

OPEN

# Hypersensitivity to Noise and Light Over 1 Year After Mild Traumatic Brain Injury: A Longitudinal Study on Self-Reported Hypersensitivity and Its Influence on Long-Term Anxiety, Depression, and Quality of Life

Marilien C. Marzolla, MSc; Melloney Wijenberg, PhD; Sven Stapert, PhD; Petra Hurks, PhD; Jan Schepers, PhD; Caroline van Heugten, PhD

**Objective:** This study aimed to investigate (1) the prevalence of self-reported sensory hypersensitivity (noise [NS] and light [LS]) over 1 year after mild traumatic brain injury (mTBI) in adults and (2) the impact of NS and LS measured 2 weeks after injury on long-term outcomes 12 months postinjury, while controlling for postconcussion symptoms. **Setting:** Participants were recruited from 6 hospitals in the south of the Netherlands and were tested 4 times (2 weeks, 3 months, 6 months, and 12 months postinjury), using self-report questionnaires. **Participants:** In total, 186 mTBI participants (diagnosed using WHO [World Health Organization]/EFNS [European Federation of Neurological Societies] criteria at the neurology/emergency department) and 181 participants with a minor orthopedic injury in their extremities (control group). **Design:** An observational, longitudinal, multicenter cohort study. **Main Measures:** NS and LS items (Rivermead Post-Concussion Symptoms Questionnaire) were used as main outcome variables to determine sensory hypersensitivity symptoms. Additional outcomes included anxiety, depression, health-related quality of life (HRQoL), and life satisfaction. **Results:** There was an elevated prevalence of NS and LS between 2 weeks and 3 months after injury in the mTBI group compared with controls. Approximately 3% of mTBI patients had persistent hypersensitivity symptoms during the whole course of the study. At 12 months postinjury, the mTBI and control groups did not differ in the prevalence of persistent hypersensitivity symptoms. There was no evidence of a predictive value of hypersensitivity within 2 weeks postinjury on anxiety, depression, HRQoL, or life satisfaction, 12 months later after controlling for postconcussion symptoms. **Conclusions:** These results not only confirm the presence of hypersensitivity symptoms after mTBI in the subacute stage but also provide assurance about the small size of the group that experiences persistent symptoms. Furthermore, there was no evidence that early NS and LS

**Author Affiliations:** Department of Neuropsychology and Psychopharmacology (Ms Marzolla and Drs Stapert, Hurks, and van Heugten), Section of Teaching and Innovation of Learning (Dr Wijenberg), and Department of Methodology and Statistics (Dr Schepers), Faculty of Psychology and Neuroscience, and Department of Psychiatry and Neuropsychology, School for Mental Health and Neuroscience (Dr van Heugten), Maastricht University, Maastricht, the Netherlands; Limburg Brain Injury Centre, Maastricht, the Netherlands (Ms Marzolla and Dr van Heugten); Department of Brain Injury Rehabilitation, Adelante Rehabilitation Centre of Expertise in Rehabilitation and Audiology, Hoensbroek, the Netherlands (Dr Wijenberg); and Department of Clinical and Medical Psychology, Zuyderland Medical Centre, Sittard-Geleen, the Netherlands (Dr Stapert).

The authors thank all participants and partaking hospitals for devoting their time. Furthermore, the authors express their gratitude to all staff and students who contributed to realize this project.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website ([www.headtraumarehab.com](http://www.headtraumarehab.com)).

The authors declare no conflicts of interest.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

**Corresponding Author:** Caroline van Heugten, PhD, Department of Psychiatry and Neuropsychology, School for Mental Health and Neuroscience, Maastricht University, Maastricht 6229 ER, the Netherlands ([caroline.vanheugten@maastrichtuniversity.nl](mailto:caroline.vanheugten@maastrichtuniversity.nl)).

DOI: 10.1097/HTR.0000000000000813

are uniquely associated with long-term emotional and quality-of-life outcomes, over and above general levels of postconcussion symptoms. **Key words:** *anxiety, depression, life satisfaction, light sensitivity, mild traumatic brain injury, noise sensitivity, postconcussion symptoms, quality of life*

**M**ILD TRAUMATIC BRAIN INJURY (mTBI) accounts for 58% to 88% of all traumatic brain injuries (TBIs).<sup>1</sup> It is typically defined by a Glasgow Coma Scale (GCS) score of 13 to 15 following an acute brain injury resulting from an external force or blow to the head.<sup>2</sup> Although it has attracted comparatively little attention in the literature, sensory hypersensitivity is a commonly reported postconcussion symptom after mTBI<sup>3,4</sup> and has been defined by Scheydt et al as “perceiving a stimulus as an atypical or excessive stimulation that exceeds an individual’s usual level.”<sup>5(p115)</sup> Individuals with sensory hypersensitivity report being easily overwhelmed in stimulus-rich environments,<sup>5</sup> which can lead to avoidance behavior, increased social isolation, and decreased quality of life.<sup>4,6</sup> Sensory hypersensitivity after mTBI has been reported across several sensory modalities; however, most frequently reported are noise sensitivity (NS) and light sensitivity (LS).<sup>4</sup> From this point onward, sensory hypersensitivity is referred to as *hypersensitivity*.

Studies assessing the occurrence of hypersensitivity after mTBI show varying results, that is, prevalence between 20% and 80%, which could be due to differences in methodology and definition of concepts.<sup>7–10</sup> Besides, longitudinal studies evaluating the course of symptoms at more than 2 time points are scarce. In a sample where NS and LS symptoms were measured 3 times over 12 months, NS increased from 9% to 25% and LS from 6% to 18%.<sup>11</sup> Other studies found decreases of NS and/or LS over a year from around 46% and 35% to 22% and 15%, respectively, between 2 weeks and 12 months postinjury.<sup>8,12</sup> However, none of these studies used a control group (for all time points) and the prevalence was not always statistically tested.

Therefore, the first aim of the present study was to investigate hypersensitivity symptoms over a period of 12 months, while measuring symptoms multiple times (ie, 4 times). Individuals with a minor orthopedic trauma injury were chosen as the control group because they are similar to individuals with mTBI in terms of medical care after their injury and expected benign recovery. Furthermore, it takes into account that hypersensitivity is common in the general population, that is, 16% of individuals in the general population rate themselves as being more sensitive than others.<sup>13,14</sup>

Next, hypersensitivity is known as a vulnerability factor that has a substantial impact on short- and long-term recovery,<sup>4,12,15</sup> and individuals with hypersensitivity report greater fatigue, neuroticism, and more negative emotional states.<sup>16</sup> In an mTBI group, NS was positively correlated with feelings of anxiety and depression,<sup>17</sup> and hypersensitivity after mTBI was associated with

poorer health-related quality of life (HRQoL), a self-report measure referring to the health aspects of quality of life.<sup>6,18,19</sup> Hypersensitivity is known to co-occur with emotional symptoms<sup>8,10</sup> after TBI; however, information is lacking on the predictive value of hypersensitivity. Subsequently, the second aim of this study was to investigate the predictive value of hypersensitivity 2 weeks post-mTBI on anxiety, depression, HRQoL, and life satisfaction, 12 months later while controlling for postconcussion symptoms.

As such, the following research questions were investigated:

- RQ1. What is the course of self-reported NS and LS symptoms over a period of 12 months in mTBI patients and controls?
- RQ2. Can levels of self-reported NS and LS within the first 2 weeks postinjury predict anxiety, depression, HRQoL, and life satisfaction, 12 months postinjury?

## MATERIALS AND METHODS

For this prospective, longitudinal, multicenter cohort study, ethical approval was received from the medical ethics committee of Maastricht University and Maastricht University Medical Centre (METC 16-4-209). Data used for the current study were collected as part of a larger data collection effort for a project investigating mTBI and fear avoidance behavior.

### Participants

Participants were adults who had an mTBI (mTBI group) and adults who had a minor orthopedic injury in at least one extremity (control group). The following inclusion criteria were used for the mTBI group:

1. Aged 18 years or older;
2. Able and willing to provide informed consent;
3. Fluent in Dutch;
4. Diagnosed by their treating healthcare professional using the WHO (World Health Organization) and EFNS (European Federation of Neurological Societies) criteria at the neurology or emergency department,<sup>20,21</sup> which include:
  - History of impact to the head,
  - Glasgow Coma Scale (GCS) score between 13 and 15, 30 minutes after the impact or later at hospital admission,
  - In case of a GCS score of 15, at least one of the following: loss of consciousness (LOC) ( $\leq 30$  minutes), posttraumatic amnesia (PTA) ( $\leq 24$  hours), other transient neurological signs such as vomiting.

Exclusion criteria for the mTBI group were as follows:

1. A history of neurological disease or injury such as epilepsy and multiple sclerosis;
2. A history of psychiatric disorders for which hospitalization was needed;
3. Under the influence of illicit substances at the time of injury or a history of drug addiction; and
4. Use of psychoactive medication known for cognitive (side) effects.

The inclusion and exclusion criteria for the control group were the same, except for a diagnosis of mTBI. Participants were instead required to have received a diagnosis of a minor orthopedic injury in the extremities (eg, bone fracture or sprain) from a healthcare professional. The injury did not involve the head and there was no LOC or PTA or transient neurological signs.

### Outcome measures

The questionnaires were self-report. Each participant was tested at 4 time points (within the first 2 weeks, at 3 months, 6 months, and 12 months postinjury).

### Noise and light sensitivity

Two items of the Rivermead Post-Concussion Symptoms Questionnaire (RPQ)<sup>22</sup> were used to assess NS and LS. The items were stated as follows: “Compared to before the accident, do you now (ie, over the last 24 hours) suffer from *noise sensitivity, easily upset by loud noise* or *light sensitivity, easily upset by bright light*. Items were assessed on a 5-point scale: 0 (not experienced at all), 1 (not a problem anymore), 2 (a mild problem), 3 (a moderate problem), and 4 (a severe problem). The use of these single items to investigate these concepts in mTBI has been reported before,<sup>6,23,24</sup> and individual item reliability lies between 0.70 and 0.94.<sup>22</sup> NS and LS were measured at all 4 time points. Finally, scores on the other 14 items of the RPQ (within the first 2 weeks) were included in RQ2 as a control measure for early postconcussion symptoms. For this, the total score was used for all items except those assessing NS and LS.

### Anxiety and depression

Symptoms of anxiety and depression were assessed at 12 months postinjury using the Dutch version of the Hospital Anxiety and Depression Scale (HADS),<sup>25</sup> which is a valid and reliable measure for screening depression and anxiety in patients with TBI.<sup>26</sup> The HADS consists of 14 questions divided over 2 subscales: Depression and Anxiety. Scores can range from 0 to 21 per subscale, with a cutoff score of 8 or higher suggesting the presence of either depression or anxiety.

### HRQoL

The EuroQoL-5D-5L (EQ-5D-5L)<sup>27</sup> assesses HRQoL on 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and, per dimension, on 5 levels of severity (ranging from *no problems* to *unable to do*). This was converted into an index value that can range between 0 and 1, with higher scores indicating a better health status. A vertical visual analog scale (VAS) was used to rate current health state ranging from 0 (worst imaginable health) to 100 (best imaginable health) (EQ-5D-5L VAS). All questions informed about the patients' health status “today.” The EQ-5D-5L exhibits good psychometric properties.<sup>28</sup>

### Life satisfaction

The Utrecht Scale for Evaluation and Rehabilitation-Participation (USER-P Satisfaction) was used to measure satisfaction with participation in life<sup>29</sup> and is a valid and reliable measure for patients with TBI.<sup>30,31</sup> Ten items were scored on a 5-point scale (*very unsatisfied* to *very satisfied*), and the total was converted into 1 outcome measure ranging from 0 to 100. Higher scores indicate higher levels of satisfaction.

### Procedure

Potential participants were given information about the study following diagnosis of mTBI or orthopedic injury at one of the 6 recruiting hospitals in the south of the Netherlands (ie, “Laurentius Ziekenhuis Roermond,” “Maastricht UMC+,” “St Jans Gasthuis Weert,” “VieCurie Medisch Centrum Venlo,” “Zuyderland Heerlen,” and “Zuyderland Sittard”). After a patient expressed interest in the study, a first measurement was scheduled within 2 weeks after the injury ( $T_1$ ), which would take place at the participant's home or a different location (ie, university). At this point, the informed consent was signed, where after the questionnaires were completed in an online testing environment. The researcher could provide to help navigate this online system. After completing the first measurement, participants received a notification for the upcoming follow-ups: after 3 months ( $T_2$ ), 6 months ( $T_3$ ), and 12 months ( $T_4$ ). Participants were given 4 weeks to complete the questionnaires after each time point. NS and LS were analyzed for all time points, whereas anxiety, depression, HRQoL and life satisfaction were only analyzed at  $T_4$ . The recruitment took place from March 2017 to August 2019 (follow-up until August 2020).

### Data analysis

All analyses were conducted in SPSS v.26 for Windows (IBM Corp, Armonk, New York), and assumptions were checked prior to analysis. Bonferroni corrections

for multiple comparisons were applied where necessary. Differences in group characteristics were assessed with 2-sample *t* tests and chi-squared tests. RQ1 was investigated using 2 binary variables (NS and LS). The presence of NS and LS was indicated when a participant scored 2 or higher on RPQ items, which is consistent with other studies.<sup>32,33</sup> Detailed description of the answers given is presented in Supplemental Digital Content 1 Figure (available at: <http://links.lww.com/JHTR/A605>). The prevalence of NS and LS was assessed using 2 different methods. First, the number of participants in each group with NS and LS was calculated at each time point separately (*independent count*). Second, the rate of *persistent symptoms* was calculated by adding up the number of participants at each time point who had reported symptoms at all the previous time points too. For example, the number reported for persistent symptoms at  $T_4$  reflects the number of participants who reported symptoms at  $T_4$  and also at  $T_1$ ,  $T_2$ , and  $T_3$ . The effects of time and group on NS/LS (*independent count*) were studied using GEE (generalized estimation equations) to account for dependency as a result of the longitudinal multicenter design of the study. Specifically, a binary logit model was used with an unstructured correlation matrix. Because of the nature of the analyses, subjects with incomplete data were not excluded from

the analyses, that is, no case-wise deletion or any data imputation was applied.

Subsequently, for *persistent symptoms*, group differences were investigated per time point, using mixed logistic regression analysis with a random intercept for “recruiting center.” If the variance of the random recruiting center effect was estimated to be zero, a logistic regression was carried out using group as a binary predictor.

RQ2 was investigated using a linear mixed model, in which NS and LS measured at  $T_1$  and group (mTBI vs control) were fixed factors, recruiting center was included as a random factor, and postconcussion symptoms at  $T_1$  were included as a covariate (total score of RPQ, excluding NS and LS items). These linear mixed-model analyses were performed for each of 5 dependent variables: HADS Anxiety and HADS Depression, EQ-5D-5L scores, and USER-P Satisfaction at  $T_4$ . If the variance of the random recruiting center effect was estimated to be zero, a 2-way analysis of variance was carried out.

## RESULTS

### Participants

In total, 186 participants with mTBI and 181 control participants consented to participate. A flowchart

**TABLE 1** Characteristics of study groups

Variable	mTBI (N = 186)	Controls (N = 181)
Age at injury, mean (SD), range	48.8 (17.3), 18-76	46.6 (14.0), 18-66
Sex, n (%)		
Female	73 (39.2)	100 (55.2)
Male	113 (60.8)	81 (44.8)
Higher education level, <sup>a</sup> n (%)	65 (35.0)	60 (33.2)
Current psychological treatment, n (%)	10 (5.4)	8 (4.4)
History of psychological treatment, n (%)	27 (14.5)	28 (15.5)
Hospital admission, n (%)	42 (22.6)	3 (1.7)
GCS score, n (%)		
13	4 (2.2)	
14	21 (11.3)	
15	161 (86.6)	
Loss of consciousness (minutes)		
n (%)	113 (60.8)	
Duration, mean (SD), range	4.8 (5.8), 0.5-29	
Posttraumatic amnesia, h		
n (%)	120 (64.5) <sup>b</sup>	
Duration, mean (SD), range	2.7 (4.8), 0.02-23	
CT brain scan abnormalities, n (%)	20 (10.8)	
Orthopedic injury type, n (%)		
Fracture		128 (70.7)
Contusion		14 (7.7)
Sprain/strain		23 (12.7)
Luxation/dislocation		9 (5.0)
Other		7 (3.9)

Abbreviations: CT, computed tomography; GCS, Glasgow Coma Scale; mTBI, mild traumatic brain injury.

<sup>a</sup>Higher education level includes completion of a college or university degree.

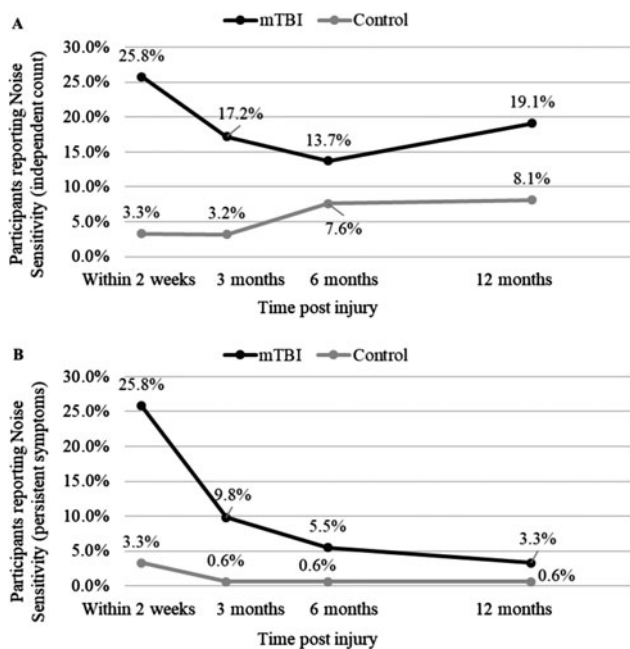
<sup>b</sup>Information on loss of consciousness, posttraumatic amnesia, and CT scan abnormalities was missing for 23, 11, and 1 participant(s), respectively.

representing participant numbers at every stage is presented in Supplemental Digital Content 2 Figure (available at: <http://links.lww.com/JHTR/A606>). Characteristics of the participants are displayed in Table 1. The mTBI and control groups were not statistically different in terms of age, education, and current and previous history of psychological treatment ( $t_{365} = 1.37$ ,  $P = .173$ ;  $\chi^2_8 = 7.00$ ,  $P = .537$ ;  $\chi^2_1 = 0.18$ ,  $P = .671$ ;  $\chi^2_1 = 0.07$ ,  $P = .798$ , respectively). They differed in distribution of sex ( $\chi^2_1 = 9.43$ ,  $P = .002$ , ie, the mTBI group contained relatively more males than the control group) and hospitalization (yes/no) ( $\chi^2_1 = 37.58$ ,  $P < .001$ , ie, hospitalization was relatively more frequent in the mTBI group than in the control group).

### Course of hypersensitivity symptoms over time

The course of hypersensitivity symptoms in both groups is displayed in Figures 1 (NS) and 2 (LS). Rates of dual sensitivity (ie, those participants reporting both NS and LS) at each time point are presented in Supplemental Digital Content 3 Table (available at: <http://links.lww.com/JHTR/A607>).

The GEE analyses showed a significant interaction between time and group for symptoms of NS ( $P = .001$ )



**Figure 1.** Noise sensitivity symptoms in the mTBI and control groups. Number of participants with noise sensitivity symptoms on each time point using independent count (A) and persistent symptoms (B). Number of people assessed: Within 2 weeks ( $T_1$ ), mTBI,  $N = 186$ ; control,  $N = 181$ . At 3 months ( $T_2$ ), mTBI,  $N = 163$ ; control,  $N = 158$ . At 6 months ( $T_3$ ), mTBI,  $N = 153$ ; control,  $N = 158$ . At 12 months ( $T_4$ ), mTBI,  $N = 152$ ; control,  $N = 160$ . mTBI indicates mild traumatic brain injury.

(independent count). This interaction was investigated further using a set of three 1 *df* interaction contrasts, each testing a  $2 \times 2$  interaction between group and time for 2 contiguous time points. Specifically, no interaction between time and group was found when focusing on  $T_1$ - $T_2$  ( $P = 1.000$ ); however, a significant effect of group was found ( $P < .001$ ) (see Figure 1A). When focusing on  $T_2$ - $T_3$ , a significant interaction was found ( $P = .048$ ), which means that the differences between groups grow smaller (see Figure 1A). Finally, when focusing on  $T_3$ - $T_4$ , no interaction was found ( $P = 1.000$ ); however, an effect of group remained ( $P = .027$ ). Concluding, the groups started with a difference in the prevalence of NS symptoms between  $T_1$  and  $T_2$ . This difference became smaller between  $T_2$  and  $T_3$ ; however, no evidence was found that it changed after  $T_3$ .

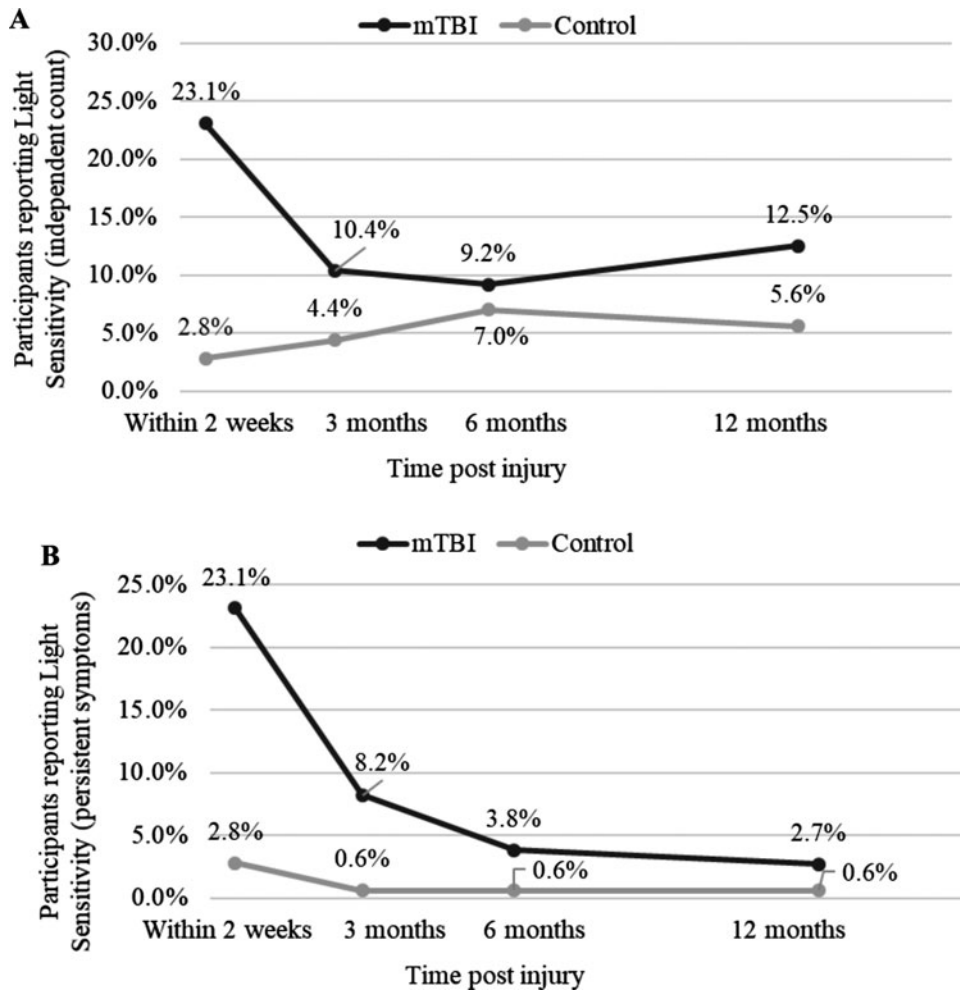
Considering *persistent symptoms* of NS (see Figure 1B), a significant difference was found between groups at  $T_1$  ( $P < .001$ ) and  $T_2$  ( $P = .016$ ) but not at  $T_3$  or  $T_4$  ( $P = .108$  and  $P = .384$ , respectively). This means there were more participants with persistent symptoms of NS in the mTBI group than in the control group in early stages ( $T_1$  and  $T_2$ ); however, in later stages ( $T_3$  and  $T_4$ ), no significant difference could be identified (see Figure 1B).

The GEE analyses showed a significant interaction between time and group (*independent count*) for symptoms of LS ( $P = .001$ ). This interaction was investigated further using a set of three 1 *df* interaction contrasts, each testing a  $2 \times 2$  interaction between group and time for 2 contiguous time points. Specifically, an interaction between time and group was found when focusing on  $T_1$ - $T_2$  ( $P = .033$ ) (see Figure 2A). When focusing on  $T_2$ - $T_3$  as well as on  $T_3$ - $T_4$ , no effects (interaction or main) were found. Concluding, a difference in terms of LS symptom prevalence between groups was found at  $T_1$  but could not be identified from  $T_2$  onward.

For *persistent symptoms* of LS (see Figure 2B), a significant difference was found between groups at  $T_1$  ( $P < .001$ ) and  $T_2$  ( $P = .028$ ) but not at  $T_3$  or  $T_4$  ( $P = .272$  and  $P = .556$ , respectively). Which means that there were more persistent symptoms of LS in the mTBI group than in the control group at  $T_1$  and  $T_2$ ; however, at  $T_3$  and  $T_4$ , no significant difference was identified (see Figure 2B).

### Effects of hypersensitivity within 2 weeks postinjury on outcomes at 12 months

When controlling for postconcussion symptoms at  $T_1$ , no effects of NS at  $T_1$  were found on HADS Anxiety ( $P = .830$ ), HADS Depression ( $P > 1.000$ ), EQ-5D-5L index score ( $P > 1.000$ ), EQ-5D-5L VAS ( $P > 1.000$ ), and USER-P Satisfaction ( $P > 1.000$ ) at  $T_4$  (see Table 2). For the EQ-5D-5L index score, a group effect was found, indicating a higher index value for the mTBI group



**Figure 2.** Light sensitivity symptoms in the mTBI and control groups. Number of participants with light sensitivity symptoms on each time point using independent count (A) and persistent symptoms (B). Number of people assessed: Within 2 weeks ( $T_1$ ), mTBI,  $N = 186$ ; control,  $N = 181$ . At 3 months ( $T_2$ ), mTBI,  $N = 163$ ; control,  $N = 158$ . At 6 months ( $T_3$ ), mTBI,  $N = 153$ ; control,  $N = 158$ . At 12 months ( $T_4$ ), mTBI,  $N = 152$ ; control,  $N = 160$ . mTBI indicates mild traumatic brain injury.

**TABLE 2** Effects of noise sensitivity within 2 weeks postinjury on anxiety, depression, and health-related quality of life at 12 months postinjury, controlling for postconcussion symptoms<sup>a</sup>

Outcome measure	No noise sensitivity		Noise sensitivity		<i>F</i>	<i>P</i>
	EMM	SE	EMM	SE		
HADS Anxiety	3.87	0.48	4.94	0.86	1.925	.830
HADS Depression	2.45	0.34	2.46	0.76	0.000	>1.000
EQ-5D-5L Index value	0.85	0.02	0.87	0.04	0.192	>1.000
EQ-5D-5L VAS	77.27	1.54	72.01	5.67	0.766	>1.000
USER-P Satisfaction	79.94	0.94	81.22	3.43	0.126	>1.000

Abbreviations: EMM, estimated marginal means; EQ-5D-5L, EuroQoL-5D-5L; HADS, Hospital Anxiety and Depression Scale; USER-P, Utrecht Scale for Evaluation and Rehabilitation-Participation; VAS, visual analog scale.

<sup>a</sup>Statistics were corrected for multiple comparisons and assessed using  $P < .05$ .

( $M = 0.91$ ,  $SD = 0.02$ ) than for the control group ( $M = 0.81$ ,  $SD = 0.04$ ;  $F_{1,303.906} = 10.722$ ,  $P = .005$ ). Otherwise, no main effects of group or interaction were found. As the results show a different pattern of the effects of NS on long-term outcomes when not controlling for postconcussion symptoms, the analyses without the covariate are reported in Supplemental Digital Content 4 Table (available at: <http://links.lww.com/JHTR/A608>).

When controlling for postconcussion symptoms at  $T_1$ , no effects of LS at  $T_1$  could be found on HADS Anxiety ( $P > 1.000$ ), HADS Depression ( $P = .975$ ), EQ-5D-5L index score ( $P > 1.000$ ), EQ-5D-5L VAS ( $P > 1.000$ ), and USER-P Satisfaction ( $P > 1.000$ ) (see Table 3). For the HADS Anxiety score, a group effect was found, indicating lower anxiety scores for the mTBI group ( $M = 3.15$ ,  $SD = 0.54$ ) than for the control group ( $M = 5.45$ ,  $SD = 0.89$ ;  $F_{1,304.905} = 7.458$ ,  $P = .035$ ). Otherwise, no main effects of group or interaction were found. As these results differed from the results when not controlling for postconcussion symptoms, the analyses without the covariate are reported in Supplemental Digital Content 5 Table (available at: <http://links.lww.com/JHTR/A609>).

## DISCUSSION

This prospective, longitudinal, multicenter cohort study aimed to examine the prevalence of hypersensitivity after mTBI and the effects on relevant long-term outcomes such as anxiety, depression, HRQoL, and life satisfaction. It was found that individuals with mTBI reported symptoms of NS between 2 weeks and 3 months postinjury more often than the control group. Although this difference grew smaller after 3 months, a group effect remained at 12 months postinjury. The prevalence of LS symptoms at 2 weeks post-mTBI was higher than that for controls; however, this difference disappeared from 3 months onward. There was a higher prevalence of persistent NS and LS symptoms after mTBI than that

for controls within 2 weeks and at 3 months postinjury. It was apparent that at 12 months postinjury, approximately 3% of mTBI patients had persistent symptoms during the course of the study (1% in the control group). At that time, the groups did not differ in persistent symptom rates.

These results confirm a higher prevalence of NS and LS up to 3 months postinjury in individuals with mTBI than in controls. However, the results also show that this difference grows smaller over time, becoming nonsignificant for LS from 3 months onward. The prevalence and an initial peak in symptoms found in this cohort are similar to those reported in previous studies.<sup>8,10,34-37</sup> At 12 months postinjury or more, other studies found a higher prevalence; however, this could be due to differences in cohorts (eg, veterans)<sup>38</sup> and smaller sample sizes.<sup>7,38</sup>

Furthermore, the results showed that NS and LS within 2 weeks postinjury were not predictive of anxiety, depression, HRQoL, and life satisfaction, 12 months later when controlling for early postconcussion symptoms. This was in contrast to the results of the analyses without using postconcussion symptoms as a covariate, which showed effects of hypersensitivity on anxiety, depression, and HRQoL. As such, there was no evidence that early NS and LS are uniquely associated with long-term emotional and quality-of-life outcomes, above general levels of postconcussion symptoms, which are known to affect quality of life<sup>11</sup> and are associated with emotional symptoms.<sup>39</sup> Finally, it should be noted that all scores for anxiety and depression were below the clinical cutoff scores.

## STRENGTHS AND LIMITATIONS

This study contains several strengths and limitations. First, multiple follow-up measures in large samples provided insights into various stages after mTBI. Because

**TABLE 3** Effects of light sensitivity within 2 weeks postinjury on anxiety, depression, and health-related quality of life at 12 months postinjury, controlling for postconcussion symptoms<sup>a</sup>

Outcome measure	No light sensitivity		Light sensitivity		F	P
	EMM	SE	EMM	SE		
HADS Anxiety	3.75	0.48	4.86	0.94	1.647	>1.000
HADS Depression	2.21	0.30	3.28	0.82	1.688	.975
EQ-5D-5L Index value	0.86	0.02	0.85	0.04	0.068	>1.000
EQ-5D-5L VAS	77.19	1.53	75.44	6.30	0.070	>1.000
USER-P Satisfaction	80.03	0.92	81.72	3.80	0.179	>1.000

Abbreviations: EMM, estimated marginal means; EQ-5D-5L, EuroQoL-5D-5L; HADS, Hospital Anxiety and Depression Scale; USER-P, Utrecht Scale for Evaluation and Rehabilitation-Participation; VAS, visual analog scale.

<sup>a</sup>Statistics were corrected for multiple comparisons and assessed using  $P < .05$ .

of the inclusion of an orthopedic injury control group, hypersensitivity symptoms could be compared with a group with similar medical care and expected recovery. Participants were required to rate their hypersensitivity compared with preinjury levels, which might have led to accuracy issues at later time points. Nevertheless, this was the same for both groups. Finally, the current study had occasional missing data, which potentially influenced the results. However, no significant differences in hypersensitivity within 2 weeks were found between participants with and without missing data at 12 months.

## FUTURE RESEARCH

Standardized procedures to measure hypersensitivity could minimize methodological differences between studies and give way to a better interpretation of findings. Instruments, possibly not solely relying on self-report, to investigate sensory modalities and identify circumstances in which symptoms occur could create a broader picture of hypersensitivity. Questionnaires focusing specifically on hypersensitivity symptoms such as the Hyperacusis Questionnaire<sup>40</sup> or Leiden Visual Sensitivity Scale<sup>41</sup> may provide better insights into the nature of the symptoms. Finally, taking into account physiological factors (eg, stress levels), cognitive measurements (eg, attention), and overall symptom reporting (eg, somatization, illness percep-

tions) may further deepen the knowledge of sensory hypersensitivity.

## CLINICAL IMPLICATIONS

Based on the current findings, clinicians could provide assurance to their patients about the low occurrence of persistent hypersensitivity symptoms after mTBI and its benign course of recovery. Furthermore, the questions arise whether hypersensitivity is caused by mTBI, and whether there are psychological factors that play a role in maintenance of symptoms, as has been described for persisting symptoms after mTBI.<sup>42</sup> With this in mind, it is important to be aware that hypersensitivity also occurs in the general population; however, it is usually assessed using different methods,<sup>14</sup> which may have led to differences in the prevalence.

## CONCLUSION

This study showed an elevated prevalence of NS and LS symptoms between 2 weeks and 3 months after injury in an mTBI group compared with minor orthopedic trauma controls. This difference grew smaller over time, even disappeared for LS. Only 3% of mTBI patients reported hypersensitivity at every time point during a year follow-up. Finally, hypersensitivity by itself did not predict long-term anxiety, depression, HRQoL, and life satisfaction, when taking early postconcussion symptoms into account.

## REFERENCES

- Bruns J Jr, Hauser WA. The epidemiology of traumatic brain injury: a review. *Epilepsia*. 2003;44(s10):2–10. doi:10.1046/j.1528-1157.44.s10.3.x
- Sussman ES, Pendharkar AV, Ho AL, Ghajar J. Mild traumatic brain injury and concussion: terminology and classification. *Handb Clin Neurol*. 2018;158:21–24. doi:10.1016/B978-0-444-63954-7.00003-3
- Assi H, Moore RD, Ellemberg D, Hébert S. Sensitivity to sounds in sport-related concussed athletes: a new clinical presentation of hyperacusis. *Sci Rep*. 2018;8(1):9921. doi:10.1038/s41598-018-28312-1
- Callahan ML, Lim MM. Sensory sensitivity in TBI: implications for chronic disability. *Curr Neurol Neurosci Rep*. 2018;18(9):56. doi:10.1007/s11910-018-0867-x
- Scheydt S, Müller Staub M, Frauenfelder F, Nielsen GH, Behrens J, Needham I. Sensory overload: a concept analysis. *Int J Ment Health Nurs*. 2017;26(2):110–120. doi:10.1111/inm.12303
- Shepherd D, Landon J, Kallour M, et al. The association between health-related quality of life and noise or light sensitivity in survivors of a mild traumatic brain injury. *Qual Life Res*. 2020;29(3):665–672. doi:10.1007/s11136-019-02346-y
- Fourtassi M, Hajjioui A, Ouahabi AE, Benmassaoud H, Hajjaj-Hassouni N, Khamlichi AE. Long-term outcome following mild traumatic brain injury in Moroccan patients. *Clin Neurol Neurosurg*. 2011;113(9):716–720. doi:10.1016/j.clineuro.2011.07.010
- Barker-Collo S, Theadom A, Starkey N, Kahan M, Jones K, Feigin V. Factor structure of the Rivermead Post-Concussion Symptoms Questionnaire over the first year following mild traumatic brain injury. *Brain Inj*. 2018;32(4):453–458. doi:10.1080/02699052.2018.1429659
- Mortera MH, Kinirons SA, Simantov J, Klingbeil H. Long-term neurobehavioral symptoms and return to productivity in Operation Enduring Freedom/Operation Iraqi Freedom veterans with and without traumatic brain injury. *Arch Phys Med Rehabil*. 2018;99(2S):S50–S57. doi:10.1016/j.apmr.2016.11.026
- Dikmen S, Machamer J, Fann JR, Temkin NR. Rates of symptom reporting following traumatic brain injury. *J Int Neuropsychol Soc*. 2010;16(3):401–411. doi:10.1017/S1355617710000196
- Emanuelson I, Andersson Holmkvist E, Björklund R, Stålhammar D. Quality of life and postconcussion symptoms in adults after mild traumatic brain injury: a population-based study in western Sweden. *Acta Neurol Scand*. 2003;108(5):332–338. doi:10.1034/j.1600-0404.2003.00155.x
- Shepherd D, Heinonen-Guzejev M, Heikkilä K, Landon J, Theadom A; BIONIC Research Group. Sensitivity to noise following a mild traumatic brain injury: a longitudinal study. *J Head Trauma Rehabil*. 2021;36(5):E289–E301. doi:10.1097/HTR.0000000000000645
- Aron EN, Aron A, Jagiellowicz J. Sensory processing sensitivity: a review in the light of the evolution of biological responsiveness. *Pers Soc Psychol Rev*. 2012;16(3):262–282. doi:10.1177/1088868311434213
- Engel-Yeger B, Dunn W. The relationship between sensory processing difficulties and anxiety level of healthy adults. *Br J Occup Ther*. 2011;74(5):210–216. doi:10.4276/030802211X13046730116407



15. Falk H, Bechtold KT, Peters ME, et al. A prognostic model for predicting one-month outcomes among emergency department patients with mild traumatic brain injury and a presenting Glasgow Coma Scale of fifteen. *J Neurotrauma*. 2021;38(19):2714–2722. doi:10.1089/neu.2021.0137
16. Jagiellowicz J, Zarinafar S, Acevedo BP. Health and social outcomes in highly sensitive persons. In: *The Highly Sensitive Brain: Research, Assessment, and Treatment of Sensory Processing Sensitivity*. Elsevier; 2020:75–107. doi:10.1016/B978-0-12-818251-2.00004-7
17. Shepherd D, Landon J, Kallor M, Theadom A. Clinical correlates of noise sensitivity in patients with acute TBI. *Brain Inj*. 2019; 33(8):1050–1058. doi:10.1080/02699052.2019.1606443
18. Hallberg LRM, Hallberg U, Johansson M, Jansson G, Wiberg A. Daily living with hyperacusis due to head injury 1 year after a treatment programme at the hearing clinic. *Scand J Caring Sci*. 2005;19(4):410–418. doi:10.1111/j.1471-6712.2005.00361.x
19. N Mayo, ed. *Dictionary of Quality of Life and Health Outcomes Measurement*. Version 1. ISOQOL; 2015.
20. Cassidy JD, Carroll L, Peloso P, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med*. 2004;36(43)(suppl):28–60. doi:10.1080/16501960410023732
21. Vos PE, Alekseenko Y, Battistin L, et al. Mild traumatic brain injury. *Eur J Neurol*. 2012;19(2):191–198. doi:10.1111/j.1468-1331.2011.03581.x
22. King N, Crawford S, Wenden F, Moss N, Wade D. The Rivermead Post Concussion Symptoms Questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. *J Neurol*. 1995;242(9):587–592. doi:10.1007/BF00868811
23. Callahan ML, Binder LM, O’Neil ME, et al. Sensory sensitivity in Operation Enduring Freedom/Operation Iraqi Freedom veterans with and without blast exposure and mild traumatic brain injury. *Appl Neuropsychol Adult*. 2018;25(2):126–136. doi:10.1080/23279095.2016.1261867
24. Forrest RH, Henry JD, McGarry PJ, Marshall RN. Mild traumatic brain injury in New Zealand: factors influencing post-concussion symptom recovery time in a specialised concussion service. *J Prim Health Care*. 2018;10(2):159–166. doi:10.1071/HC17071
25. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand*. 1983;67(6):361–370. doi:10.1111/j.1600-0447.1983.tb09716.x
26. Whelan-Goodinson R, Ponsford J, Schönberger M. Validity of the Hospital Anxiety and Depression Scale to assess depression and anxiety following traumatic brain injury as compared with the Structured Clinical Interview for DSM-IV. *J Affect Disord*. 2009; 114(1/3):94–102. doi:10.1016/j.jad.2008.06.007
27. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727–1736. doi:10.1007/s11136-011-9903-x
28. Feng Y-S, Kohlmann T, Janssen MF, Buchholz I. Psychometric properties of the EQ-5D-5L: a systematic review of the literature. *Qual Life Res*. 2021;30(3):647–673. doi:10.1007/s11136-020-02688-y
29. van der Zee CH, Priesterbach AR, van der Dussen L, et al. Reproducibility of three self-report participation measures: the ICF Measure of Participation and Activities Screener, the Participation Scale, and the Utrecht Scale for Evaluation of Rehabilitation-Participation. *J Rehabil Med*. 2010;42(8):752–757. doi:10.2340/16501977-0589
30. Post MW, van der Zee CH, Hennink J, Schaftrat CG, Visser-Meily JM, van Berlekom SB. Validity of the Utrecht scale for Evaluation of Rehabilitation-Participation. *Disabil Rehabil*. 2012; 34(6):478–485. doi:10.3109/09638288.2011.608148
31. Domensino A-F, van Haastregt JC, van Heugten CM. One-year follow-up results of a community-based treatment programme for people with acquired brain injury in the chronic phase. *Disabil Rehabil*. 2020;42(21):3106–3111. doi:10.1080/09638288.2019.1582719
32. Spronk I, Polinder S, Bonsel G, Janssen M, Haagsma J. The relation between EQ-5D and fatigue in a Dutch general population sample: an explorative study. *Health Qual Life Outcomes*. 2021;19(1):35. doi:10.1186/s12955-021-01771-3
33. Voormolen DC, Haagsma JA, Polinder S, et al. Post-concussion symptoms in complicated vs. uncomplicated mild traumatic brain injury patients at three and six months postinjury: results from the CENTER-TBI study. *J Clin Med*. 2019;8(11):1921. doi:10.3390/jcm8111921
34. Dischinger PC, Ryb GE, Kufera JA, Auman KM. Early predictors of postconcussive syndrome in a population of trauma patients with mild traumatic brain injury. *J Trauma*. 2009;66(2):289–297. doi:10.1097/TA.0b013e3181961da2
35. Kashluba S, Paniak C, Blake T, Reynolds S, Toller-Lobe G, Nagy J. A longitudinal, controlled study of patient complaints following treated mild traumatic brain injury. *Arch Clin Neuropsychol*. 2004; 19(6):805–816. doi:10.1016/j.acn.2003.09.005
36. Heitger MH, Jones RD, Frampton CM, Ardagh MW, Anderson TJ. Recovery in the first year after mild head injury: divergence of symptom status and self-perceived quality of life. *J Rehabil Med*. 2007;39(8):612–621. doi:10.2340/16501977-0100
37. Merezhinskaya N, Mallia RK, Park D, Millian-Morell L, Barker FM II. Photophobia associated with traumatic brain injury: a systematic review and meta-analysis. *Optom Vis Sci*. 2021;98(8): 891–900. doi:10.1097/OPX.0000000000001757
38. Elliott JE, Opel RA, Weymann KB, et al. Sleep disturbances in traumatic brain injury: associations with sensory sensitivity. *J Clin Sleep Med*. 2018;14(7):1177–1186. doi:10.5664/jcsm.7220
39. Losoi H, Silverberg ND, Wäljas M, et al. Recovery from mild traumatic brain injury in previously healthy adults. *J Neurotrauma*. 2016;33(8):766–776. doi:10.1089/neu.2015.4070
40. Khalfa S, Dubal S, Veuillet E, Perez-Diaz F, Jouvent R, Collet L. Psychometric normalization of a hyperacusis questionnaire. *ORL J Otorhinolaryngol Relat Spec*. 2002;64(6):436–442. doi:10.1159/000067570
41. Perenboom MJ, Najafabadi AHZ, Zielman R, Carpay JA, Ferrari MD. Quantifying visual allodynia across migraine subtypes: the Leiden Visual Sensitivity Scale. *Pain*. 2018;159(11):2375–2382. doi:10.1097/j.pain.0000000000001343
42. van der Horn HJ, Out ML, de Koning ME, et al. An integrated perspective linking physiological and psychological consequences of mild traumatic brain injury. *J Neurol*. 2020;267(9):2497–2506. doi:10.1007/s00415-019-09335-8