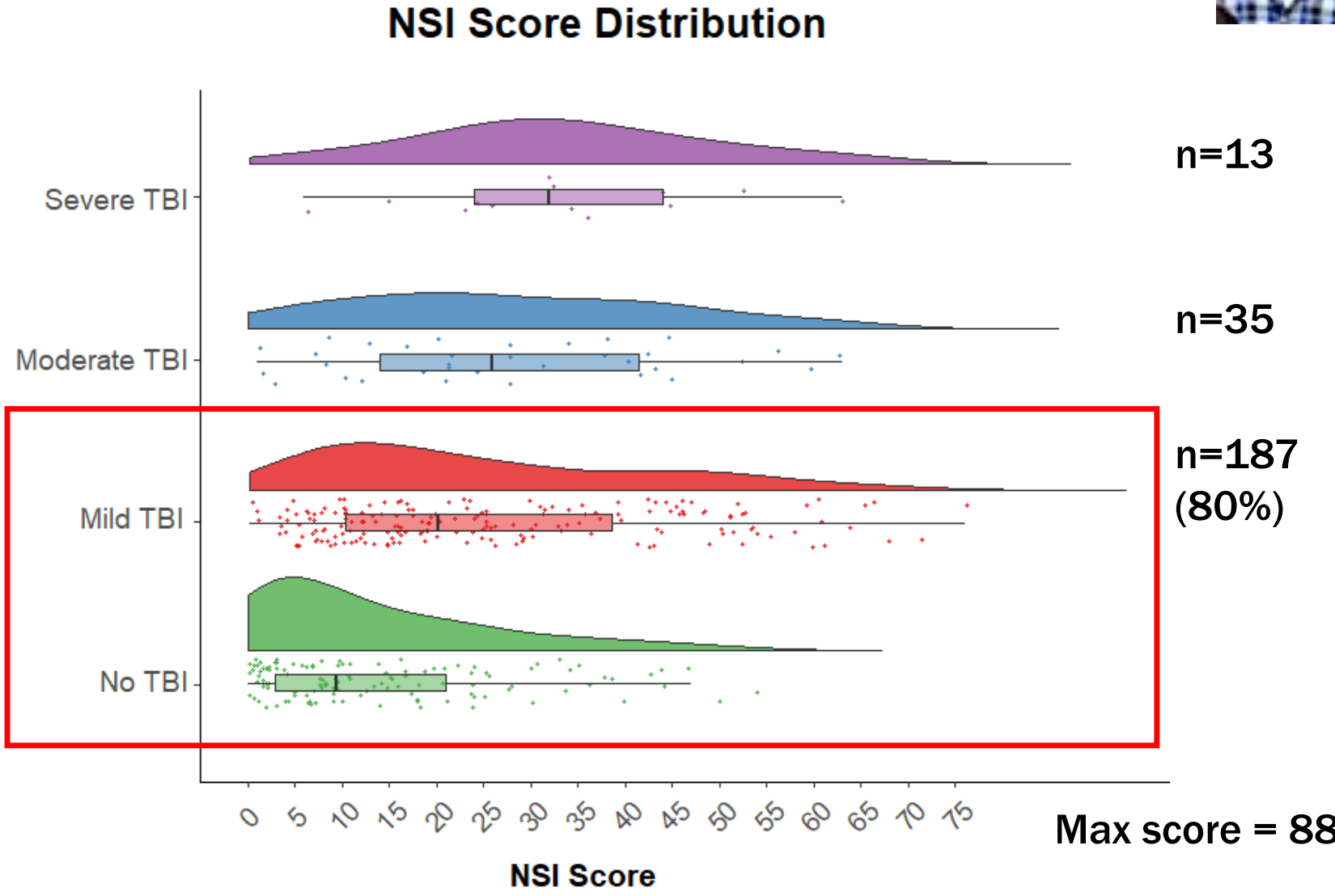
n=395 subjects



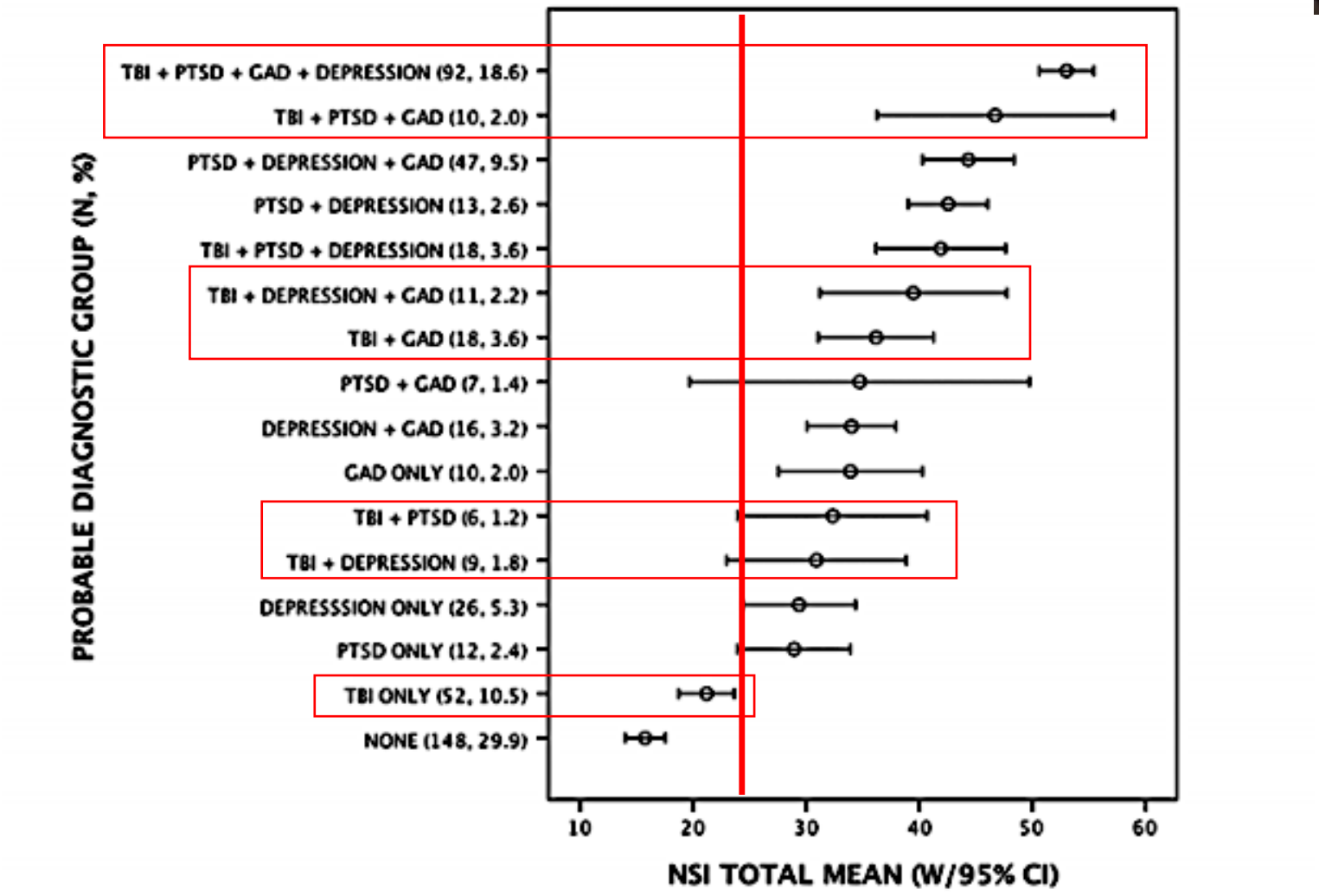


Adapted from: Verriotto et al., 2017

Taking a closer look at our TBI groups

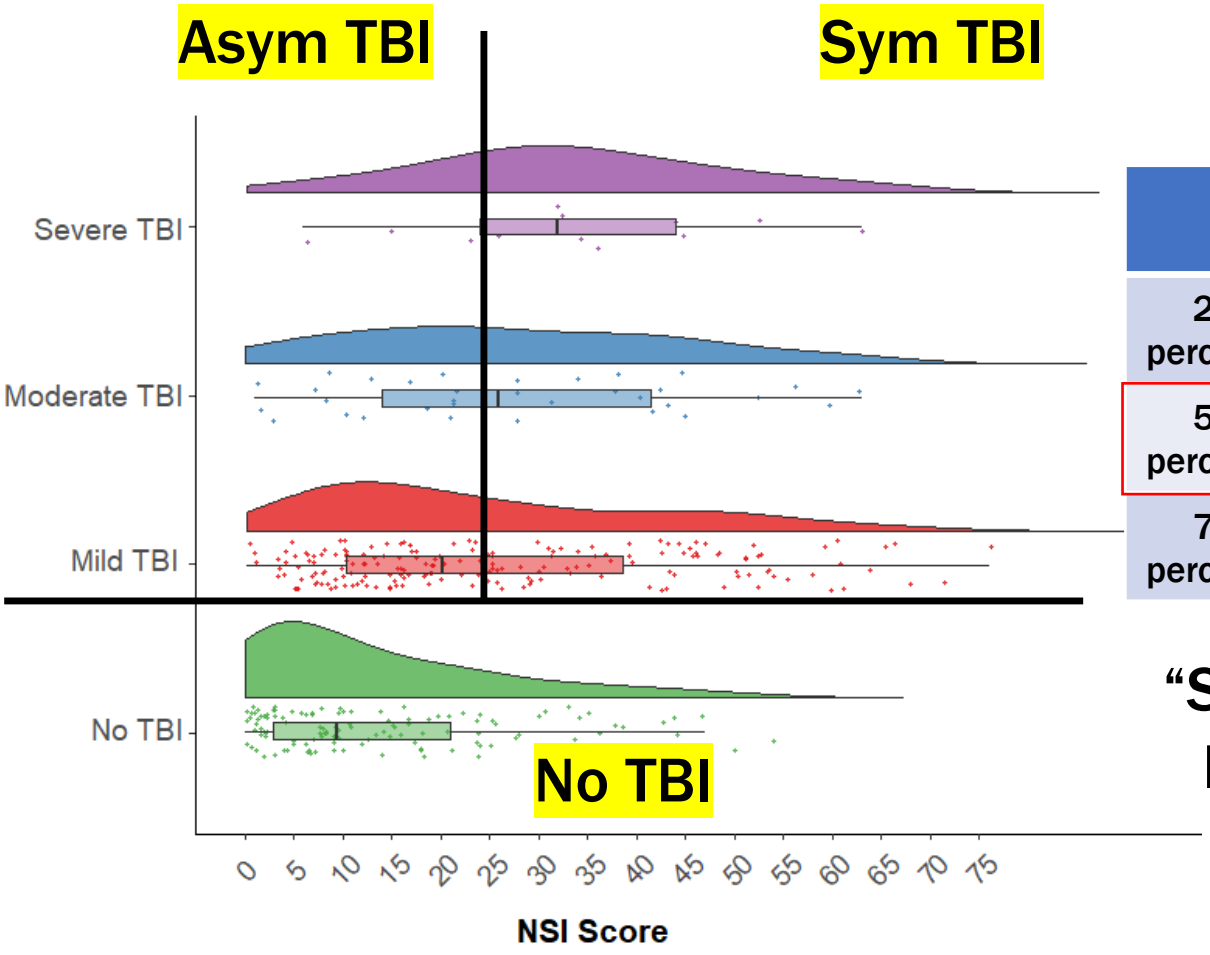


Taking a closer look at our TBI groups



King et. al., 2012, *J Rehab Res Dev*

Redefining our TBI groups

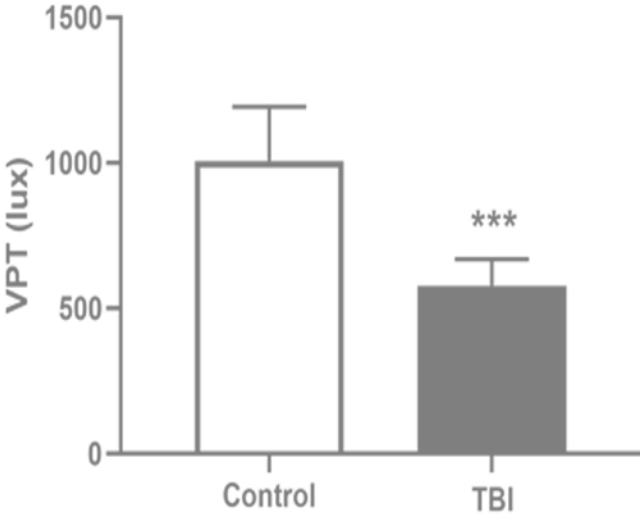


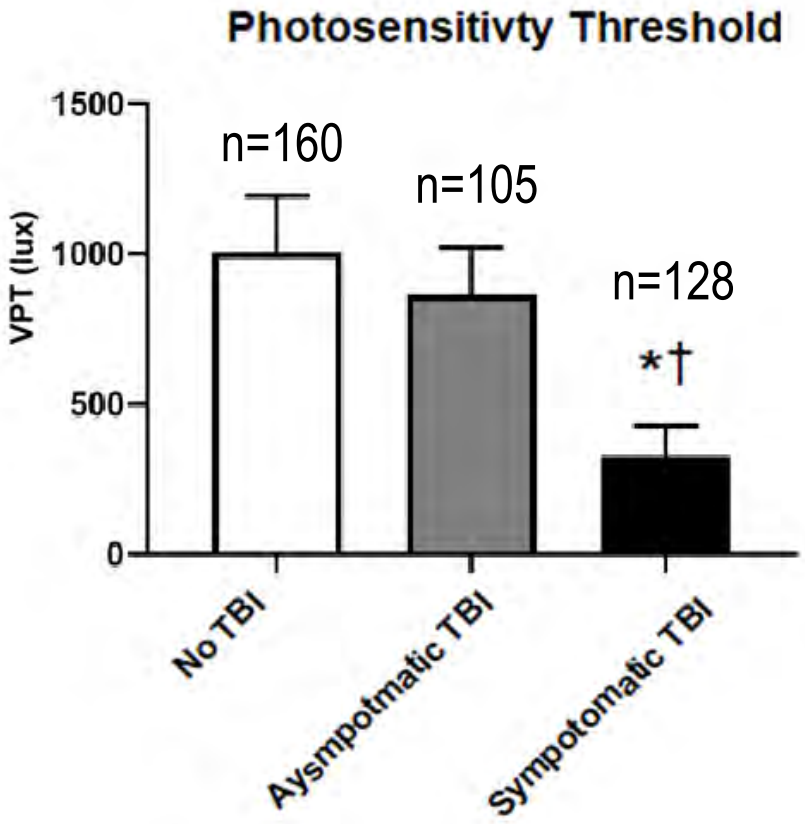
	TBI NSI score	No TBI NSI score
25th percentile	13	3
50th percentile	23	12
75th percentile	42	13

"Symptomatic TBI"
NSI cutoff >= 24

Photosensitivity threshold is reduced in Symptomatic TBI (NSI>=24)

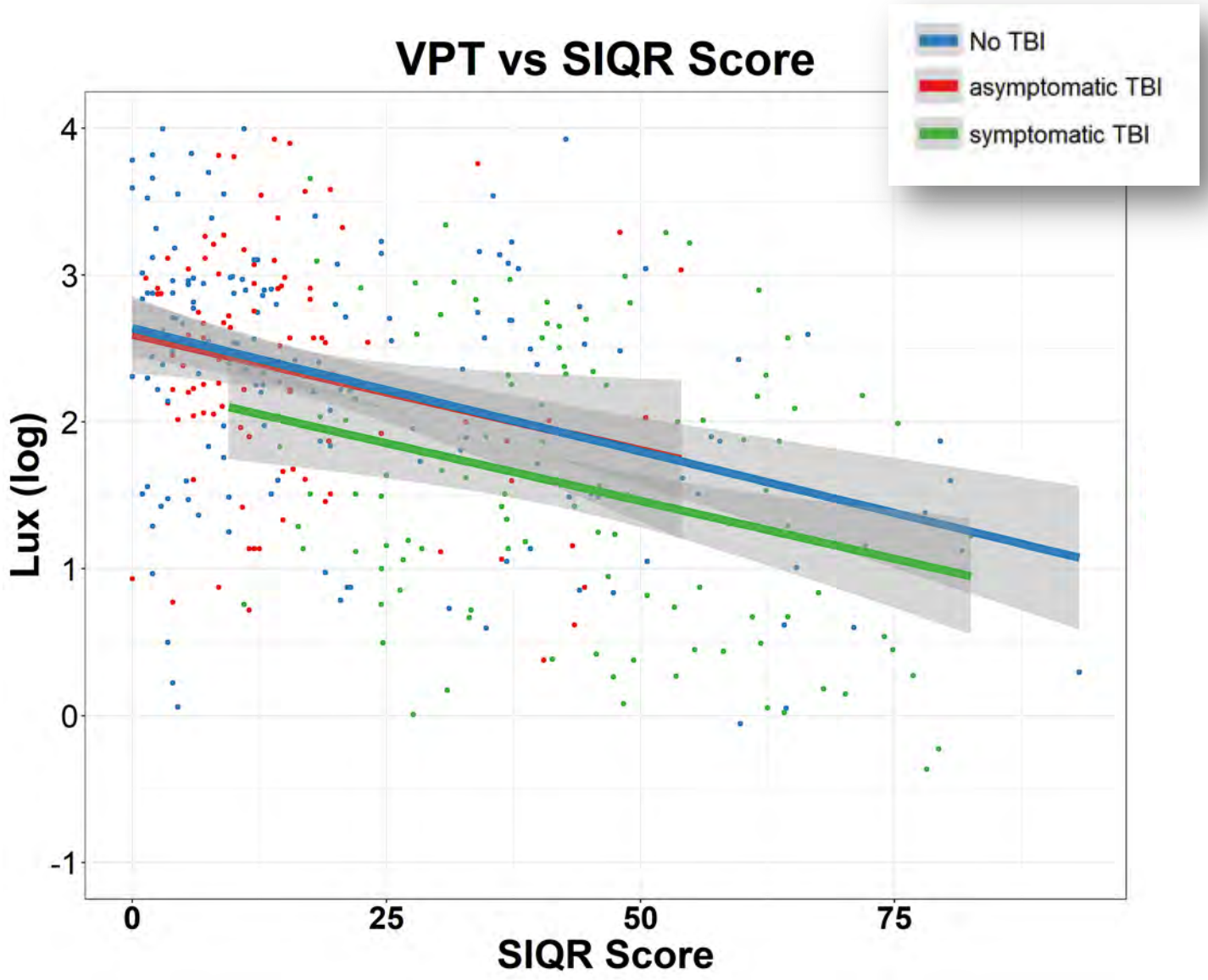
n=395 subjects





*** = P <0.001 vs Control
* = P <0.05 vs No TBI
† = P <0.05 vs Asymptomatic TBI

Photosensitivity strongly correlates with chronic pain complaints

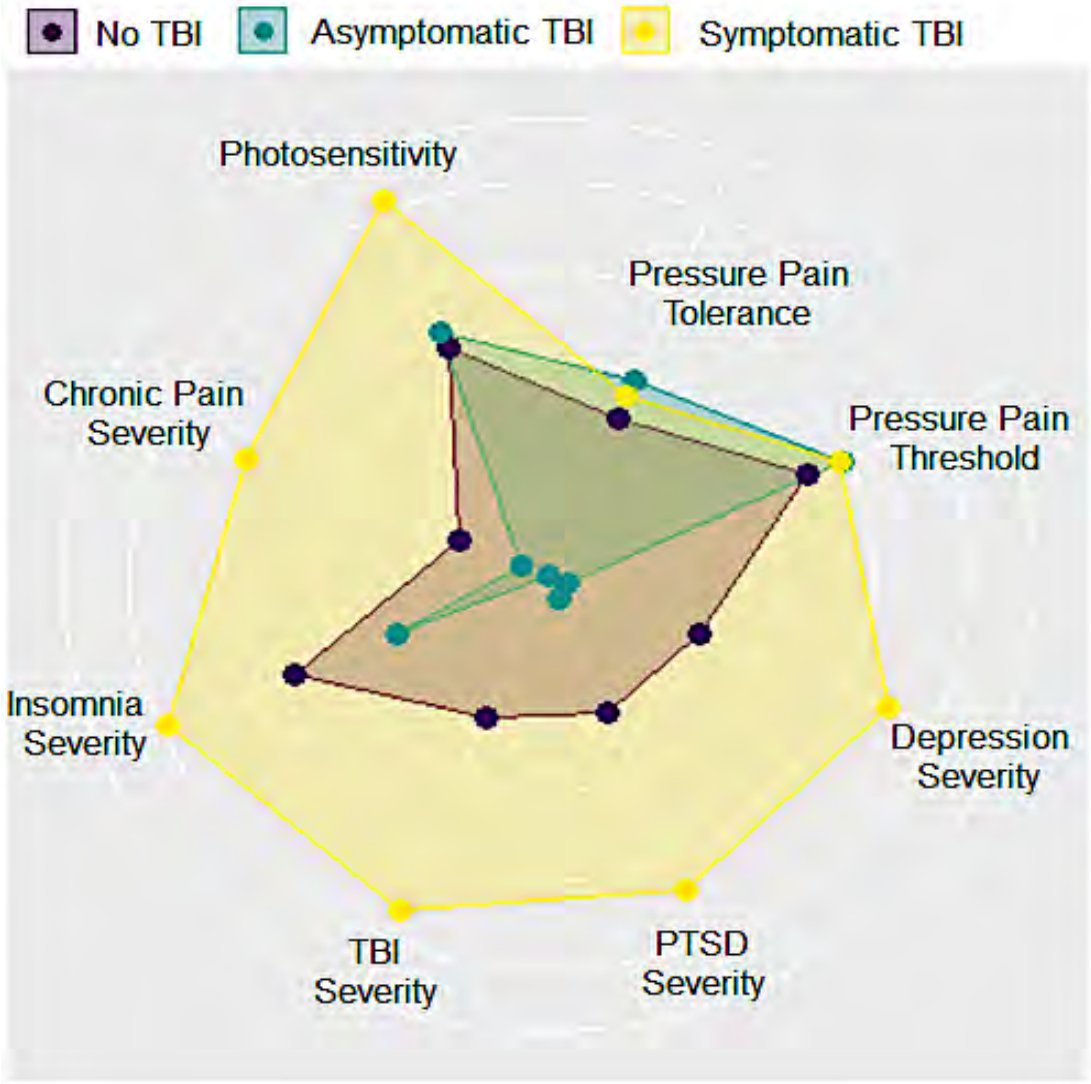


No TBI:
R = -0.384
P <0.001

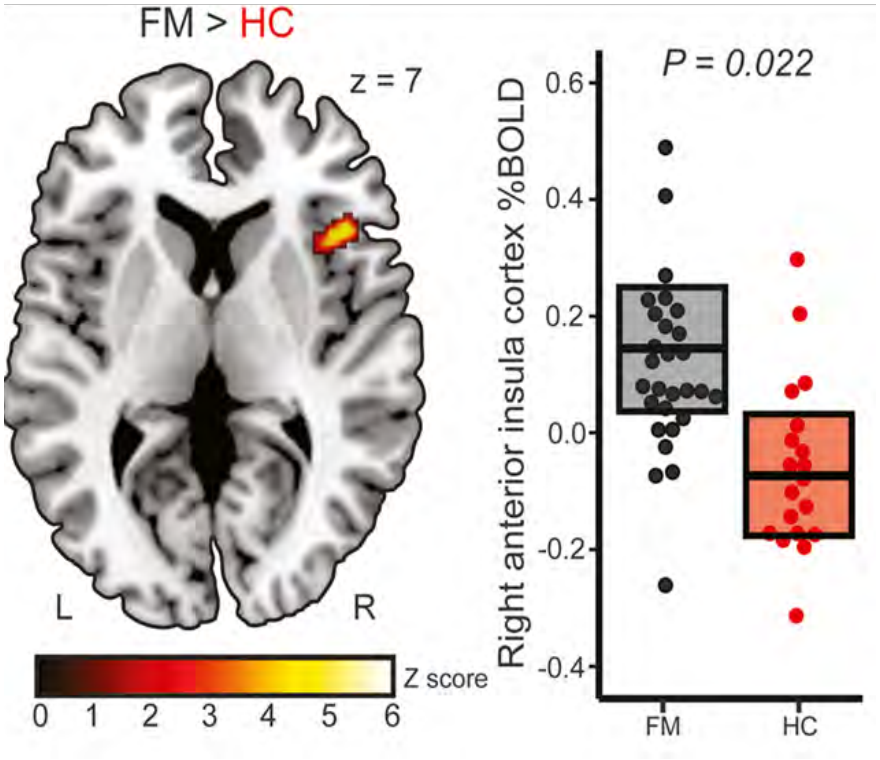
Asym TBI:
R = -0.231
P = 0.021

Sym TBI:
R = -0.308
P <0.001

Photosensitivity is not the only problem in Symptomatic TBI…



Photosensitivity as a window into CNS pain: fMRI studies



Harte et al., 2016

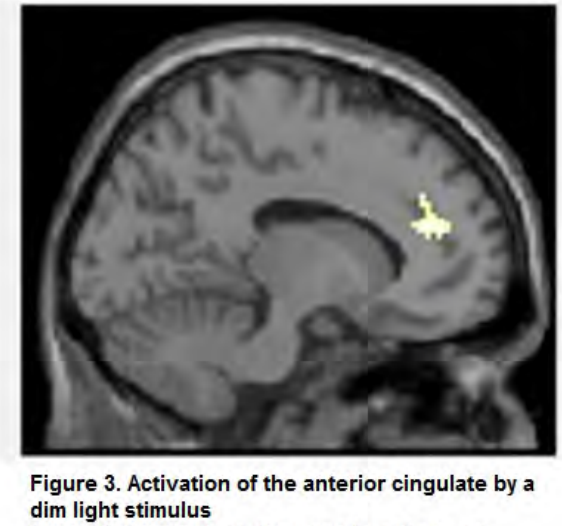


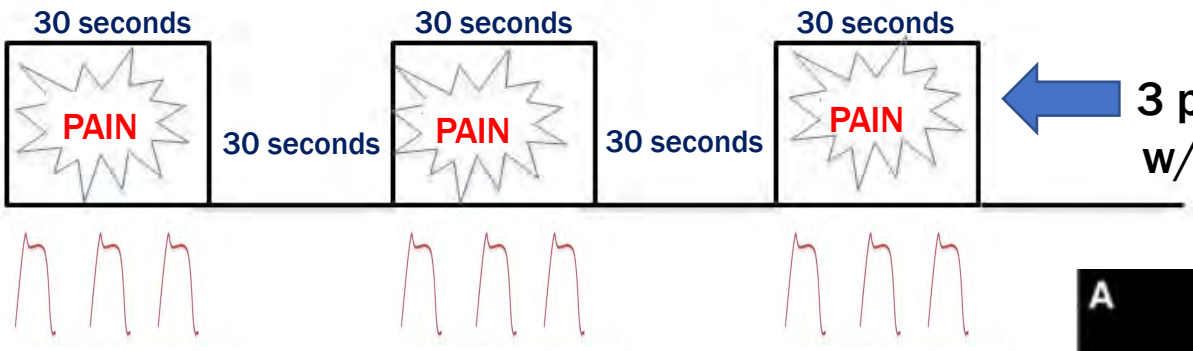
Figure 3. Activation of the anterior cingulate by a dim light stimulus

(Unpublished Data on FM patient)

Photosensitivity as a window into CNS pain: fMRI studies

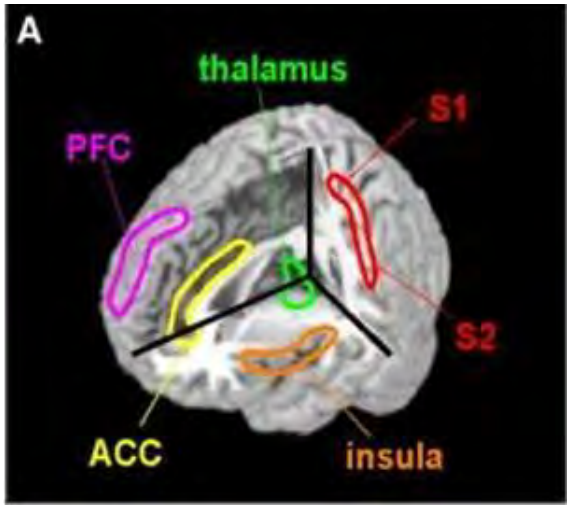

Does dim light activate pain circuitry in Veterans with Symptomatic TBI??

1. Identify pain-related regions using pressure-evoked pain block-design



3 pain stimuli per block w/ 7 sec intervals

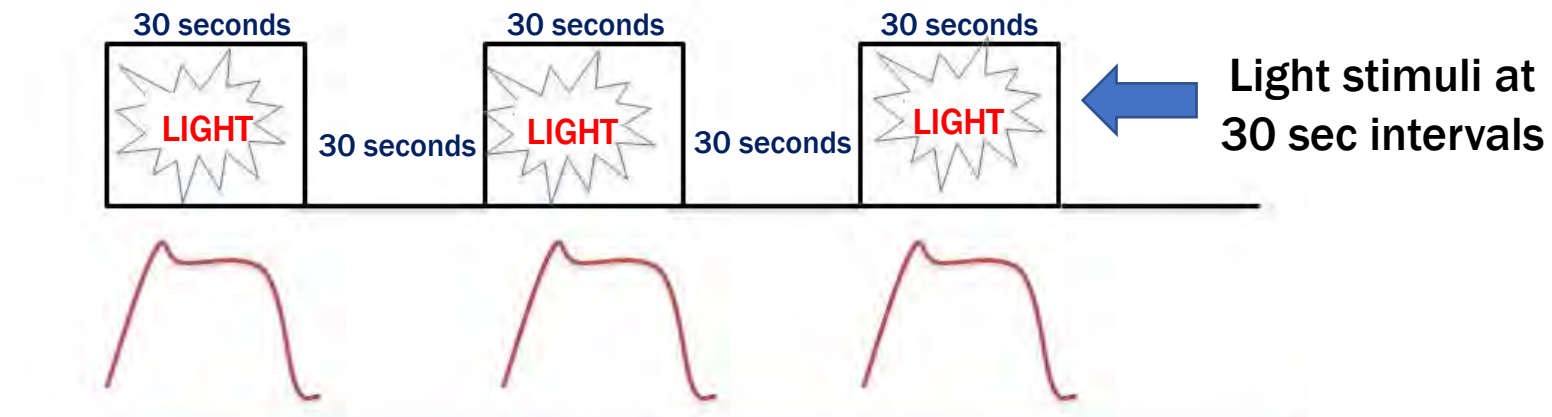
- Primary Somatosensory Cortex (S1)
- Secondary Somatosensory Cortex (S2)
- Insula
- Anterior Cingulate Cortex
- Thalamus
- Prefrontal Cortex



Photosensitivity as a window into CNS pain: fMRI studies


Does dim light activate pain circuitry in Veterans with Symptomatic TBI??

2. Create task-activation maps based on ROIs defined by evoked pain. Contrast Light blocks with Rest.

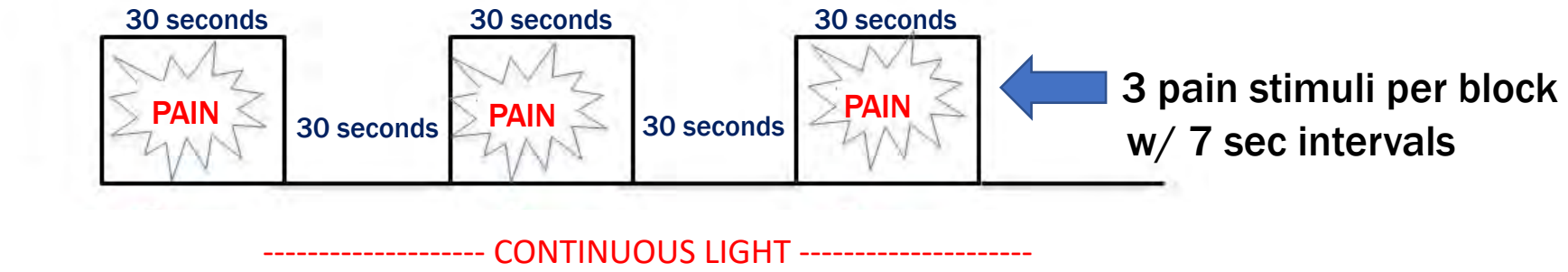


Hypothesis: Light will activate pain-related circuitry in Symptomatic TBI group but not in Controls.

Photosensitivity as a window into CNS pain: fMRI studies

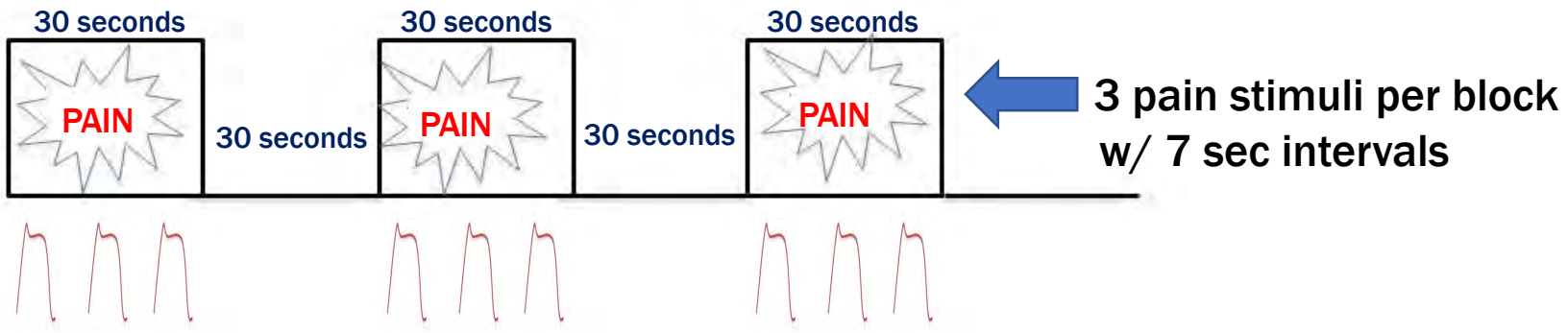

Does dim light activate pain circuitry in Veterans with Symptomatic TBI??

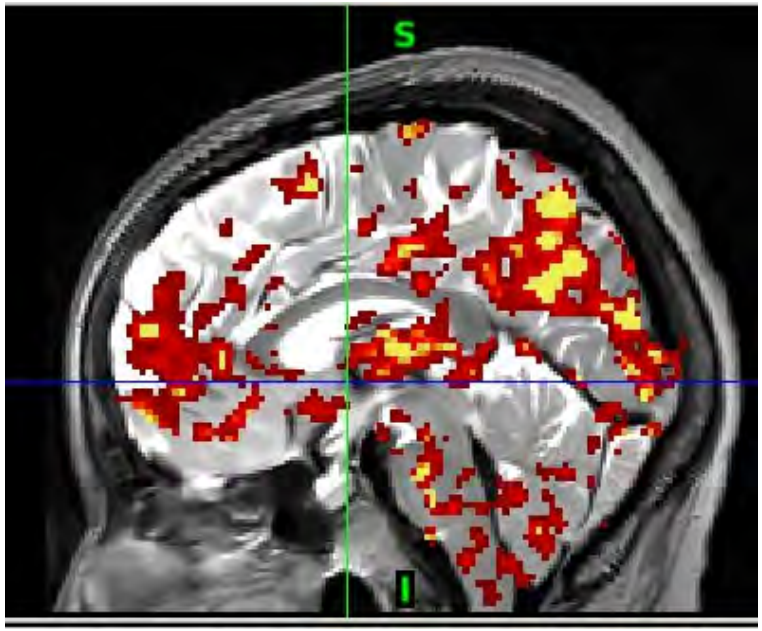
3. Does light exacerbate pain?
   Contrast Light+Pain blocks with Light alone.

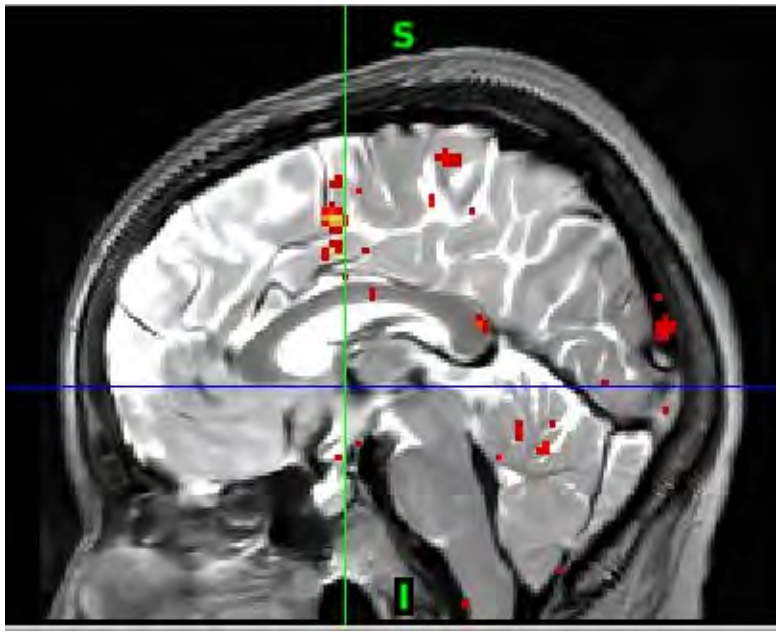


Hypothesis: Light will exacerbate pain in Symptomatic TBI group but not in Controls.

Pain activates pain circuits in Symptomatic TBI



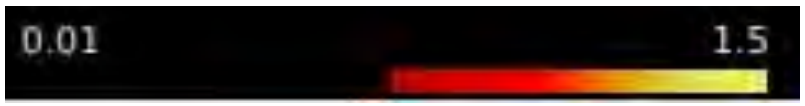




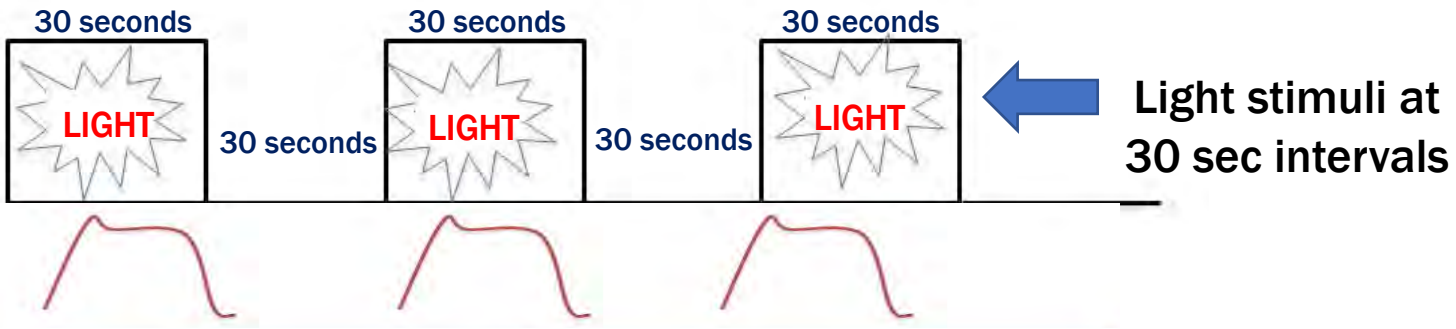
Chronic pain (n=3) – Controls (n=4)

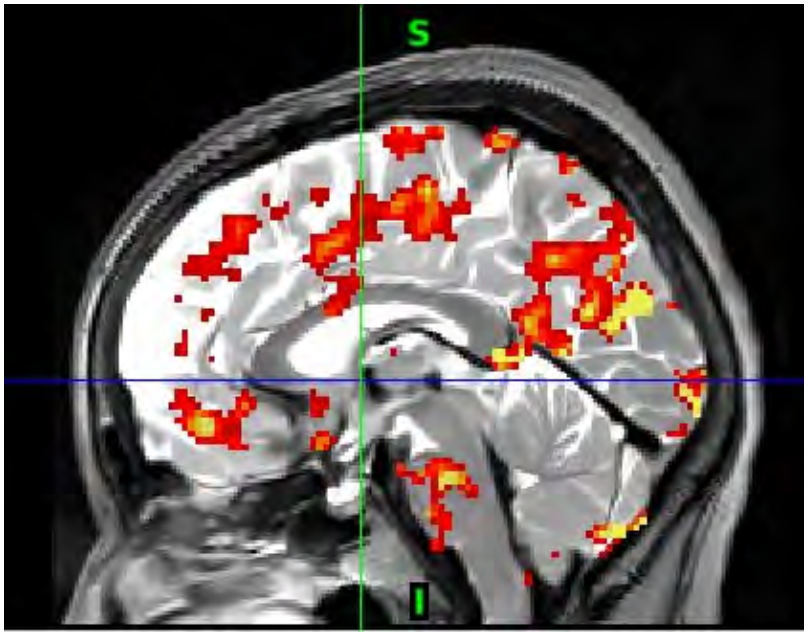
unpaired t-test
z-scores

Controls (n=4) – Chronic pain (n=3)

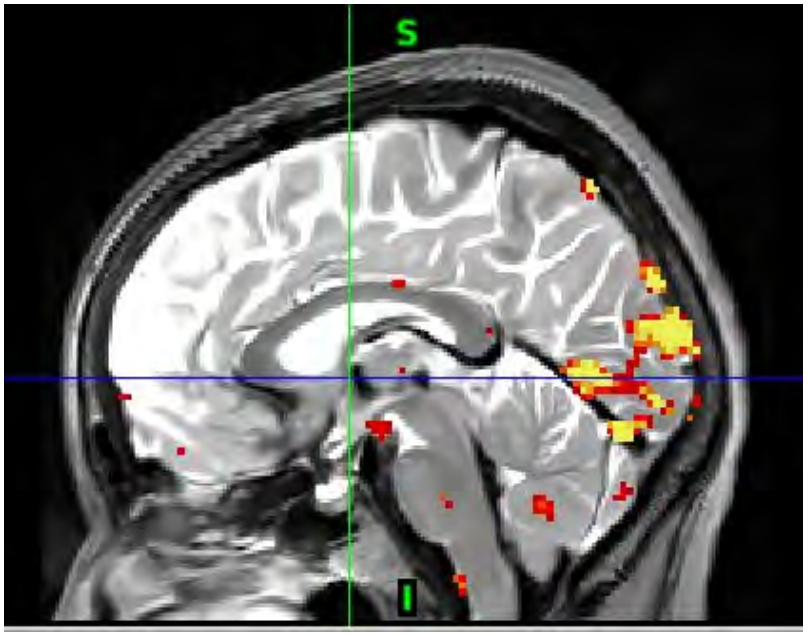


Light activates pain circuits in Symptomatic TBI

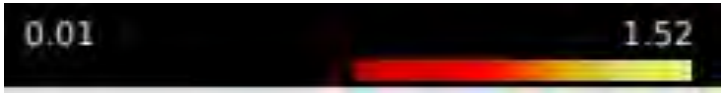




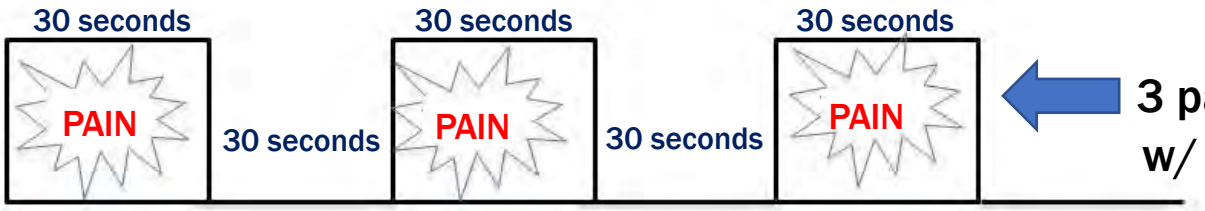
Chronic pain (n=3) – Controls (n=4)



Controls (n=4) – Chronic pain (n=3)

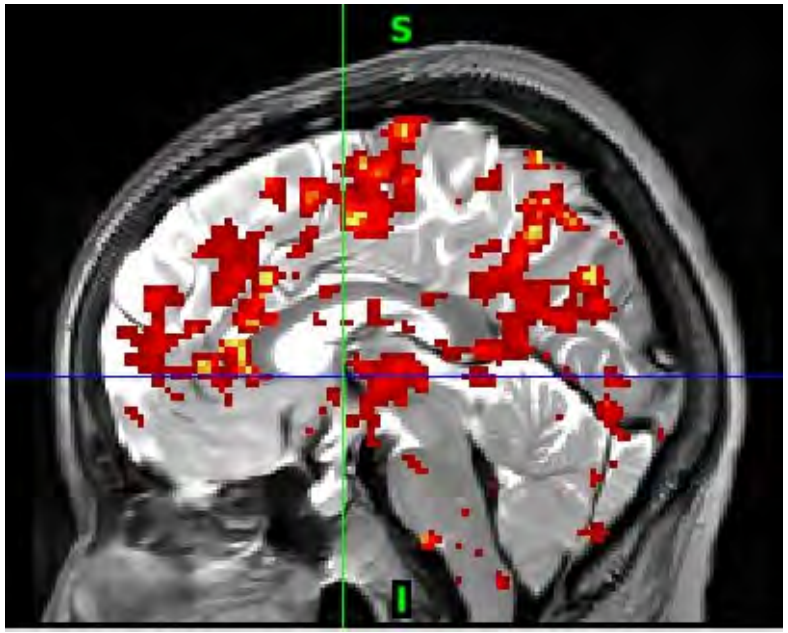


Light+Pain circuits in Symptomatic TBI

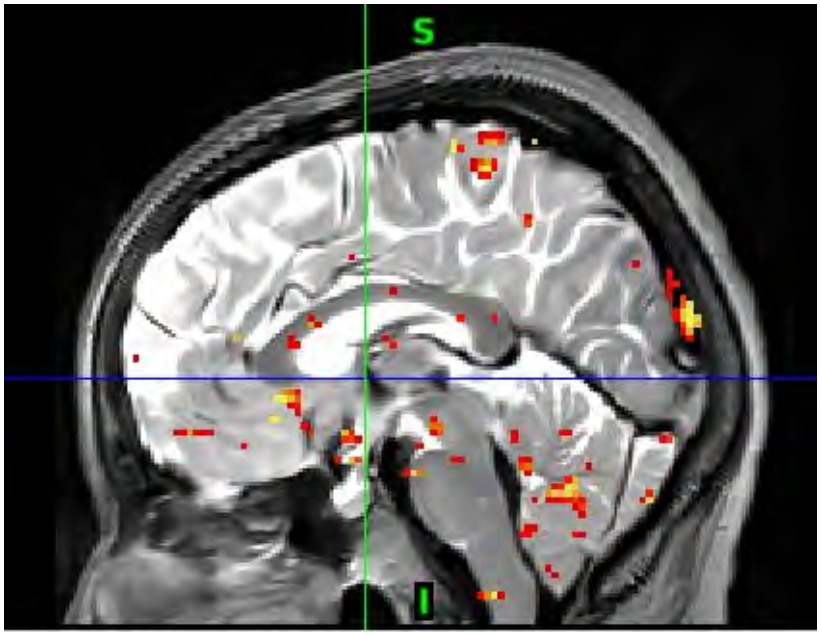


3 pain stimuli per block
w/ 7 sec intervals

---------- CONTINUOUS LIGHT ----------

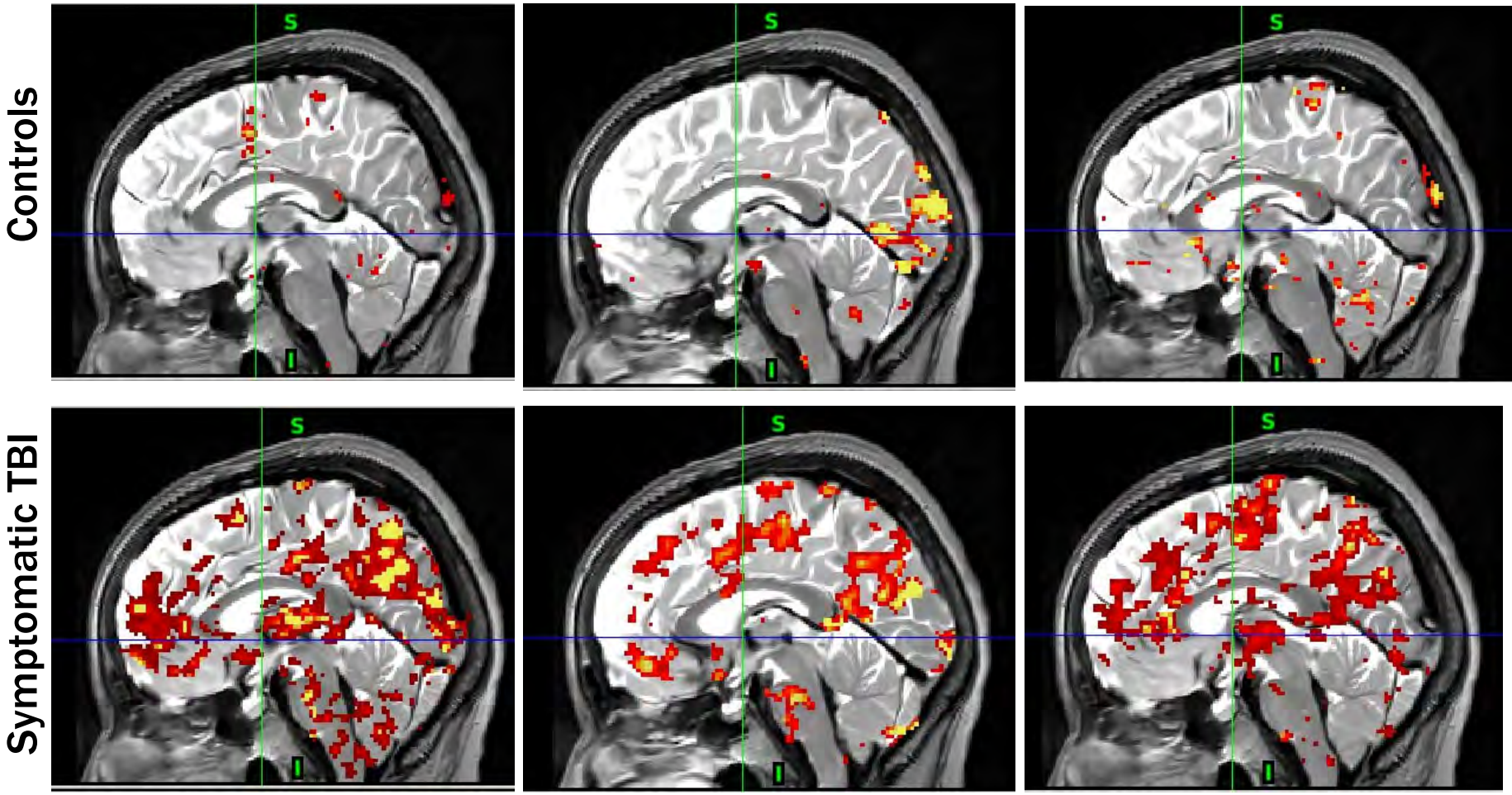


Chronic pain (n=3) – Controls (n=4)



Controls (n=4) – Chronic pain (n=3)

Photosensitivity may be a window into central sensitization of pain



Summary

- TBI is associated with photosensitivity and chronic pain.
- Light activates pain circuits in those with symptomatic TBI, but not controls.
- Photosensitivity may be a window into central sensitization of pain.

Lessons Learned: How is TBI evaluated in research studies?

3 Typical Methods:

1. Self-Report
2. Chart Review
3. Clinical interv

11. Have you ever had a concussion or traumatic brain injury (TBI)?

☐ No
☐ Yes

What year(s) did the event(s) occur?

Was it mild or severe?

☐ Mild
☐ Severe (hospitalized)

Head Trauma Events Checklist (HTEC)

VA HEALTH CARE | Defining EXCELLENCE in the 21st Century

Version: 12-21-18

Structured TBI Interview

Subject ID:_____ **Date:**_____ **Interviewer:**_____ **Phone/in person:**_____

1. "At any point in your life, have you had an accident or injury to your head that resulted in confusion, feeling dazed/stunned, or seeing stars?"
   1. ☐ No
   2. ☐ Yes ⇒
      1. "How many times has this happened in your lifetime?" ☐
      2. "Can you tell me about one injury that was **most significant** to you?" Briefly describe:

         a. # of years since injury: ☐

         b. Was the injury before, after, or during military duty?
            ☐ Before
            ☐ After
            ☐ During

         c. Was the injury a result of a direct or indirect blow to head?
            ☐ Direct
            ☐ Indirect
            ☐ Unknown

         d. Was there evidence of an intracranial injury (bleeding) or skull fracture?
            ☐ No
            ☐ Yes

         e. Cause
            ☐ MVC ☐ MVC-Ped ☐ Fall
            ☐ Assault ☐ Sports ☐ Blast
            ☐ Other: ☐

         f. Location of Impact:
            ☐ Frontal ☐ L Temporal ☐ R Temporal
            ☐ L Parietal ☐ R Parietal ☐ Occipital
            ☐ Neck ☐ Indirect Force ☐ Unknown

         g. Did you lose consciousness?
            ☐ No
            ☐ Yes ⇒ Duration (hours): ☐

         h. Are there events before or after the event that you have no memory of?
            ☐ No
            ☐ Before ⇒ Duration (hours): ☐
            ☐ After ⇒ Duration (hours): ☐

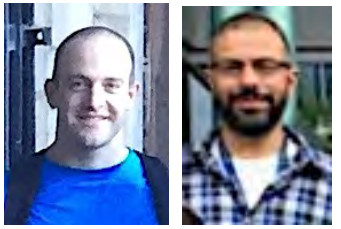
         i. Were seizures observed?
            ☐ No
            ☐ Yes ⇒ Details: ☐

- **Semi-structured interview with both closed and open-ended questions.**
- **Considered "gold standard," but still relies on subject's self-report of injury.**

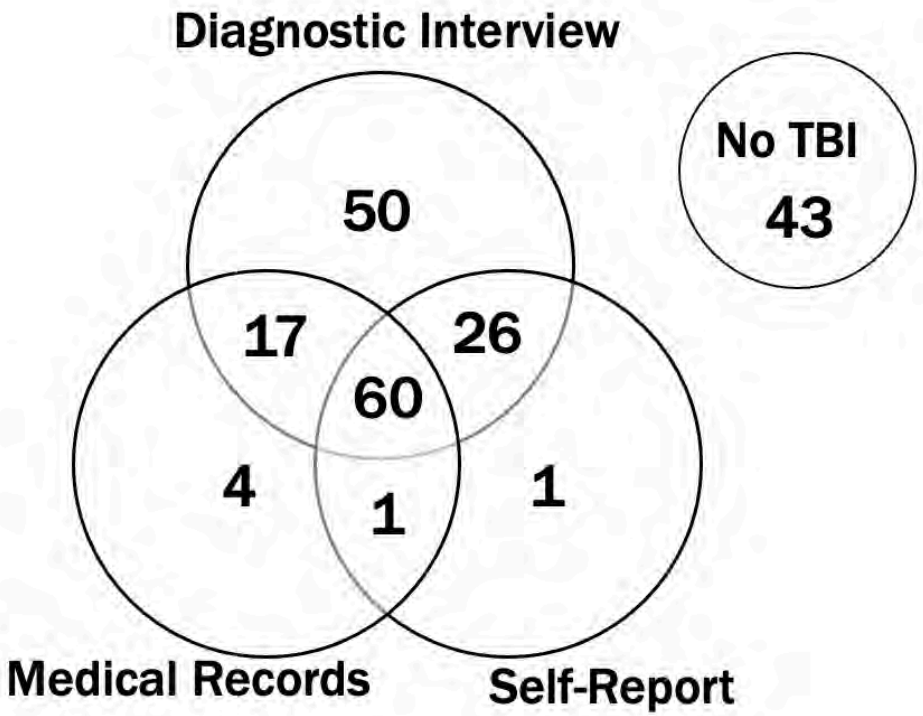
Do rates of TBI differ based on the method of diagnosis?

Are there differences in TBI symptoms based on these different methods?

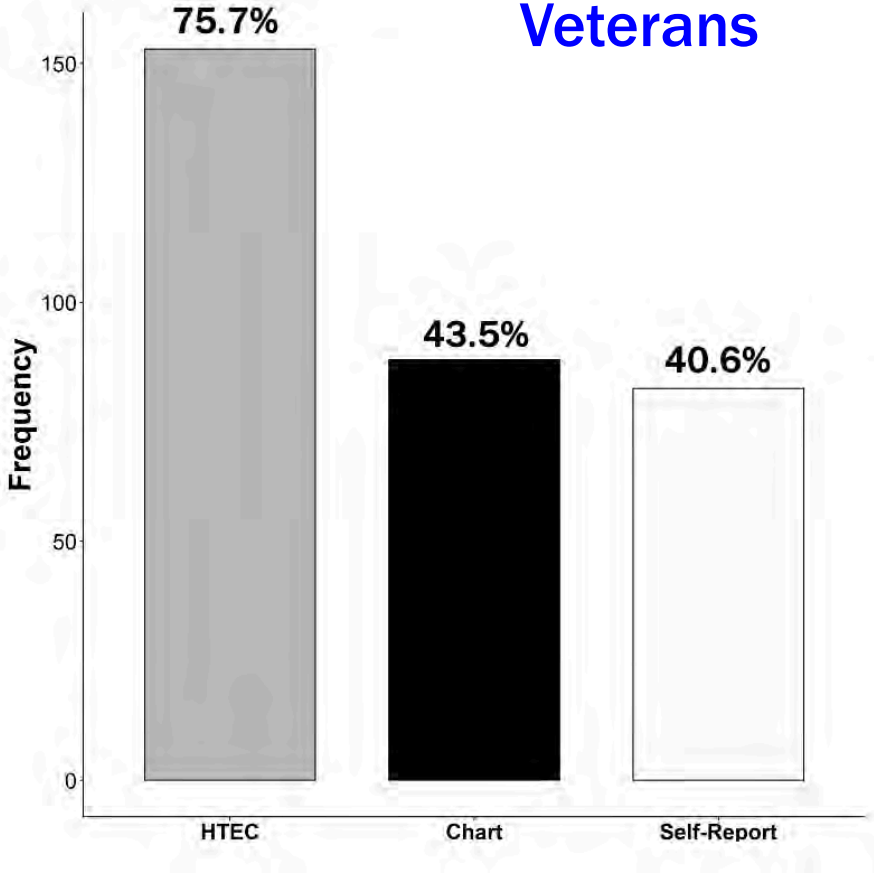
Rates of TBI Diagnoses by Evaluation Type



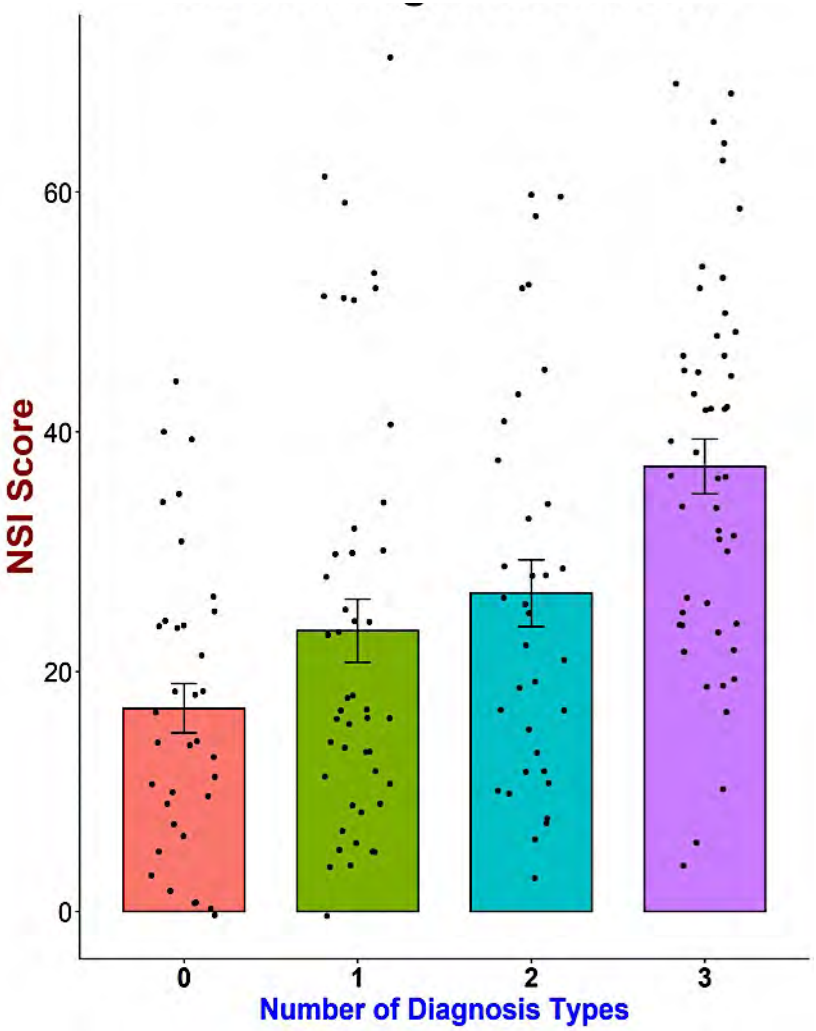
TBI-1dx
TBI-2dx
TBI-3dx

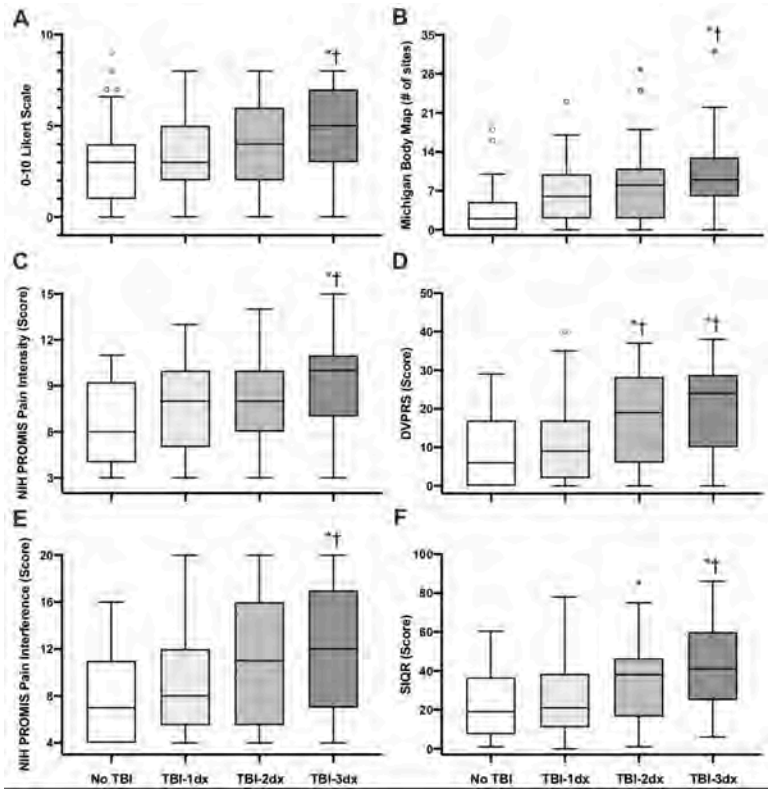


n=200 consecutive Veterans



TBI-3dx group has highest NSI and pain scores





Balba & Elliott et al., in prep

TBI-3dx group has higher #TBIs

Table 3. *TBI specific information.*

	Whole group	No TBI	TBI-1dx	TBI-2dx	TBI-3dx
TBI Recency					
<1 year	4 (2.0%)	-	1 (2.0%)	2 (4.5%)	2 (3.4%)
1-5 years	19 (9.5%)	-	4 (8.0%)	3 (6.8%)	9 (15.2%)
6-10 years	9 (4.5%)	-	1 (2.0)	3 (6.8%)	5 (8.5%)
11-30 years	51 (25.5%)	-	19 (38.0%)	14 (31.8%)	18 (30.5%)
>30 years	70 (35.0%)	-	25 (50.0%)	22 (50.0%)	23 (40.0%)
Average, years	18.2 ± 16.4	-	31.8 ± 17.4	27.7 ± 16.3	24.4 ± 19.0
Age of injury, years	27.8 ± 17.9	-	25.9 ± 16.5	28.0 ± 15.5	28.0 ± 14.5
Number of TBIs					
1	28 (18.3%)	-	15 (28.3%)	9 (20.0%)	4 (6.8%)‡
2-4	61 (39.9%)	-	18 (34.0%)	18 (40.0%)	25 (42.4%)
5-10	42 (27.4%)	-	11 (20.8%)	12 (26.7%)	19 (32.2%)
11-25	13 (8.5%)	-	5 (9.4%)	3 (6.7%)	5 (8.5%)
>25	7 (4.6%)	-	1 (1.9%)	2 (4.4%)	4 (6.8%)
Maximum	160	-	26	46	160
Average, number	7.1 ± 14.8	-	5.1 ± 6.3	5.9 ± 8.3	9.7 ± 21.9

TBI-3dx group was deployed more

Table 4. *Military-specific information.*

	Whole group	No TBI	TBI-1dx	TBI-2dx	TBI-3dx
Service duration, years	6.9 ± 6.9	6.8 ± 6.8	7.3 ± 7.7	5.9 ± 5.1	7.5 ± 7.6
Exposure to combat, *n* (%)	57 (28.5%)	8 (18.6%)	12 (22.6%)	13 (28.9%)	24 (40.7%)
Service connection, %	55.3 ± 30.8	44.4 ± 29.4	50.7 ± 32.6	60.0 ± 26.5	60.6 ± 31.7
Branch					
Army	82 (41.0%)	17 (39.5%)	19 (35.8%)	19 (42.2%)	27 (45.8%)
Navy	33 (16.5%)	10 (23.3%)	10 (18.9%)	6 (13.3%)	7 (11.9%)
Air Force	31 (15.5%)	9 (20.9%)	8 (15.1%)	7 (15.6%)	7 (11.9%)
Marines	27 (13.5%)	3 (7.0%)	7 (13.2%)	9 (20.0%)	8 (13.6%)
Coast Guard	3 (1.5%)	1 (2.3%)	1 (1.9%)	0	1 (1.7%)
Reserve	11 (5.5%)	1 (2.3%)	4 (7.5%)	2 (4.4%)	4 (6.8%)
National Guard	3 (1.5%)	0	1 (1.9%)	1 (2.2%)	1 (1.7%)
Multiple Branches	7 (3.5%)	1 (2.3%)	3 (5.7%)	1 (2.2%)	2 (3.4%)
Unknown	3 (1.5%)	1 (2.3%)	0	0	2 (3.4%)
Number of Deployments					
Not deployed	68 (34.0%)	15 (34.9%)	22 (41.5%)	17 (37.8%)	14 (23.7%)
1	70 (35.0%)	16 (37.2%)	17 (32.1%)	15 (23.3%)	22 (37.3%)
2 to 3	47 (23.5%)	9 (20.9%)	13 (24.5%)	13 (28.9%)	12 (20.3%)
4 to 5	15 (7.5%)	3 (7.0%)	1 (1.9%)	0	11 (18.6%)†‡

Why is this important?

- Differences in diagnostic methods may explain the wide range in estimated rates of TBI and presence/severity of chronic symptoms.
  - Some researchers believe that mTBI does not ever lead to chronic symptoms;
  - Others (like us) have data that suggest it does.
- TBI diagnostic congruency across multiple approaches will yield more robust and consistent symptoms than a single TBI diagnosis (even HTEC alone).
  - Perhaps consider using all 3 methods in studies?

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