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## First- and second-order contrast sensitivity functions reveal disrupted visual processing following mild traumatic brain injury



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### ABSTRACT

Vision is disrupted by traumatic brain injury (TBI), with vision-related complaints being amongst the most common in this population. Based on the neural responses of early visual cortical areas, injury to the visual cortex would be predicted to affect both 1<sup>st</sup> order and 2<sup>nd</sup> order contrast sensitivity functions (CSFs)—the height and/or the cut-off of the CSF are expected to be affected by TBI. Previous studies have reported disruptions only in 2<sup>nd</sup> order contrast sensitivity, but using a narrow range of parameters and divergent methodologies—no study has characterized the effect of TBI on the full CSF for both 1<sup>st</sup> and 2<sup>nd</sup> order stimuli. Such information is needed to properly understand the effect of TBI on contrast perception, which underlies all visual processing. Using a unified framework based on the *quick* contrast sensitivity function, we measured full CSFs for static and dynamic 1<sup>st</sup> and 2<sup>nd</sup> order stimuli. Our results provide a unique dataset showing alterations in sensitivity for both 1<sup>st</sup> and 2<sup>nd</sup> order visual stimuli. In particular, we show that TBI patients have increased sensitivity for 1<sup>st</sup> order motion stimuli and decreased sensitivity to orientation-defined and contrast-defined 2<sup>nd</sup> order stimuli. In addition, our data suggest that TBI patients' sensitivity for both 1<sup>st</sup> order stimuli and 2<sup>nd</sup> order contrast-defined stimuli is shifted towards higher spatial frequencies.

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### 1. Introduction

Traumatic brain injury (TBI) is one of the most common causes for disability amongst the North American population affecting approximately 3.2–5.3 million people (Coronado et al., 2011; Corrigan, Selassie, & Orman, 2010). Some of the most common complaints after TBI are visual deficits (Greenwald, Kapoor, & Singh, 2012; Kapoor & Ciuffreda, 2002). Clinically, these complaints include image blur, problems with reading, double vision, motion sensitivity, and light sensitivity (for a comprehensive review see (Kapoor & Ciuffreda, 2002)). The fact that many visual symptoms persist despite normal ocular function suggests that post-chiasmatic visual processing involving the thalamus or the occipital cortex may be affected. The prevalence of visual complaints in a subset of TBI patients may be indicative of more general disruption

of vision—patients who are unaware of symptoms may nonetheless suffer from sub-clinical disruptions to visual performance.

While total loss of the primary visual cortex (V1) results in effective blindness (blindsight) (Covey, 2010; Stoerig & Covey, 1997), injury to the rest of the visual cortex results in contrast sensitivity loss for both 1<sup>st</sup> and 2<sup>nd</sup> order stimuli—stimuli that vary in a dimension other than luminance such as texture, motion and contrast, thought to involve extra-striate cortical regions (El-Shamayleh & Movshon, 2011; Larsson, Heeger, & Landy, 2010; Merigan, 2000). First-order or luminance modulation losses are smaller in magnitude than the 2<sup>nd</sup> order losses, suggesting that the extra-striate cortex may be specifically involved (Hayes & Merigan, 2006; Merigan, Nealey, & Maunsell, 1993; Schiller, 1993). For example, a lesion to the macaque visual area V2 resulted in a mild 1<sup>st</sup> order contrast sensitivity loss within the lesioned cortical region whereas perception of orientation-defined 2<sup>nd</sup> order stimuli was severely impaired (Merigan et al., 1993). Chemical lesions to macaque monkey V4 resulted in deficits in both 1<sup>st</sup> order contrast sensitivity and 2<sup>nd</sup> order contour discrimination and these findings were in notable agreement with human data from stroke patients with lesions in corresponding cortical area

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(Hayes & Merigan, 2006). Thus, the processing of 1<sup>st</sup> and 2<sup>nd</sup> order stimuli (non-luminance modulation) can be affected in TBI, suggesting that the putative diffuse injury involves both extra-striate as well as striate processing.

Describing a deficit in terms of 1<sup>st</sup> and 2<sup>nd</sup> order processing is challenging for two reasons. For example, contrast perception for 1<sup>st</sup> order stimuli might be affected by whether the stimulus is static or moving. Second-order stimuli can be defined in a number of ways, e.g., being defined solely by contrast variation, texture variation, or dynamic variations over space. Independent of the stimulus type, it is imperative that a range of stimulus parameters be tested so as to not obtain biased estimates of group differences—for instance, TBI and normal subjects may have a difference in performance at only high or only medium spatial frequencies. This information is important to identify the affected mechanisms as well as the potential means of treatment. Critically, 2<sup>nd</sup> order stimuli all have equi-detectable carriers (i.e. all carriers were set to a contrast factor above threshold). We do this to ensure that any 2<sup>nd</sup> order loss in sensitivity is not simply a consequence of a less detectable carrier (i.e. a first order loss).

Previous findings with fixed stimulus parameters suggest that sensitivity, particularly for 2<sup>nd</sup> order contrast modulated stimuli, can be affected by TBI. While sensitivity to a 1<sup>st</sup> order low spatial frequency luminance grating was not affected, sensitivity to both static and dynamic contrast-defined 2<sup>nd</sup> order stimuli at the same spatial frequency was lower in children who suffered a mild TBI (Brosseau-Lachaine, Gagnon, Forget, & Faubert, 2008). Another study showed that reaction times on a motion direction discrimination task were longer in mild TBI participants for both 1<sup>st</sup> and 2<sup>nd</sup> order stimuli using parameters comparable to a previous study. However, unlike in the control group, the reaction times for 2<sup>nd</sup> order stimuli were longer compared to 1<sup>st</sup> order stimuli in the TBI group (Piponnier et al., 2015).

Electrophysiological results appear to corroborate the psychophysical findings. Lachapelle, Ouimet, Bach, Ptito, and McKerral (2004) recorded visual evoked potentials (VEPs) to 1<sup>st</sup> and 2<sup>nd</sup> order visual stimuli and assessed the delays as well as the amplitudes of the low- and high-level VEP components. While the amplitudes did not significantly differ between the two groups in either condition—albeit on average being diminished in the TBI group—the delay was significantly longer for motion- and texture-defined 2<sup>nd</sup> order stimuli. A later study by the same group showed a prolonged event-related potential latency to motion-defined texture (2<sup>nd</sup> order) but not simple (1<sup>st</sup> order) motion or pattern reversal (Lachapelle, Bolduc-Teasdale, Ptito, & McKerral, 2008).

A particular challenge in interpreting previous findings is that the spatial frequencies tested are often limited, for example some studies used only low spatial frequency (0.5 cpd) for both 1<sup>st</sup> and 2<sup>nd</sup> order stimuli (Brosseau-Lachaine et al., 2008; Piponnier et al., 2015). In addition, the carriers contrast of the 2<sup>nd</sup> order stimuli were fixed at a constant contrast (usually 50% or 100%) and were not scaled by the 1<sup>st</sup> order sensitivity of each participant (Brosseau-Lachaine et al., 2008; Lachapelle et al., 2008; Piponnier et al., 2015). We have addressed these issues by estimating the full contrast sensitivity function (CSF) for both static and dynamic 1<sup>st</sup> and 2<sup>nd</sup> order stimuli. Our approach—utilizing the *quick* contrast sensitivity method (qCSF; (Lesmes, Lu, Baek, & Albright, 2010; Reynaud, Tang, Zhou, & Hess, 2014))—allowed us to match the 2<sup>nd</sup> order stimulus presentation parameters to their 1<sup>st</sup> order detectability across the spatial frequency range, allowing us to accurately measure alterations in 2<sup>nd</sup> order contrast perception that are independent of any 1<sup>st</sup> order performance deficit. We also measured the 2<sup>nd</sup> order sensitivity for three fundamentally different types of stimuli—stimuli defined by contrast, orientation, or motion. Using this unified approach, we observed changes to both

1<sup>st</sup> order and 2<sup>nd</sup> order visual perception, with particular differences relating to dynamic vs. static stimuli.

## 2. Methods

### 2.1. Participants

A group of 26 mild TBI participants (17 females, 9 males, mean age 34.69 years  $\pm$  14.7 SD) was recruited either from the McGill University Health Center Out-Patient TBI Program or via public advertisements. The criteria of mild TBI were as follows: (1) any amnesia of events immediately before or after the accident lasting no longer than 24 h and (2) a Glasgow Coma Score ranging between 13 and 15. If loss of consciousness was present, it had to be shorter than 30 min. Mild TBI could be sub-classified as trivial, simple or complex (presence of a positive acute intracerebral bleeding in CT scan). The time between the TBI and the testing session varied between 35 days and 96 months. All participants had normal or corrected-to-normal visual acuity and wore their habitual refractive correction during the experiment. All procedures were in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and were approved by the Research Ethics Board of the McGill University Health Centre. Informed consent was obtained from all participants prior to data collection. A short verbal screening for relevant medical history e.g. visual and psychiatric disorders, recurrent migraines, or vertigo was administered prior to participation. The exclusion criteria were: general anesthesia within the past six months, other acquired brain injuries in the past, severe tremors, and/or epilepsy. All participants successfully completed a quick neuropsychological screening of visual attention—the Trail Making Test A (Giovagnoli et al., 1996), the Bells Test (Gauthier, Dehaut, & Joannette, 1989)—and spatial neglect—the Clock-drawing test (Ishiai, Sugishita, Ichikawa, Gono, & Watabiki, 1993) (see Table 1).

### 2.2. Subjective visual complaints

In order to evaluate how the TBI affected vision of our group of participants we used a modified version of the questionnaire included in the Defense Centers of Excellence guidelines for assessment of visual dysfunction associated with mTBI (Defense Centers of Excellence for Psychological Health & Traumatic Brain Injury, 2013). The questionnaire is included in Table 2. In brief, the questionnaire probes for common complaints after concussion, including blurred vision, reading difficulties, discomfort during use of computer screens, etc. Twenty two participants completed the questionnaire, and were asked to rank their responses on a scale from 1 to 10 where 1 = “not at all” and 10 = “totally”. There were 11 ranked questions therefore the minimum total score was 11 and the maximum total score was 110.

### 2.3. Stimuli and experimental procedure

The stimulus generation procedures have been previously described in detail (Gao et al., 2014; Reynaud et al., 2014). The 1<sup>st</sup> order orientation-defined stimuli were created by filtering a white noise with horizontally- or vertically-oriented Gabor filters with a half-response spatial frequency bandwidth of 1.84 octaves, resulting in horizontally- or vertically-oriented patterns (Fig. 1B). The motion-defined stimuli were created by filtering the white noise by both orthogonal filters and were drifted either along the horizontal or vertical directions at a temporal frequency of 2 Hz. The 2<sup>nd</sup> order stimuli are best described in terms of a carrier (high-frequency texture) and an envelope (lower-frequency constraint on the carrier contrast variations over space). Thus, the

**Table 1**  
TBI participants.

ID	Age	Gender	Trail making test time	Trail making test errors	Bells test time	Bells test missed	TBI type
T1	51	F	49.68	0	106.27	0	Self-reported
T2	59	M	56.22	0	157.88	2	Mild simple
T3	19	F	37.82	0	126.03	1	Mild simple
T4	22	M	30.02	0	100.01	0	Mild simple
T5	28	M	22.42	0	114.72	2	Mild simple
T6	23	F	37.24	0	79.22	1	Mild simple
T7	48	M	39.77	0	40.08	8	Mild simple
T8	18	F	25.933	0	76.599	4	Mild simple
T9	55	F	39.204	0	80.945	7	Mild simple
T10	50	F	23.369	1	68.446	6	Mild simple
T11	20	F	27.62	0	50.909	13	Mild simple
T12	57	F	23.107	0	89.576	10	Self-reported
T13	59	M	33.646	0	82.928	6	Mild complex
T14	19	F	19.98	0	46.6	6	Mild simple
T15	19	F	19.98	0	46.6	6	Mild complex
T16	34	F	32.72	0	101.05	3	Mild simple
T17	44	F	19.93	1	32.18	5	Mild simple
T18	24	F	33	1	60.02	11	Mild simple
T19	31	F	23.28	0	78.48	0	Self-reported
T20	18	F	23.11	1	62.04	1	Mild simple
T21	33	F	20.23	0	38.09	10	Mild simple
T22	28	M	32.35	1	119.65	2	Mild complex
T23	26	M	27.73	0	125.43	7	Mild simple
T24	50	M	26.16	1	87.71	3	Self-reported
T25	23	F	24.49	1	88.21	1	Mild simple
T26	44	M	22.35	0	88.36	1	Mild simple

measurable spatial frequency for 2<sup>nd</sup> order is necessarily lower than the 1<sup>st</sup> order stimuli—the 2<sup>nd</sup> order envelope must include 1<sup>st</sup> order modulations, hence it must be larger. The 1<sup>st</sup> order stimuli were used as carriers for the 2<sup>nd</sup> order stimuli that were defined by orientation, motion, and contrast (Fig. 1B). The carrier-to-envelope spatial frequency ratio was set to 4-to-1 has been shown to be optimal for psychophysical assessment of low-level vision (Meso & Hess, 2010; Reynaud & Hess, 2012; Sutter, Sperling, & Chubb, 1995), but see (Dakin & Mareschal, 2000). Stimuli were presented on a grey background within a Gaussian envelope with 10° of standard deviation.

The contrast and spatial frequency of each stimulus were determined by the quick contrast sensitivity function method (qCSF; (Lesmes et al., 2010)). The qCSF is an adaptive Bayesian procedure that estimates multiple parameters of psychometric function allowing for quick estimates of thresholds across the whole spatial frequency range. Before each stimulus presentation, the qCSF

algorithm searches for the optimal spatial frequency and contrast in order to maximize the information gain about the subjects' CSF. For the 2<sup>nd</sup> order stimuli, the qCSF routine (Lesmes et al., 2010) controlled the envelope's spatial frequency and the level of modulation. The carrier's spatial frequency was also adjusted in order to maintain a 4-to-1 carrier-to-envelope spatial frequency ratio. The validity of this approach has been successfully established for first-order (Lesmes et al., 2010) and second order (Gao et al., 2014; Reynaud et al., 2014) sensitivities.

Participants performed a two-alternative forced choice (2AFC) task of identifying the orientation of the grating in the 1<sup>st</sup> order orientation condition, orientation of motion (horizontal vs. vertical) in the 1<sup>st</sup> order motion task, and the orientation of the envelope in all 2<sup>nd</sup> order conditions (Fig. 1B). The order of conditions was pseudo-random, following previous schemes—for half of the participants, the order consisted of 1<sup>st</sup> order orientation, 2<sup>nd</sup> order orientation, 1<sup>st</sup> order motion, 2<sup>nd</sup> order motion-defined, and finally 2<sup>nd</sup> order contrast modulation, while for the other half of the subjects the order was 2<sup>nd</sup> order contrast modulation, 1<sup>st</sup> order motion, 2<sup>nd</sup> order motion modulation, 1<sup>st</sup> order orientation, 2<sup>nd</sup> order orientation (Gao et al., 2014; Reynaud et al., 2014). Each participant completed one repetition per condition, with each qCSF estimate requiring 100 trials preceded by five training trials that were discarded from analysis. All stimuli were created by Psychtoolbox (Brainard, 1997; Pelli, 1997) under Matlab 2012a (MathWorks, Natick, US) installed on a PC (Intel Core i7 processor, 4 GB RAM, 2.67 Hz, ATI Radeon HD 3400 8 bit graphics card) and viewed on a gamma-corrected CRT screen (LG Flatron F900P, 1024 × 768, 85 Hz). The monitor was positioned at 60 cm and viewed monocularly (half of the participants used their right eye) with an opaque patch over one eye.

#### 2.4. Analysis

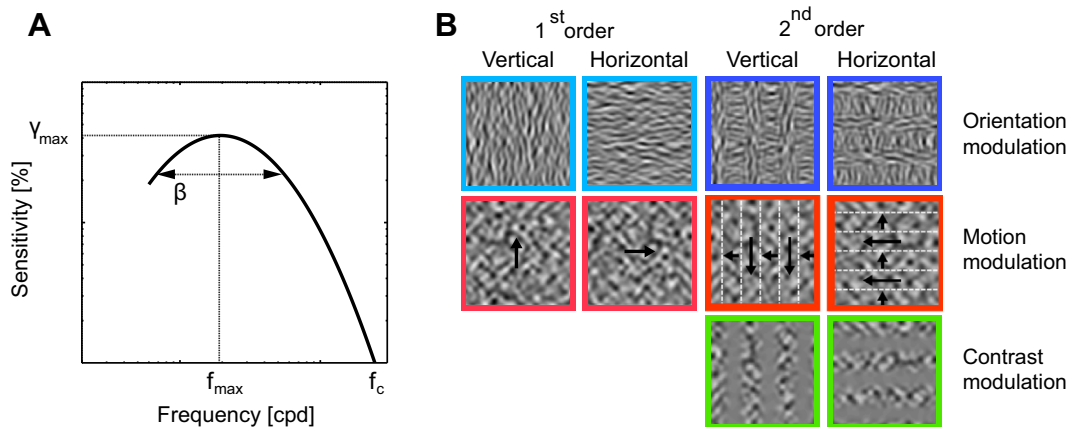
The qCSF method provides estimates of five parameters (Fig. 1) the maximum gain, the peak frequency, the bandwidth, truncation, and the cut-off frequency of the CSF (Gao et al., 2014; Lesmes et al., 2010; Reynaud et al., 2014). In line with our previous application of qCSF (Gao et al., 2014; Reynaud et al., 2014), the truncation parameter was discarded from our analyses.

Data from this study were compared to an extension of the normative dataset of Reynaud et al. (2014) which expands the age-range of the dataset. The extended normative dataset consisted of qCSF measurements in 102 healthy adults (49 males, 53 females, mean age 46.3 ± years 22 SD). All parameter estimates for each condition were compared between the TBI and the normative dataset using the non-parametric Mann-Whitney *U*-test. To evaluate the relationship between the 1<sup>st</sup> order orientation and motion CSFs, we calculated sensitivity difference in decibels between the maximum gain estimates for the 1<sup>st</sup> order sensitivity functions. This measure was then subjected to the Mann Whitney *U*-test. Alpha level of 0.05 was adopted for all analyses. In addition, we conducted a non-parametric Bayes factor analysis (Holmes, Caron, Griffin, & Stephens, 2015) (Supplementary material). Spearman's correlation was used to assess the relationships between time-since-TBI, neuropsychological test measures, and summed score from the visual complaints questionnaire and maximum gain estimates for each condition (Supplementary Figs. 2–6). To account for multiple comparisons (time-since-TBI, all neuropsychological measures, and the questionnaire score were subjected to 20 correlations – 5 conditions × 4 qCSF parameters), we adopted a Bonferroni-corrected alpha 0.0025 for this analysis.

Prior to the group analysis, all individual data were visually inspected. In one participant (T19), the 2<sup>nd</sup> order motion-modulation sensitivity function (Supplementary Fig. 1) was not log-parabola shaped. For the purpose of the group analysis of 2<sup>nd</sup> order motion condition, this participant's data were excluded.

**Table 2**  
Visual complaint questionnaire. The questionnaire contains 11 ranked questions with scores between 1 and 11 where 1 = “not at all” and 10 = “completely”. The minimum total score was 11 and the maximum total score was 110. 5th and 95th = 5th and 95th percentile (N = 22).

After your concussion, did you...	5th	Median	95th
1. Did you experience any change in vision? Rating: 1 2 3 4 5 6 7 8 9 10	1	1	9.45
2. Did you experience blurred vision (far or near)? Far rating: 1 2 3 4 5 6 7 8 9 10 Near rating: 1 2 3 4 5 6 7 8 9 10	1 1	1 1	8.45 7.8
3. Did you experience any vision loss? Rating: 1 2 3 4 5 6 7 8 9 10	1	1	2
4. Did you experience sensitivity to light or glare? Rating: 1 2 3 4 5 6 7 8 9 10	1	7	10
5. Did you see equally with each eye? Yes vs No	n/a		
6. Did you experience problems with balance or dizziness? Rating: 1 2 3 4 5 6 7 8 9 10	1	5	10
7. Did you have difficulty maintaining clear vision for extended time periods? Rating: 1 2 3 4 5 6 7 8 9 10	1	2	8.45
8. Did you have problems reading across a page or computer screen? Rating: 1 2 3 4 5 6 7 8 9 10	1	5	9
9. Did you get a headache when reading or using a computer? Rating: 1 2 3 4 5 6 7 8 9 10	1	6	10
10. Did you experience any changes to visual habits such as cell phone/texting use, driving, video games, etc.? Rating: 1 2 3 4 5 6 7 8 9 10	1	3	10
11. Did you see better if you tilted your head? Rating: 1 2 3 4 5 6 7 8 9 10	1	1	6
12. When did you notice visual problems? Free entry:			
13. What were you doing when you notice the visual problems? Free entry:			
14. Record any spontaneous thoughts: Free entry:			



**Fig. 1.** Adapted from (Reynaud et al., 2014). Panel A: qCSF is described by the log-parabola model as a function of the spatial frequency. Four parameters are studied: the maximum gain ( $\gamma_{max}$ ), the peak frequency ( $f_{max}$ ), the bandwidth ( $\beta$ ), and the cut-off frequency ( $f_c$ ). Panel B: example of the stimuli. Left part 1<sup>st</sup> order stimuli, right part 2<sup>nd</sup> order stimuli. Note that the stimuli were presented within a Gaussian aperture during the experiment. For detailed description of stimuli construction refer to Reynaud et al. (2014) and Gao et al. (2014).

While the results reported here reflect the exclusion, the results were unaffected by the inclusion of this subject's data (see Supplementary material).

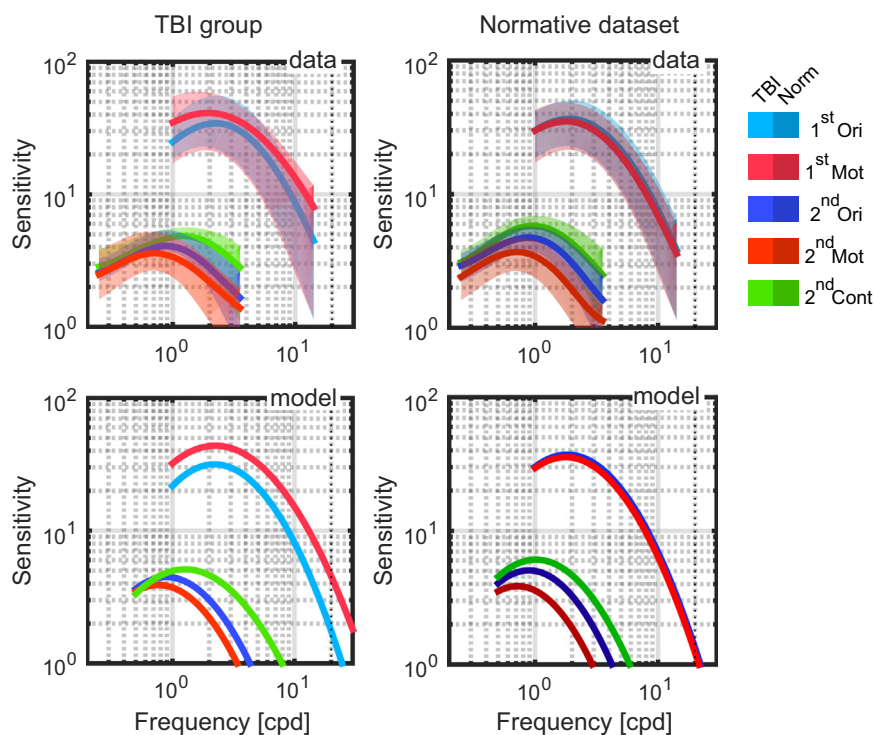
### 3. Results

Average sensitivity functions and measured model estimates for all sensitivity functions based on pseudomedian estimates of qCSF parameters for both groups are depicted in Fig. 2. Values for frequencies smaller than 1 cpd in the 1<sup>st</sup> order conditions and

0.5 cpd in the 2<sup>nd</sup> order conditions are plotted as the truncation parameter was discarded from our analysis. Broadly, the sensitivity functions are clustered in two groups corresponding to the 1<sup>st</sup> and 2<sup>nd</sup> order vision whereby the 1<sup>st</sup> order functions show higher maximum gain and sensitivities at higher spatial frequencies.

#### 3.1. First order perception

On average there was a significant trend for decreased sensitivity for the orientation condition and increased sensitivity for the



**Fig. 2.** Averaged CSFs (top row) and model estimates based on the group pseudomedian estimates of qCSF parameters (bottom row). Averaged CSFs represent geometric mean with shading representing the standard deviation. Left panels TBI group; right panels normative dataset. cpd = cycles per degree. 1<sup>st</sup> Ori – 1<sup>st</sup> order orientation, 1<sup>st</sup> Mot – 1<sup>st</sup> order motion, 2<sup>nd</sup> Ori – 2<sup>nd</sup> order orientation modulation, 2<sup>nd</sup> Mot – 2<sup>nd</sup> order motion modulation, 2<sup>nd</sup> Cont – 2<sup>nd</sup> order contrast modulation.

motion condition in the TBI group across all tested spatial frequencies. This resulted in a separation of the two functions in the TBI group which is in contrast to the normative data where the two functions practically overlap. Quantified as decibel ratio of the maximum gain estimates, the separation of the two functions was significantly larger between the TBI compared to the normative groups ( $U = 1619$ ,  $p = 0.001$ ). Furthermore, direct comparison of the maximum gain estimates revealed a significantly higher 1<sup>st</sup> order motion sensitivity in the TBI group ( $U = 2017$ ,  $p = 0.047$ ); the individual parameters are reported in Fig. 3. There was no significant correlation between the maximum gain estimate and time-since-TBI, visual complaints questionnaire score, or any of the neuropsychological measures.

There was a small but significant shift of the CSF peak towards higher spatial frequencies in the TBI group for both orientation ( $U = 1529$ ,  $p < 0.001$ ) as well as motion 1<sup>st</sup> order stimuli ( $U = 1906$ ,  $p = 0.02$ ). In addition, the variance of the peak spatial frequency values was higher in the TBI group compared to the normative dataset ( $W > 7.0$ ,  $p < 0.001$ ). The bandwidth estimate for the motion condition ( $U = 1363$ ,  $p < 0.001$ ) and cut-off spatial frequency ( $U = 718$ ,  $p < 0.001$ ) were significantly larger compared to the normative dataset (Fig. 3).

### 3.2. Second order perception

Analysis of the CSF parameters for the 2<sup>nd</sup> order conditions revealed a decreased sensitivity for orientation-defined ( $U = 1710$ ,  $p = 0.003$ ) and contrast-defined stimuli ( $U = 1211$ ,  $p < 0.001$ ) but not for motion-defined stimuli ( $U = 2532$ ,  $p = 0.954$ ) as estimated by the maximum gain parameter (Fig. 3). However, for the motion-defined stimuli, there was a larger variance in the maximum gain parameter estimates in the TBI group  $W = 1.71$ ,  $p = 0.04$ ). Similarly to 1<sup>st</sup> order conditions, we found no correlation

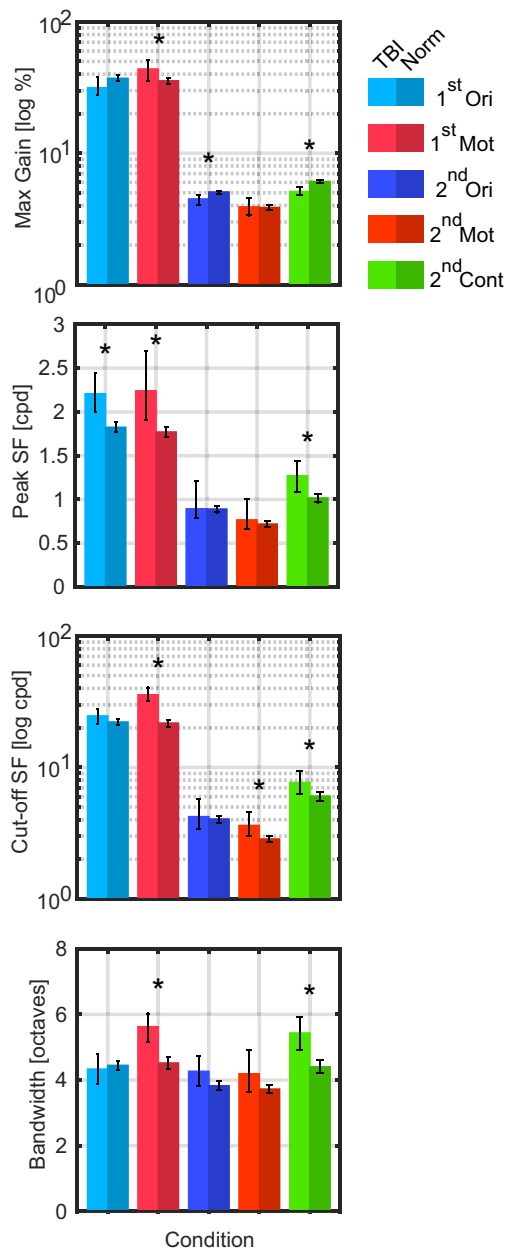
between the maximum gain and the time since TBI, visual complaints questionnaire score, or the neuropsychological measures.

In terms of peak spatial frequency, there was an average shift of the CSFs towards higher spatial frequencies in all 2<sup>nd</sup> order conditions, but the effect was significant only for the contrast-defined condition ( $U = 1736$ ,  $p = 0.04$ ). The variance of the peak spatial frequency estimates was higher in the TBI group for all conditions ( $W > 2.5$ ,  $p < 0.006$ ). Similarly, the cut-off spatial frequency of the CSFs was higher in all conditions on average but reached significance only for the 2<sup>nd</sup> order contrast-defined ( $U = 1911$ ,  $p = 0.02$ ) and motion-defined stimuli ( $U = 1779$ ,  $p = 0.014$ ). Finally, the bandwidth was significantly broader for contrast-defined stimuli ( $U = 1566$ ,  $p = 0.001$ ); Fig. 3.

### 3.3. Visual complaints questionnaire

Twenty two out of the 26 TBI participants completed our visual complaints questionnaire (Table 2). Five of these participants (23%) reported a change in vision associated with the TBI (score of 5 and above); Table 2. The most common complaint was sensitivity to light and glare (59%) followed by headaches and/or difficulties associated with work with a computer screen (45–54%). Also, nine participants reported that they had to change their visual habits post-concussion. On the other hand, only three and four participants reported blurred vision at near and distance, respectively.

In addition to the Spearman ranked correlation analysis reported above, we carried out a further exploratory analysis of the most vs. the least symptomatic patients based on their questionnaire responses. Based on their ranking on the aggregate score from the questionnaire, we did not observe any significant differences between the five most versus the five least symptomatic patients on the qCSF parameters ( $U > 4$ ,  $p > 0.095$ ).



**Fig. 3.** Pseudomedian estimates of the sensitivity function parameters. Error bars represent  $\pm$  nonparametric 95% confidence intervals. \*  $p < 0.05$  Mann-Whitney  $U$  test. 1<sup>st</sup> Ori – 1<sup>st</sup> order orientation, 1<sup>st</sup> Mot – 1<sup>st</sup> order motion, 2<sup>nd</sup> Ori – 2<sup>nd</sup> order orientation modulation, 2<sup>nd</sup> Mot – 2<sup>nd</sup> order motion modulation, 2<sup>nd</sup> Cont – 2<sup>nd</sup> order contrast modulation.

#### 4. Discussion

In this study, we evaluated several aspects of 1<sup>st</sup> and 2<sup>nd</sup> order visual processing following TBI using a unified approach that measured the full contrast sensitivity function for both 1<sup>st</sup> and 2<sup>nd</sup> order stimuli, with both dynamic and static stimuli, and with 2<sup>nd</sup> order stimuli scaled for 1<sup>st</sup> order performance. The three most notable results are that (1) TBI patients have altered relative sensitivity between dynamic and static 1<sup>st</sup> order stimuli, (2) TBI patients' sensitivity to orientation-defined and contrast-defined stimuli is lower, and (3) TBI patients' sensitivity for both 1<sup>st</sup> order and 2<sup>nd</sup> order contrast-defined stimuli is shifted towards higher spatial frequencies. Because of our experimental design in which carriers for 2<sup>nd</sup> order orientation and motion contrasts were set

to be a constant times their 1<sup>st</sup> order contrast threshold, we can be sure that these deficits for 1<sup>st</sup> and 2<sup>nd</sup> order stimuli are independent.

Visual disturbances are prevalent after TBI, and many patients complain of blurred vision, increased sensitivity to visual motion (e.g. watching TV, scrolling on computers and tablets etc.) and/or sensitivity to flicker (e.g. photosensitivity to fluorescent lighting) (Ciuffreda, 2008; Kapoor & Ciuffreda, 2002). Altogether, these observations suggest an altered temporal processing of visual information, this is in agreement with previous psychophysical studies as well as our results. For example, TBI patients have been shown to have elevated thresholds for global motion, as assessed by the random dot kinematogram (Patel, Ciuffreda, Tannen, & Kapoor, 2011), and the increase may be related to visual motion sensitivity and vertigo—increased sensitivity to local motion would amplify the iso-directional dots in a global motion task, thereby decreasing sensitivity. Similarly, it has been shown that TBI patients—at least within the first 30 days post injury—have impaired adaptation to optic flow (Slobounov, Tutwiler, Sebastianelli, & Slobounov, 2006), suggesting heightened sensitivity to this motion signal. The sensitivity to optic flow motion can be so severe within the three days post injury so as to prevent the patients from performing the task as it produced sickness, disorientation and nausea (Slobounov et al., 2006). Interestingly, another index of temporal visual processing, the critical flicker frequency (i.e. the highest temporal frequency allowing a distinction of flickering vs. steady stimulus), does not seem to differ in TBI population (Chang, Ciuffreda, & Kapoor, 2007; Schrupp, Ciuffreda, & Kapoor, 2009). However, the critical flicker frequencies may be related to severity of light sensitivity symptoms in mild TBI patients compared to TBI patients without light sensitivity symptoms or controls (Chang et al., 2007).

Increase of intracortical excitation and/or decrease of GABAergic inhibition—a well-known sequel of TBI (Cantu et al., 2014; Guerriero, Giza, & Rotenberg, 2015; Spiegel, Laguë-Beauvais, Sharma, & Farivar, 2015)—may be the cause of this increased motion sensitivity. Support for this proposition can be found in studies investigating neural excitation in the motion visual area MT+/V5 in normal participants. Anodal transcranial direct current stimulation (tDCS)—a noninvasive brain stimulation technique that can increase excitation (Antal, Kincses, Nitsche, & Paulus, 2003) and reduce GABAergic inhibition (Spiegel, Hansen, Byblow, & Thompson, 2012; Stagg et al., 2009)—improved motion direction discrimination task performance for fully coherent motion but lowered performance with decreased coherence (Antal et al., 2004). These findings suggest that changes in the global excitation/inhibition balance affect signal extraction from noise, likely by amplifying the noise.

Migraineurs, who are also known to have increased cortical excitability (Aurora & Wilkinson, 2007), also exhibit superior performance for fully coherent motion condition (Antal et al., 2005) but perform worse than the control group in the non-coherent motion condition (Antal et al., 2005; McKendrick & Badcock, 2004). These findings are notable for two reasons. Firstly, migraines are also a very common consequence of TBI (Mayer, Huber, & Peskind, 2013) suggesting that motion sensitivity alteration in both conditions may be driven by similar neuronal mechanisms. Secondly, the findings explain the seemingly contradictory findings between our results (in particular increased sensitivity for the 1<sup>st</sup> order motion condition) and the previous study on motion sensitivity in TBI participants (Patel et al., 2011). Whereas Patel and colleagues used the random dot kinematogram, i.e. incoherent environment, our 1<sup>st</sup> order stimuli represent fully coherent motion.

We observed a lower gain for orientation- and contrast-defined 2<sup>nd</sup> order stimuli in the TBI group. This corroborates and extends

previous studies. For example, Brosseau-Lachaine et al. (2008) showed reduced sensitivity to 2<sup>nd</sup> order contrast-defined stimuli of low spatial frequency (0.5 cpd). Lachapelle et al. (2004) reported a significant time delay of the later VEP peak that is believed to reflect higher-order visual processing (Lachapelle et al., 2004, 2008) and the patients showing more pronounced higher-order visual deficits measured by evoked potentials had lower expectations of returning to their normal occupational activities.

It is unlikely that refractive and/or undiagnosed ocular pathologies would explain our observations. While we did not specifically carry out a full optometric evaluation, patients wore their up to date refractive corrections. Furthermore, the carrier contrast was set at ten times its contrast threshold to be fully visible. Therefore, any ocular disorders that might have resulted in an elevation of contrast thresholds would have had negligible impact on the 2<sup>nd</sup> order sensitivity measurements.

The observed CSFs' shift towards higher spatial frequencies indicated by increased peak and cutoff spatial frequency in both 1<sup>st</sup> order and 2<sup>nd</sup> order contrast-defined stimuli in TBI participants is intriguing. This may suggest that in our sample of mild TBI patients, low spatial frequencies may be more affected. This observation is in agreement with some previous findings showing that a proportion of patients with cerebral lesions or injury exhibit mid- to lower-spatial frequencies impairment (Bodis-Wollner & Diamond, 1976; Hess, Zihl, Pointer, & Schmid, 1990).

Our data show a significant increase of bandwidth in the 1<sup>st</sup> order motion and 2<sup>nd</sup> order contrast conditions. The CSF bandwidth is recognized as a range of spatial frequencies detectable at a given contrast and it has been shown to be a reliable index of spatial vision. Therefore, this finding is not surprising for the 1<sup>st</sup> order motion condition where TBI participants also showed an increased sensitivity. However, this result is unexpected for the 2<sup>nd</sup> order contrast condition in light of the decreased maximum gain for this condition. This finding indicates that despite the decreased sensitivity, the range of detectable envelope spatial frequencies is broader to contrast-modulated 2<sup>nd</sup> order stimuli.

While we did not specifically test patients for visual symptoms, some patients did report visual disturbances. Interestingly, these reports were uncorrelated with any of our measures, suggesting that contrast sensitivity changes are a separate potential concern, independent of the common vision complaints after concussion. The discrepancy is not necessarily surprising—our qCSF measures probe very low-level pattern perception functions, while the common visual complaints of patients are typically related to “high-level” tasks such as reading or computer use. Thus it is possible that in some patients, there is either different or extended brain injury that combines with the low-level losses, and it is these additional losses related to high-level deficits that trigger the visual complaints.

Using a statistically-optimized method such as the qCSF imposes a risk of generating misleading estimates due to incorrect selection of the prior for each parameter—this may be particularly concerning in a neurologically abnormal population. We do not think this is a critical factor in our study. Firstly, the qCSF method was thoroughly validated in normal population for both 1<sup>st</sup> and 2<sup>nd</sup> order stimuli (Lesmes et al., 2010; Reynaud et al., 2014) and secondly, using the qCSF with the same priors has been successfully used with a clinical population with amblyopia (Gao et al., 2014). Another possible limitation is that the qCSF estimate may not be sensitive to possible losses of contrast sensitivity in particular bands of the spatial frequency, deficits that are well-described in brain-lesioned population (Bodis-Wollner & Diamond, 1976; Hess et al., 1990).

In summary, this study brings a unique dataset that provides a comprehensive summary of TBI-related effects on fundamental aspects of low-level visual processing in TBI patients. Our approach

utilizing the qCSF allowed us to evaluate—for the first time—the whole CSF curves for five different types of 1<sup>st</sup> and 2<sup>nd</sup> order visual stimuli. Comparing the data to a large normative dataset provided psychophysical evidence of increased sensitivity to 1<sup>st</sup> order motion stimuli, and decreased sensitivity to orientation- and contrast-defined stimuli following TBI. These findings are in general agreement with the clinical reports (Kapoor & Ciuffreda, 2002), however do not correlate with the complaints within our sample. The underlying neural causes for the alterations reported here require an integrated approach combining precise psychophysical characterization of the full CSF, in conjunction with neurophysiological measurements as well as temporary neuromodulation.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.visres.2016.03.004>.

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