Critical Flicker Frequency in Traumatic Brain Injury

M.S. Thesis
Tina T. Chang B.S.,
Advisors: Dr. Kenneth J. Ciuffreda O.D., Ph.D.
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Keywords: Traumatic brain injury, acquired brain injury, critical flicker fusion frequency, temporal processing, magnocellular pathway, motion sensitivity, light sensitivity

Abstract

Primary Objective: To determine whether critical flicker frequency (CFF) thresholds are elevated in individuals with traumatic brain injury (TBI) and correlated with the degree of motion and light sensitivity.

Methods and procedures: The foveal CFF threshold was assessed in individuals with TBI (n=18) having varying degrees of light and motion sensitivity. Mean CFF values were obtained using the ascending and descending psychophysical method of limits with binocular viewing at 40 cm. A rating-scale questionnaire was used to assess the degree of light sensitivity and motion sensitivity. These parameters were also assessed in a visually-normal cohort.

Main outcomes and results: CFF in the TBI group was not significantly different across age groups from the visually- normal cohort. However, mean CFF among the TBI subjects was significantly higher for the "light sensitive" and "motion sensitive" subgroups when compared to the "not light sensitive" and "not motion sensitive" subgroups. The majority of TBI subjects had both light and motion sensitivity.

Conclusion: An elevated CFF among a subgroup of TBI subjects may be related to the symptoms of light and motion sensitivity that many TBI patients experience. Underlying mechanisms involving disinhibition of the magnocellular pathway as a result of brain injury may be causal of the hypersensitivity to light and motion. CFF thresholds can potentially aid clinicians in determining methods of treatment for TBI patients.

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Introduction

Critical flicker fusion frequency (CFF) is defined as the lowest frequency at which a physically flickering light is perceived to be non-flickering or "steady" [1]. CFF is a rapid and simple technique for providing information about the temporal responsiveness of the visual system by defining the upper limits of one's temporal resolution. It has been found to increase with an increase in target luminance, target size [2], and retinal eccentricity [3]. CFF has been found to decrease with increasing age, which suggested age-related neural changes in the visual system [3-5]. CFF is also affected by viewing distance, duty cycle, and the spectral properties of the light source [6].

Recent studies have suggested that CFF may be useful for providing insight into a range of abnormal vision and neurological conditions [6,7]. For example, it has been used to determine the integrity of the retina in the presence of cataracts [8]. In glaucoma, CFF has been used in determination of the temporal sensitivity across the visual field for earlier detection of damaged retinal regions [9]. With respect to migraine, Coleston and Kennard [10] found CFF to be reduced in migraineurs without aura, but not in migraineurs with aura. Furthermore, Kowacs *et al*. [11] found that migraineurs had lower flicker fusion thresholds and hypothesized that this may be an indicator of the underlying neurological dysfunction in migraines.

CFF is important not only in assessing the integrity of the retina, but also in ascertaining temporal processing beyond the retina [12]. It reflects the capabilities and limitations of neural processing with respect to the speed and transmission of the neural response. Visual information processing commences at the retina, where parvocellular and magnocellular pathways are differentiated into separate pathways, and proceeds to the lateral geniculate nucleus, [12,13]. Visual information is conducted relatively independently by the two pathways, although they

may overlap in the visual cortex [6]. Studies have found that the magnocellular system is primarily involved in the processing of rapid flicker and motion [7,14]. Thus, if the magnocellular pathways are damaged, this may result in impaired temporal-based flicker and motion processing ability as reflected by a reduction in the CFF level. However, if other neural structures involved in regulating these pathways are also damaged, and neural adaptation occurs, the magnocellular function may appear to be normal or even become relatively enhanced under certain conditions [15], thus leading to apparent anomalous and paradoxical temporal processing. Therefore, with respect to head trauma, dysfunction of light and motion processing may be indicated by measures of temporal sensitivity using parameters such as CFF.

Among traumatic brain-injured (TBI) individuals, many present with a range of visual and neurological impairments, including accommodative deficiency, vergence oculomotor dysfunctions, versional oculomotor deficits, and/or visual field loss [16-18]. In addition, they often report sensitivity to light and sensitivity to visual motion, in the presence of otherwise apparent normal ocular health [15,17,19]. In such cases, these individuals also reported visual discomfort and an inability to read efficiently under normal lighting conditions, to view computer screens for prolonged periods of time, to watch television in a darkened room, to function in busy supermarkets or office buildings, or even to go outdoors on sunny days. This may be due to the overall variation in illumination level and/or flicker of the illumination conditions. For example, there are frequent complaints from this population that fluorescent lighting is especially bothersome (i.e, flickering effect), and often times causes them extreme visual discomfort inside offices, supermarkets, or hospitals that are typically illuminated in this manner [20]. Subsequently, it has been hypothesized that these symptomatic TBI patients may have hypersensitive temporal processing relative to the non-brain-injured normal population.

This hypersensitive temporal processing would be analogous to the frequently evident perceptual hypersensitivity to overall ambient lighting (i.e., photosensitivity) [15,19] and to auditory stimuli (i.e., hyperacusis) [21]. Under normal conditions, the flickering of fluorescent lights is above the human flicker threshold [6]. However, if TBI patients have an elevated CFF threshold due to an enhanced magnocellular contribution, normal fluorescent lighting and its related apparent flicker and motion may cause significant visual and general discomfort in these patients. Therefore, an abnormality in temporal processing of TBI patients may be related to their symptoms.

Thus, the purpose of the present study was to determine whether an elevated foveal CFF threshold is found in TBI patients previously hypothesized, and if so, does it relate to their sensitivity to light and visual motion frequently experienced following TBI. If the CFF threshold is different from the normal population, then this would provide insight into the neurological effects of TBI on the temporal visual processing of light and perhaps even motion.

Methods

Subjects:

Fifty-six faculty, staff, and students of the SUNY State College of Optometry served as the visually-normal control group (see Table 1). Ages ranged from 22 to 83years, with a mean of 45 years and a standard deviation of ±15 years. There were 25 males and 31 females. Only two subjects reported mild light sensitivity, while all others reported neither light nor visual motion sensitivity. None reported past or present retinal or neurological disease, nor brain injury. All reported to be in good health.

The TBI group consisted of 18 subjects recruited from the Raymond J. Greenwald Rehabilitation Center at the SUNY State College of Optometry (see Tables 1 and 2). Subjects were selected through sampling of convenience. Ages ranged from 19-72 years, with a mean and standard deviation of 45.7 years ±13.6 years, respectively. There were 6 males and 12 females. All subjects were tested at least 3 months post-injury, with a range of 3 months to 15 years and a mean of 5.2 years. They received comprehensive vision examinations, including assessment of refractive state, binocular status, and ocular health.

Individuals with glaucoma, cataracts, and other retinal or optic nerve disorders were excluded from the study due to the possible effects on CFF [22]. Those with myopia above -8.00D were also excluded, as lower CFF values have been reported in this highly myopic population [23].

The study was approved by the SUNY State College of Optometry Institutional Review Board and followed the tenets of the Declaration of Helsinki. All subjects provided written, informed consent.

Apparatus:

The foveal CFF was measured using an experimental device developed and fabricated at the college. It consisted of an array of 4 adjacent white LED's with a spectrum of 460-555 nm (The LED Light Inc, Carson City, NV, theledlight.com) that provided diffuse illumination through a circular piece of translucent white plexiglass 4 cm in diameter (Figure 1A). The device was mounted onto an optical bench and placed 40 cm away along the subject's midline in primary position (Figure 1B). The CFF test device was enclosed within a flat matte black foamboard enclosure to reduce stray illumination, as well as to minimize visual distractions. The right side panel had an opening for the experimenter to view the subject and align the outer canthus of the subject's right eye with the center of the CFF device, as well as to monitor eye fixation. A headrest/chinrest setup was mounted to the front of the optical bench. The target luminance was 304.4 cd/m^2, while background luminance was 0.86 cd/m^2. Contrast of the target was 99.9% against the black background. The size of the white test field was 5.7°. A calibrated black knob was mounted on the back of the CFF device, which allowed the researcher to slowly change (~1 Hz/sec) the frequency of the test target flicker rate. The frequency range was 30-60 Hz.

Procedures:

Subjects placed their head into the chin and forehead assembly. They were asked to fixate the center of the test field. The test procedure was conducted binocularly with the normal refractive correction in place. Subjects were instructed to indicate by depressing a hand-held clicker when they first saw the perceptually flickering light stop flickering or "fused", and then to indicate when the now perceptually non-flickering light again appeared to flicker. Thus, the ascending and descending psychophysical method of limits was used [1]. A demonstration of

both a flickering and non-flickering light was provided for the subject followed by several practice trials. Once the subject understood the instructions, and a consistent response level was obtained, then 10 ascending and 10 descending measurements were taken, with the direction being counterbalanced across subjects. Mean values for the separate ascending and descending CFF values were calculated and then averaged. Normal subject data were averaged and compiled into 5-year bins (i.e., from 21-25, 26-30…). Subjects were allowed as many rest periods as needed during the course of the experiment if fatigued.

Subjects were also administered a seven-item, rating-scale questionnaire (see Appendix 1) covering the topics of light and motion sensitivity developed by Du et al [15]. Specifically, individuals were requested to rate the degree of light sensitivity and the degree of visual motion sensitivity on a scale of 1-4:: 1= never, 2 = mild, 3 = moderate, or 4 = marked. They were also asked to classify the discomfort associated with their light sensitivity on a scale of 1-5: 1 = no discomfort, 2 = somewhat bothersome, 3 = bothersome with no pain or headaches, 4 = very bothersome, with some pain associated, and 5 = very bothersome and very painful. The survey also included additional questions regarding the different types of illumination that were most bothersome, as well as questions regarding the onset of their light sensitivity. Lastly, subjects were asked to identify factors that either exacerbated (e.g.. fatigue) or reduced (e.g., spectacle lens tints, brimmed hats, or eye lid squinting) their light sensitivity.

Results

Foveal CFF as a function of age in the visually-normal control population is presented in Figure 2. The CFF averaged over the entire population was 47.26 Hz (SEM = ±0.43Hz), with subgroup variability appearing to be independent of age. It ranged from 38.5 to 53.9 Hz, with a SEM of 0.43Hz. Despite the lack of a significant difference in CFF with age [$F(3,14)= 0.64$, $p=0.60$], the lowest mean subgroup CFF and individual CFF values were found in the oldest population (i.e., 66+ years of age).

CFF as a function of age in both the visually-normal control group and TBI group is presented in Figure 3. In the control group, linear regression analysis indicated no significant change with age ($y=-0.013x +47.84$, $r= -0.059$, $p=0.67$). Similarly, in the TBI group, linear regression analysis showed no significant change with age ($y=0.146x+ 41.97$, $r=+0.44$, $p=0.067$), although a trend was noted. There was no correlation between CFF and the number of years since the most recent TBI ($r=+0.06$, $p=0.83$).

Figure 4 presents the overall mean CFF for the visually-normal control group and the TBI group. In the control group, the mean CFF was 47.26 Hz (SEM ± 0.43 Hz, SD ± 3.18 Hz). In the TBI group, the mean CFF was 48.65 Hz (SEM ±1.05 Hz, SD± 4.52Hz). These mean differences in CFF were not statistically significant [$t(72)= -1.45$, $p=0.15$]. However, variability was more than two times greater in the TBI group (0.42 Hz vs. 1.05 Hz).

Figure 5A presents the mean CFF values in the TBI group averaged across all ages as a function of the degree of light sensitivity. There was a trend for CFF to be related to the degree of light sensitivity [$F(3,14)= 3.095$, $p=0.061$]. Furthermore, when the data were combined into only two subgroups, namely “light-sensitive” and “not light-sensitive” as shown in Figure 5B, there was a significant effect with regard to the mean CFF threshold [$t = -2.698$, $p = 0.016$]. TBI

patients who were “light sensitive” had a significantly higher CFF threshold value than those who were “not light sensitive.”

Figure 6A presents the mean CFF values in the TBI group across all ages as a function of the degree of motion sensitivity. There was a trend for CFF to be related to the degree of motion sensitivity [$F(3,14) = 3.129$, $p=0.060$]. Furthermore, when the data were combined into only two subgroups, namely “motion sensitive” and “not motion sensitive” as shown in Figure 6B, there was a significant effect with regard to the mean CFF threshold [$t(16)=-2.813$, $p = 0.013$]. TBI patients who were “motion-sensitive” had significantly higher CFF threshold value than those who were “not motion sensitive.”

Table 3 summarizes the responses for TBI subjects to the questionnaire (see Appendix 1). For question 1, the most frequently reported response was a “moderate” degree of light sensitivity. For question 2, they most frequently characterized the severity of symptoms associated with their light sensitivity as either “bothersome with no pain or HA” or “very bothersome, some pain.” None of the subjects reported that the severity of their light sensitivity to be “very bothersome and very painful.” Subjects reported in question 3 that the type of lighting that bothered them the most was fluorescent light. Among the subjects with light sensitivity, only one subject (S#12) reported having symptoms of light sensitivity prior to their traumatic brain injury event. However, S#12 reported that the TBI event further exacerbated the symptoms. When asked what exacerbated their light sensitivity, the most frequent response was the sensation of general fatigue. In question #6, subjects most frequently reported that the use of tints and brimmed hats was most effective in reducing their sensitivity to light. Finally, in question #7, subjects most frequently reported a marked sensitivity to motion. In a comparison of light and motion sensitivity (questions #1 and #7), all but one subject who reported some

degree of light sensitivity also reported some degree of motion sensitivity. Only S#11 reported a "mild" degree of light sensitivity, but no degree of motion sensitivity. Fourteen of the 18 TBI subjects reported increased sensitivity to both light and motion.

Statistical analysis was performed on key questionnaire responses. In Figure 7A, CFF threshold was plotted as a function of the severity of symptoms associated with light sensitivity in the TBI group according to the responses derived from question #2. One-way ANOVA revealed a significant difference related to CFF and severity of symptoms [$F(3,14) = 3.38$, $p=0.049$]. The Fisher LSD post-hoc test revealed a significant difference between the "no symptoms" and "very bothersome, some pain" subgroups ($p=0.007$), and a trend between the "no symptoms" and "bothersome, no pain no HA" subgroups ($p=0.053$). Thus, CFF was higher in the two above symptomatic subgroups. In Figure 7B, the subjects were divided into two subgroups, "symptoms" and "no symptoms", revealing a significantly higher CFF in the "symptoms" subgroup [$t = -2.698$, $p = 0.016$]. Due to the categorization used in questions 1 and 2, the same populations were represented in Figure 7B and in Figure 5B.

Discussion

The results of the present study demonstrated that the foveal CFF was not significantly different between the TBI population and the visually-normal control group. This is consistent with some of the past studies (e.g., Battersby et al)[24]. Although the TBI population did not exhibit an overall difference in CFF with respect to the visually-normal age-matched population, it did bear significant relation to many of their symptoms. Some TBI individuals who exhibited photosensitivity had a higher CFF than found in those without photosensitivity. The results of the present study also revealed that a relatively elevated CFF was present in TBI patients who had both light and motion sensitivity. Furthermore, CFF was found to be significantly elevated in TBI patients who had an increased severity of symptoms as well. This relative hypersensitivity to normal illumination conditions [15,19] is consistent with related findings in the literature, which have reported that TBI individuals manifest hypersensitivity to normal sounds (i.e., hyperacusis) in the presence of normal auditory sensitivity [21].

Age effects and possible ocular disease

Age was not found to affect CFF in the present study. Previous literature suggests a decrease in CFF with age, beginning at the age of 50 years [3, 25], but this disparity may be due to differences in target luminance and perhaps the presence of early and/or subtle ocular disease. First, the high target luminance of 304 cd/m^2 used in the present study may explain the absence of an age effect. Any subtle subclinical age-related changes in the crystalline lens or retina would not be evident with such a high luminance target [5, 26]. The much lower target luminances of 7.4 to 50 cd/m^2 used in earlier studies did reveal an age effect in conjunction with CFF thresholds [3, 25]. Thus, the CFF threshold is higher and more robust at higher luminance levels [5]. Second, the age effect on CFF found in previous study may be related subclinical or

undetected macular or optic nerve disease. Studies have noted that macular disease produces a significant reduction in the CFF threshold [8, 26]. Despite the lack of an age effect in CFF thresholds in the present study, it should be noted that the oldest subject and the oldest subgroup presented with the lowest CFF values, as compared to the remainder of the normative sample data.

Effect of ABI on the neurosensory threshold

Earlier studies have reported a decrease in CFF following ABI. Battersby [27] found that CFF was decreased after penetrating injury to the occipital lobe with hemianopia, but there was no decrease in CFF when there was injury only to the frontal lobe. These data are not necessarily in disagreement with the present findings, as the subjects in Battersby's study had penetrating head injuries rather than the closed-head injuries as in the present study. Furthermore, no persons in the present study presented with hemianopia, which would be expected to exhibit a much lower CFF in the affected hemifield [28]. In a study conducted by Kooi, *et. al.* [29], decreased CFF was found in patients manifesting neurological signs of brain lesions from cerebral vascular accidents and encephalopathy, resulting in hemianopic field loss, but again not conventional closed-head traumatic brain injury. Similar arguments can be made here for lack of decrease of CFF in the present study. Each of these studies suggested that when brain injury was sustained, there were consequent decreases in overall neurological function and sensitivity. Yet in many cases of closed-head injuries, hypersensitivity has been noted[18,30]. For example, Du *et. al.* [15] also found that in photosensitive subjects with TBI, there was an elevated threshold for dark adaptation, thus suggesting reduced retinal and neurological sensitivity in selected vision functions, an apparent paradox. However, they too found that dark adaptation thresholds did not differentiate the subjects with TBI from the normal population, but

rather revealed a relatively elevated dark adaptation threshold correlated with the degree of photosensitivity experienced by the TBI subjects. This finding is similar to that of the present study demonstrating that the overall CFF does not differ between TBI and normal groups, but rather within the light-sensitive and visual motion-sensitive TBI symptomatic subgroups.

Relation to symptoms:

Although the results of this study did not reveal a significant difference between the mean CFF of the normal population and the TBI population, the findings did reveal that those TBI patients with symptoms of light sensitivity and motion sensitivity had relatively elevated CFF thresholds when compared with those who were asymptomatic. Similarly, when CFF was compared with the severity of symptoms (Figure 7A), it was found to be higher in the two subgroups that exhibited the worst symptoms when compared to the asymptomatic subgroup. These findings suggest that the TBI population does not exhibit abnormal basic temporal processing abilities per se as compared to the normal population, but rather an inability to perceptually tolerate temporal stimuli that normally would not provoke symptoms. One possibility is that those with TBI also manifesting hypersensitivity to normal temporal stimuli have abnormal disinhibition (i.e., reduced normal inhibition) of temporal processing leading to an increased gain in sensitivity. This is similar to the phenomenon of hyperacusis experienced by post-TBI subjects who had normal auditory processing [21,30]. In such cases, individuals with TBI who initially had higher temporal resolution may not have shown awareness of light and motion sensitivity symptoms prior to head trauma due to the presence of a normal process of inhibition. However, after sustaining a head injury that may not have directly damaged the magnocellular pathways, but rather rendered damage to inhibitory pathways in another area of the cortex, TBI patients may no longer exhibit normal inhibition of temporal stimuli, thus leading

to the experience of light and motion sensitivity. For example, in a study conducted using post-concussional patients, Bohnen et al [31] found a lowered tolerance to light and sound when compared to a normal age-matched population. They also speculated that the reduced tolerance to normal lighting conditions could be due to disinhibition from the orbital frontal cortex on sensory pathways. Additionally, in the present study, the difference between the TBI patients who were asymptomatic and those who were symptomatic could be explained by a difference in the site of injury to the brain. In observing the differences between CFF thresholds of subjects #9 and 16 who had notably lower thresholds and absence of symptoms, we speculate that magnocellular pathways may have sustained damage as a result of the TBI, thus leading to neurological adaptation through lowering CFF threshold. On the other hand, subjects who reported marked degrees of light and motion sensitivity (e.g., subject #17), and also a marked degree of light sensitivity, may not have sustained damage to the magnocellular pathway, but rather to related inhibitory pathways that control neural gain and sensory awareness. In those groups of subjects manifesting symptoms yet normal CFF thresholds, perhaps hypersensitivity may result from disinhibition of surrounding areas in the cortex, such as the parietal or frontal lobes which are indirectly involved in regulating motion processing [15,31]. In other words, efferent pathways affecting awareness may be involved in producing a greater sensitivity to bright flickering stimuli [32].

Relation to the neurology of motion processing:

The processing of CFF beyond the retina involves much of the optic pathway, visual cortex, and extrastriate cortex [7]. Motion processing mainly occurs in magnocellular pathways by traveling in the dorsal processing stream of the parietal lobe. The M-ganglion cells of the retina project to the dorsal lateral geniculate nucleus of the thalamus, from which the projections

continue in magnocellular pathways to reach the primary visual cortex layer 4Cα, and then onto layer 4B. These projections then input into visual area 2 (V2) bypassing the blobs and interblob regions. These neurons further project into extrastriate cortex in area MT (middle temporal area, V5), where primary motion processing occurs [12]. Most of the projections to the parietal lobe originate from the magnocellular pathways, while the temporal lobe receives projections from both magnocellular and parvocellular pathways. Therefore, while the primary contributor to area MT and the parietal lobe is the magnocellular pathway, there is also evidence of some parvocellular input into area MT as well as projection pathways from 4B [33,34]. There may also be influences from the magnocellular pathway in other areas of the brain as well. Areas such as the posterolateral thalamic nuclei and superior colliculus, which also carry visual information and input into area MT and V5, may be involved in the perceptual function of CFF threshold [35]. In studies involving humans, rats, and cats, lesions in the visual cortex usually produces a decrease in CFF [27,35,36]. However, in Schwartz and Cheney's [35] study of CFF in cats, they found that when the tectal area (i.e., superior and inferior colliculus) was lesioned, there was an increase in CFF threshold. Although their findings were inconclusive, they too are suggestive of possible inhibitory influences by the superior colliculus on temporal processing. Thus, the possible neural pathways involved in determining the CFF threshold may be manifold. Other reports have indicated the involvement of frontal and parietal lobe regions that are important in the awareness of CFF flicker [32]. Future neuro-imaging studies in humans will likely reveal the neural substrate involved in regulating CFF processing.

Clinical Implications

Functionally speaking, common light stimuli such as normal room illumination may cause symptoms in TBI subjects that are otherwise well-tolerated by normal subjects. As noted

from the present study, eight of the18 TBI subjects reported sensitivity to fluorescent lighting alone, while the others reported sensitivity to outdoor lighting or to all forms of lighting. In identifying these factors, simple measures can then be taken to reduce these symptoms. Such aids as wide-brimmed hats for outdoor lighting, and tints for indoor fluorescent lighting, can be notably used to reduce these symptoms experienced by patients after a TBI event [17]. Clinicians may also advise patients to replace household fluorescent lighting with incandescent lighting, thereby ameliorating these flicker-based symptoms. This could then improve their quality of life.

Study Limitations:

There are two potential limitations in the present study . First, in future studies, an increased number of subjects should be tested to determine more comprehensively subtle differences of the foveal CFF threshold between TBI and normals that may not have been revealed in the present study. A greater number of TBI subjects in each of the categories with a wider range symptoms would be useful in showing a stronger relationship between CFF threshold and the severity of symptoms. Secondly, testing was only done at the fovea. Therefore further testing should be conducted at additional retinal regions to assess the effectiveness of using CFF as a measure of brain damage and visual field integrity after a traumatic event. This would contribute to a better understanding of the overall pathways affected in this population to cause hyperaesthesia such as light and motion sensitivity.

Future studies:

Future studies should be conducted to compare CFF in TBI subjects with other types of brain injuries, such as brain tumors and post-surgical complications. Other testing may also conducted in conjunction with fMRI scans to localize areas of the brain are involved in the

determination of CFF. This may be useful in differentiating the areas affected from the brain injury itself, as well as the areas that could be involved in light and motion processing. Studies could also be conducted to assess if varying either target luminance or size would affect CFF in this population, perhaps making it a more sensitive indicator of brain injury in general and more specifically temporal processing deficits. Clinically speaking, studies using CFF as an objective psychophysical measure of symptoms pre- and post- vision therapy should be conducted to determine its efficacy with respect to producing improvements at a basic level of temporal processing. If results of future studies are consistent with the present study, then CFF could be used as a predictor of light and visual motion related symptoms. In addition, CFF could provide a measure of the extent of neurological impairment in TBI patients and indicate the level of neural plasticity for this most basic vision function. Lastly, CFF could therefore aid clinicians by allowing them to use a rapid and easy method to determine the severity of a patient's symptoms,and furthermore to predict the outcomes of prescribed treatments.

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Figure 1A- Schematic representation of CFF device (side view)

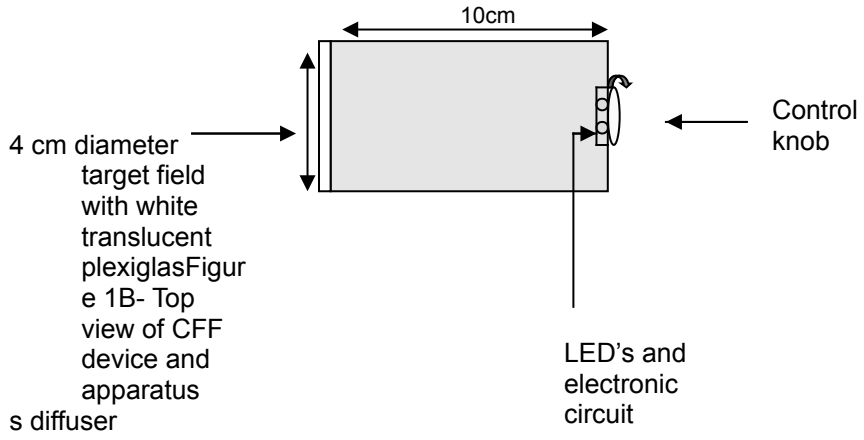
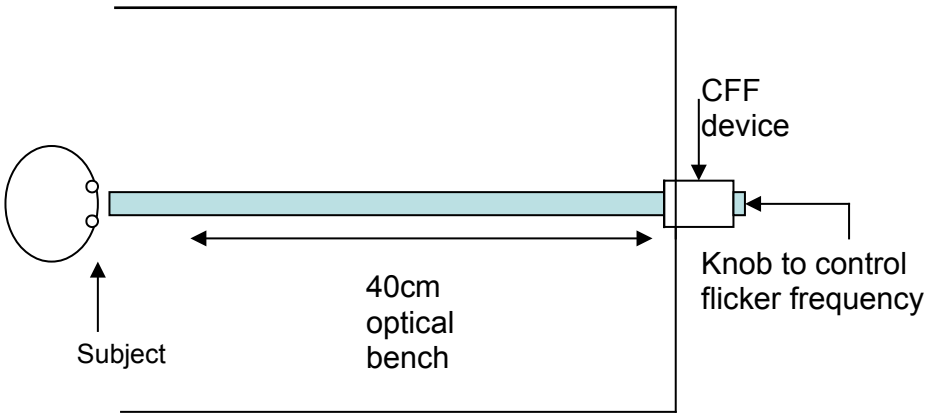


Figure 1B- Top view of CFF device and apparatus



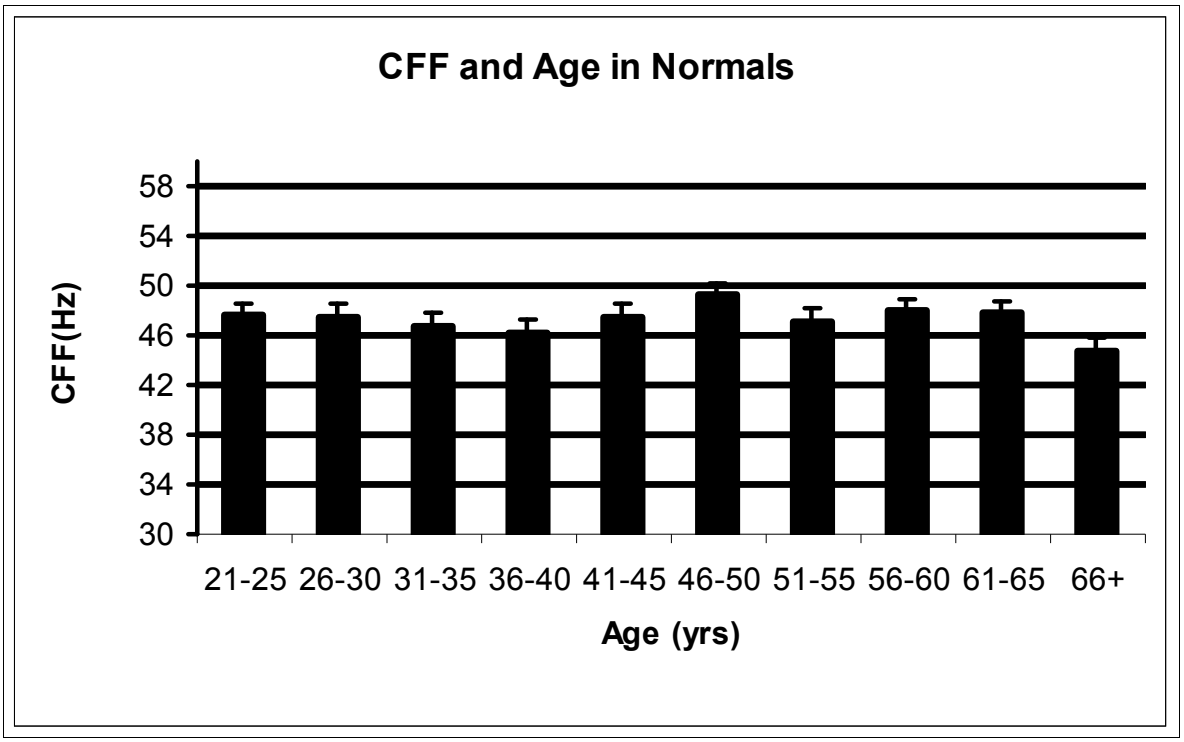


Figure 2: CFF as a function of age in the visually-normal control group. Plotted is the mean CFF +1 SEM for each 5-year bin. Each bin has 4-7 subjects.

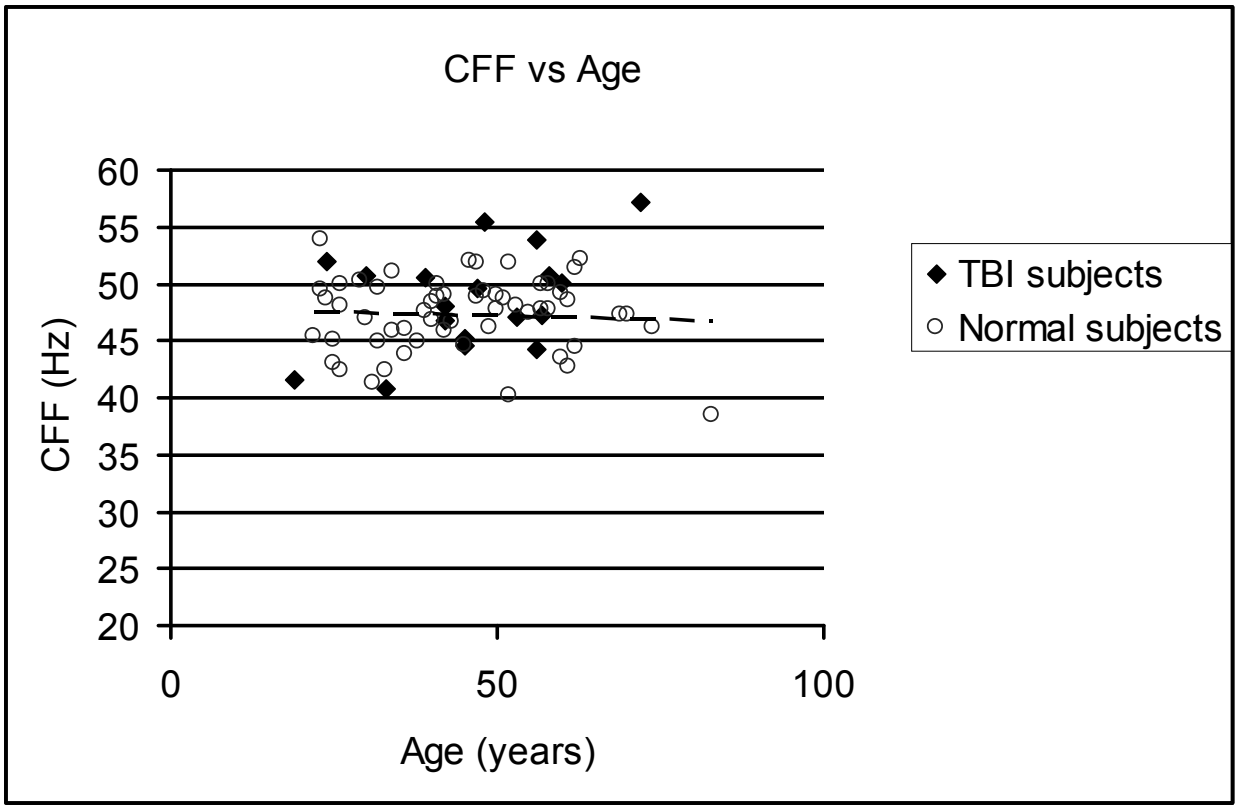


Figure 3: CFF as a function of age in the visually-normal control and TBI group. Dashed line is the linear regression for the control group (y = -0.013x + 47.84, r=-0.059), and the solid line is the linear regression for the TBI group (y = 0.146x + 41.97, r=0.44).

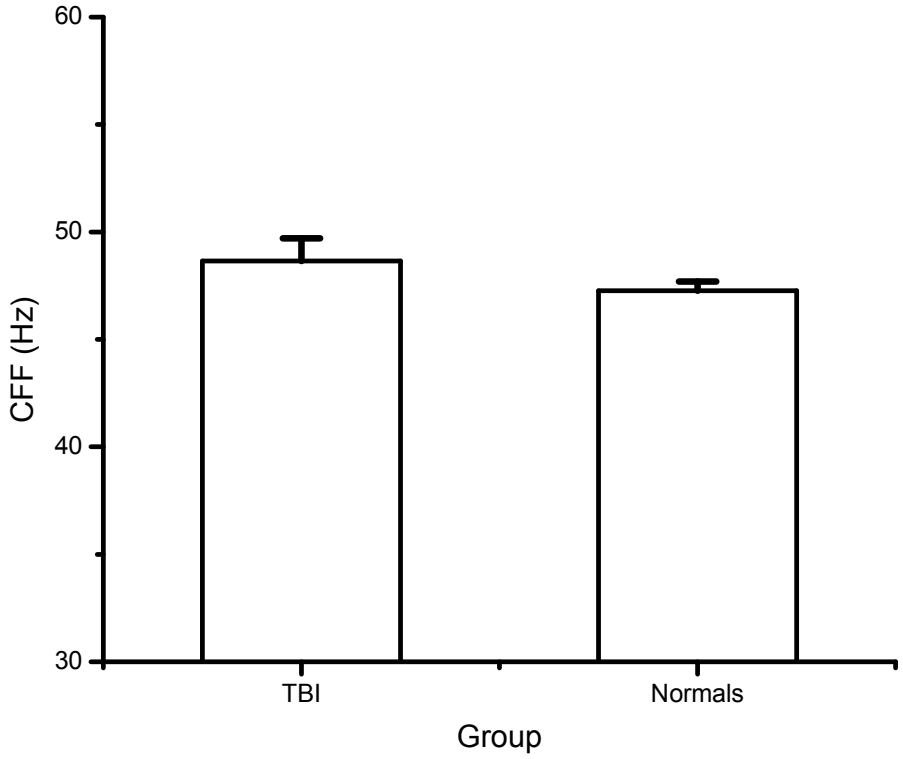


Figure 4: CFF for the visually-normal control group and the TBI group. Plotted is the mean +1 SEM.

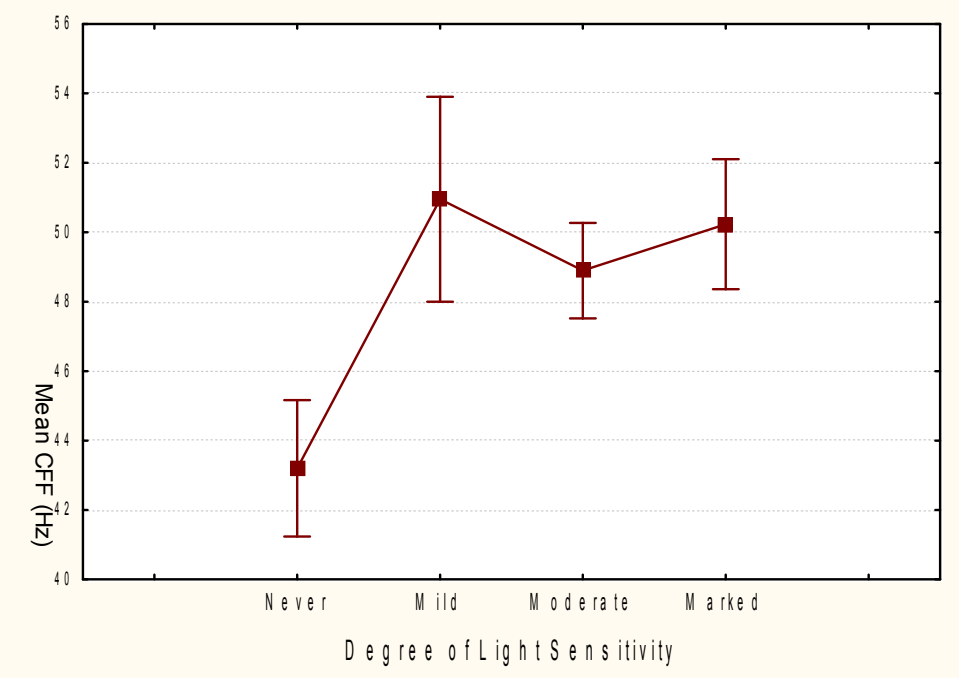


Figure 5A: CFF as a function of degree of light sensitivity in the TBI group. Plotted is the mean ± 1 SEM for the 4 levels of light sensitivity.

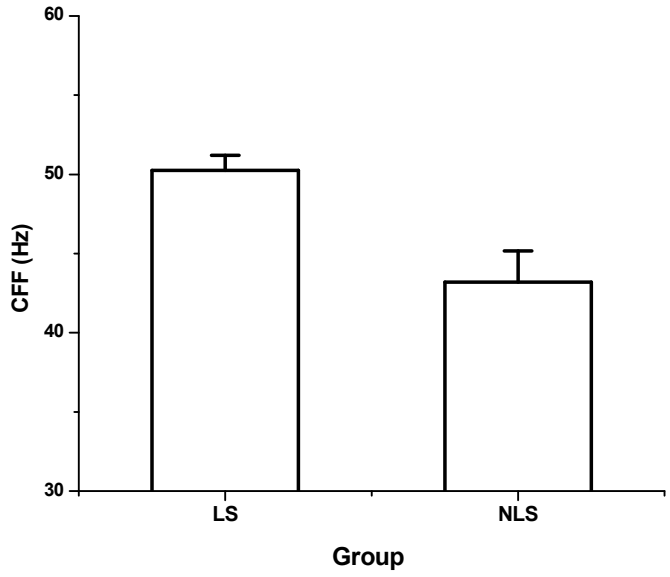


Figure 5B: CFF in the "light sensitive" versus "not light sensitive" subgroups. Plotted is the mean + 1 SEM. Symbols: LS= light sensitive, and NLS= not light sensitive.

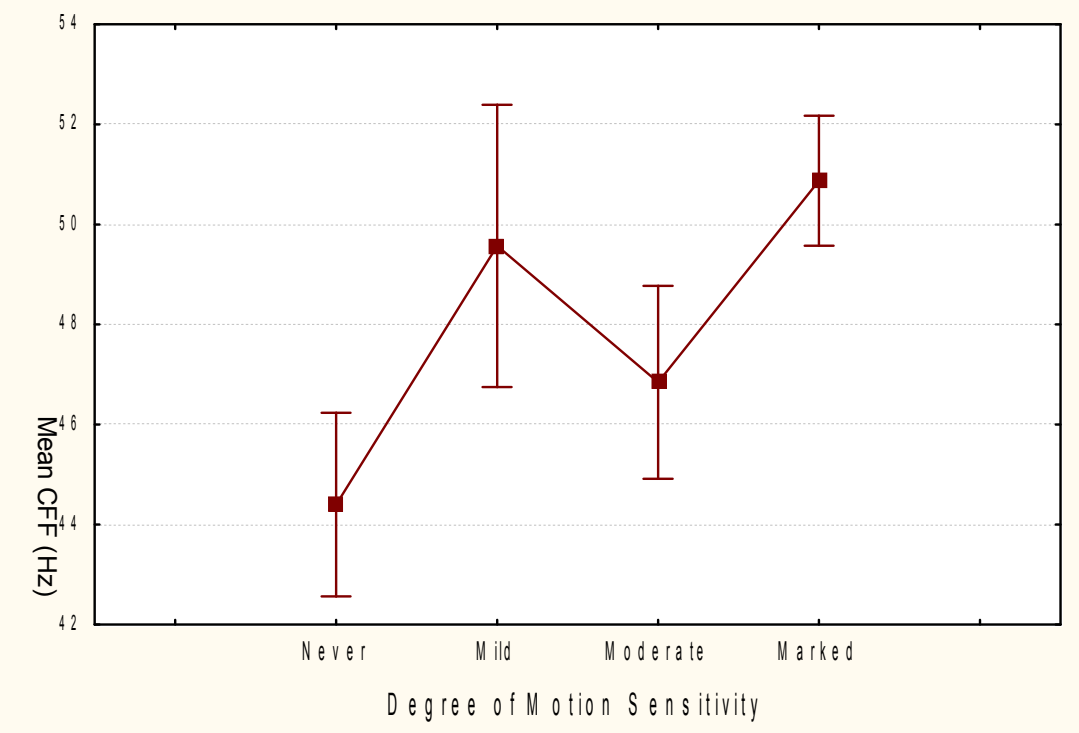


Figure 6A: CFF as a function of degree of motion sensitivity in the TBI group. Plotted is the mean ±1 SEM for the 4 levels of motion sensitivity.

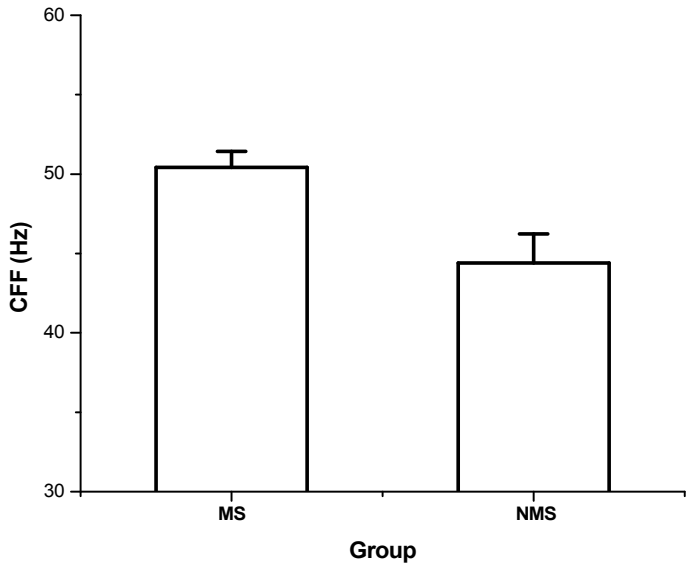


Figure 6B: CFF in "motion sensitive" versus "not motion sensitive" subgroups. Plotted is the mean +1 SEM. Symbols: MS= motion sensitive and NMS= not light sensitive.

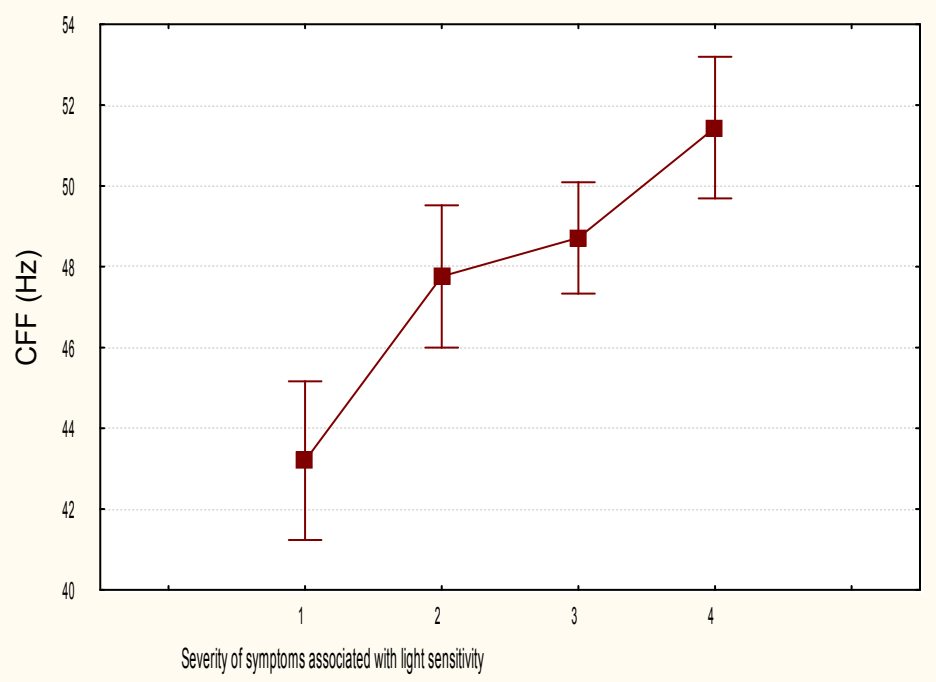


Figure 7A: CFF plotted as a function of severity of symptoms associated with light sensitivity in the TBI group. 1= no symptoms; 2 = somewhat bothersome; 3= bothersome, no pain, no HA; 4 = very bothersome, some pain

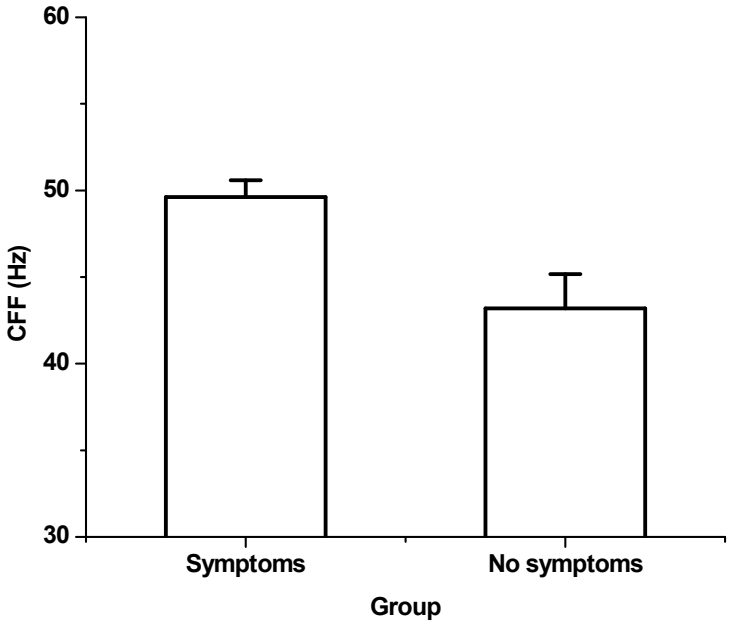


Figure 7B: CFF in the "symptoms" vs. "no symptoms" subgroups. Plotted is the mean +1 SEM.

Table 1: Comparison of Normal and TBI Groups

	Normal	TBI
Age range:	22-83 yrs	19-72 yrs
Mean ± 1SD	45 ± 15 yrs	45.7±13.6 yrs
Male:female ratio	25:31	6:12
Range of time post-injury	--	3 mos-15 yrs
Mean years post injury	--	5.2 yrs

Table 2: Clinical Data of Subjects

S#	Age (yrs)	Mean CFF (Hz)	Most recent TBI	Etiology of TBI	Medications
1	39	49.96	15 yrs	Domestic violence	Zoloft, Wellbutrin, Hydrochlorothriazide, Potassium, Chromagen
2	24	50.54	3 mos	Fall	none
3	56	44.27	10 yrs	Fall	Synthroid
4	48	55.45	3 yrs	MVA	Skelaxin, hydrocodone-Ibuprofen, Quinine sulfate , Flurbiprofen, trazoane HCl
5	58	50.68	3 mos	Assault	Wellbutrin, Adderall, Namenda, Mobil, pain patch pads
6	47	49.62	1 yr	MVA	None
7	57	47.25	3 yrs	MVA	Effexor, Ultracet, Lidoderm, Nasonex, Percocet, Maxalt, Hydromorphone HCl
8	53	47.10	8 mos	Skull fracture, unknown	Atenolol
9	19	41.65	1.5 yrs	MVA	Ibuprofen, Zoloft, Zyprexa, Depakote
10	72	57.20	unknown	Fall	None noted
11	42	48.00	5 yrs	Fall, MVA	Hespera, Naproxen, Tramadol HCl
12	56	53.90	8 yrs	Fall	Qvar, Levoxyl, Cytomel
13	45	45.25	5 yrs	Fall	Lexapro, Cozaar, Vicodin, Prilosec, Albuterol, Advair Diskus, Allegra, Topamax, Effexor
14	45	44.60	4 yrs	MVA	Effexor, Allegra, Lidoderm, Neurontin, Arthrotec
15	42	46.70	1 yr	MVA	Metformin HCL, Cholestryramine, Zoloft , Avandamet, Potassium Chloride , Hydrocodone-acetominophen, Aleve
16	33	40.85	8 yrs	Blunt head injury (football)	Risperdal, Acipax, Patanol
17	60	50.05	10 yrs	mva	Estrace, Ambien, Zoloft
18	30	50.75	3 yrs	MVA	Zoloft, Amitrex

Table 3: Responses to Questionnaire

S#	Q1. Degree of light sensitivity	Q2. Discomfort, HA, pain associated with LS	Q3. Most bothersome lighting	Q4. Onset of LS	Q5. Triggers for LS	Q6. Form of relief to LS	Q7. Degree of motion sensitivity
1	Marked	Very bothersome, some pain associated	Fluorescent	After	All, headlights on cars, lamps without shades	Does not go out when bright, lid squinting, turns off lights	Marked
2	Moderate	Bothersome, but no pain or headache	Fluorescent, Outdoor	After	Fatigue, reflections and glare	Tints, brimmed hats, lid squinting	Mild
3	Moderate	Bothersome, but no pain or headache	All lighting	After	Time (worsens as day goes on)	Tints, brimmed hats, lid squinting	Mild
4	Moderate	Very bothersome, some pain associated	All lighting	After	All	All	Marked
5	Moderate	Somewhat bothersome	Fluorescent	After	Fatigue, computers	Tints, brimmed hat, lid squinting	Moderate
6	Moderate	Bothersome, but no pain or headache	Fluorescent, Outdoor	After	Computers TV, movies	Brimmed hat	Marked
7	Marked	Bothersome, but no pain or headache	Fluorescent	After	All	All	Marked
8	Never	n/a	n/a	n/a	n/a	n/a	Never
9	Never	n/a	n/a	n/a	n/a	n/a	Never
10	Marked	Very bothersome, some pain associated	Fluorescent	After	Fatigue	Tints, brimmed hat	Marked
11	Mild	Somewhat bothersome	Outdoor	After	Emotional issues, anxiety	Tints	Never
12	Mild	Bothersome, but no pain or headache	Fluorescent	Before	Fatigue, time (worsens as day goes on), Computer	Tints, brimmed hat, anti-reflective coatings	Mild
13	Moderate	Very bothersome, some pain associated	All lighting	After	Light adaptation, dark adaptation	Tints, brimmed hat	Moderate
14	Moderate	Somewhat bothersome	Fluorescent	After	Fatigue	Tints	Moderate
15	Marked	Bothersome, but no pain or headache	All lighting	After	Computer	Tints, does not go out when bright, brimmed hat, turn off lights	Marked
16	Never	n/a	n/a	After	n/a	n/a	Never
17	Marked	Very bothersome, some pain associated	All lighting	After	Fatigue, TV/movies, complex environments	Tints, brimmed hat, looking at blank walls	Marked
18	moderate	Very bothersome, some pain associated	All lighting	After	Fatigue, time (worsens as day goes on)	Turn off lights	Marked

Appendix 1: Symptom rating-scale questionnaire

1. Are you sensitive to light? Please rate it from1-4 as listed below.

   1 – never
   2 – mild
   3 – moderate
   4 – marked

2. Is there any discomfort, headaches or pain associated with the light sensitivity?

   1- no discomfort associated
   2- somewhat bothersome
   3- bothersome, but no pain or headaches associated with it
   4- very bothersome with some pain associated
   5- very bothersome and very painful

3. What kind of light bothers you the most?

   1- indoor incandescent lighting
   2- outdoor light
   3- fluorescent lighting
   4- all lighting

4. Did you start experiencing light sensitivity before or after the head trauma?

   1- before the traumatic brain injury
   2- after the traumatic brain injury

5. What increases the light sensitivity?

   1- fatigue
   2- time (worsens as the day goes on)
   3- computer use
   4- television and movies
   5- Other (specify) _____

6. What do you do to reduce the light sensitivity?

   1- tints
   2- don't go out when it's bright
   3- brimmed hat
   4- squint
   5- other (specify)_____

7. Do you ever experience increased sensitivity to visual motion?

   1 – never
   2 – mild
   3 – moderate
   4 – marked