

Case Report: Second-order Contrast Sensitivity in Tourette Syndrome



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ABSTRACT

Gilles de la Tourette Syndrome (GTS) is a neuropsychiatric developmental disease, characterized by motor and vocal tics with no changes in the ocular structures in the ophthalmological evaluations. The visual field evaluations suggest a reduction in central visual field sensitivity. The studies on visual function in this population is scarce. In this case report we present a patient with GTS who has significant alterations in the measure of contrast sensitivity for second order vision without any vision complaints. This reduction occurred in the measure of contrast sensitivity with a white noise carrier for practically all tested space frequencies. The mean contrast sensitivity for first and second-order stimuli with a pink-noise carrier was normal. The second order contrast sensitivity with a white noise carrier is dependent on local and lateral inhibition since it includes many local luminance components. The existence of this sensitivity suggests that specific visual processing mechanisms are affected.

Keywords: Tourette Syndrome, Contrast Sensitivity, Contrast Psychophysical Channels, Second-Order Perception

INTRODUCTION

Gilles de la Tourette Syndrome (GTS) is a neuropsychiatric developmental disease, the clinical characteristic of which is multiple motor or vocal behaviors without self-control, such as repetitive but non-rhythmic patterned stereotyped movements in a single part or multiple parts of the body, motor and vocalizations called tics, occurring for at least 1 year, with the age of onset before 18 years of age (Dale 2017). The clinical spectrum, in which the severity, frequency, fluctuation, and localization of vocal tics and motor tics are highly individual, is extremely complex. Gilles de la Tourette Syndrome is more prevalent in men than in women, with a ratio of 3:1 (Cavanna et al. 2020). In addition to compulsions and motor tics, there is often the presence of coproponema (inappropriate verbal gestures and expressions) and ecophonema (imitation of gestures and phrases) and other socially inappropriate non-obscene behaviors (Cox et al. 2018).

In the cortical area, we have the striatum, it is a ganglia base (controlling the motion) that is the junction of caudate nucleus and putamen (both a part of dorsal striatum)

localized between anterior perforated substance and anterior commissure and it is responsible for functional controls, such as leading impaired sensory integration and motor planning, execution and reward system (Beste et al. 2016, Dale 2017). Sensory changes are poorly reported in GTS and these studies were centered on the somatosensory aspect. GTS patients often report premonitory hypersensitivity in other sensorial domains as visual or olfactory, which occurs before motor movement (Beste et al. 2016).

Clinical ophthalmological evaluations do not find changes in the ocular structures or the visual acuity recognition measures (Tatlipinar et al. 2001, Kovacich 2008) as well as the light detection measure in the visual field (Whitefield et al. 1995, Enoch et al. 1989), being classified as normal from the medical-ophthalmological perspective. However, functional visual perceptual measurements, besides visual acuity, have found different results.

A study showed that chromatic discrimination measures in a hue ordering task show that adults and children with GTS have reduced specific discrimination for the blue-yellow axis, but normal discrimination for the green-red axis (Melun et

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al. 2001). These authors suggested a relationship between the changes found in color vision and changes in the retinal dopamine pathway. Other visual functions, such as face perception, are also altered in patients with TS (Rae et al. 2018). In that study, the authors found no differences in the perception of emotion in neutral and angry faces, in addition to correlating with the adequate activity of the amygdala in a measure of Functional Magnetic Resonance. However, the authors report a high positive correlation between the severity of GTS with the measure of functional connectivity of the insular cortex with the visual areas V1, V2, V4, and V5/MT. A few studies showed that functional changes in the visual system can occur both for simple sensory functions (V1 and V2), and for complex functions (V4 and V5/MT). The visual changes can help us understand the pathophysiological mechanisms of the disease. Therefore, we present in this study a case report of a young patient with GTS, in which we evaluated the spatial contrast sensitivity of first and second-order luminance contrast. The choice of these measures is due to the fact that pathophysiological mechanisms are well defined and the sensitivity to first-order contrast is related to the processing of the Magnocellular and Parvocellular groups of the visual pathway, primarily V1 (Campbell et al. 1968, Baker et al. 2001). Recent studies in cannabis users suggest the reduction in first-order contrast sensitivity measured was due to an impairment in glutamatergic neurotransmission, including glutamate and GABA neurons (Lalanne et al. 2017). Second-order contrast sensitivity measurements, whether modulated by white noise or pink noise carriers, are processed in distinct visual areas, V2 and V4, respectively (Schofield et al. 2003, Callaway 2004, Yang et al. 2019). Besides, these measures have been established as efficient biomarkers to identify specific changes in various neurological and psychiatric diseases such as Alzheimer's disease (Crow et al. 2003), Duchenne Muscular Dystrophy (Costa et al. 2005, Costa et al. 2011), occupational mercury vapor intoxication (Costa et al. 2008), and Autism Spectrum Disorder (Svetozarskiy 2019).

To put in a real world example: When you are searching for a mosquito in a clean room with a white wall, finding the mosquito is going to be quite simple, however, assume that you are in the Amazon forest and you have to find the same mosquito, which is going to be harder than in the clean room.

White noise is a binary noise, which means it is created using a binary function, such as (0,1,0), to generate a stimulus that resembles the appearance of a TV without a signal. In this type of noise, the visual system is more sensitive to low frequencies (0.5-1cpG). To create pink noise, the stimulus is subjected to a Fourier transformation, resulting in a 1/f distribution. This gives the noise a textured appearance. This noise is more sensitive to high frequencies (4-8cpG) (Schofield et al. 2003).

CASE

Patient History

20 year-old female patient CMSM is a psychology student diagnosed with Gilles de La Tourette's Syndrome in childhood, does not use any medicaments (due to her refusal), presents with normal visual acuity, visual field, and an absence of ophthalmic complaints. In the Yale Global Tic Severity Scale (YGTSS), current motor and vocal tics are rated on 5 dimensions: number, frequency, intensity, complexity, and interference, with scores ranging from 0 to 5 each. Those results are summed to yield separate motor and vocal tic severity scores (ranging 0-25) and a combined total tic severity score (ranging 0-50). An associated impairment scale (ranging 0-50) assesses tic-related disability during the last week.

The patient's YGTSS result was 13 for motor tic severity and 7 for vocal tic severity, with a combined total tic severity score of 20. The auto-reported impairment was rated as a minimum. Reported simple motor tics occurred in the previous week were blinking, eye movements, facial grimace, mouth movements, head, hand, shoulder, arm and leg movements, and abdominal tensing. Reported complex motor tics were only writing tics, body bending and gyrating. Current simple phonic symptoms were production of sounds and noises. No complex symptoms were related to occur recently.

The study belongs to the Research Project for the Development of Psychophysical Measures, approved by the Human Research Ethics Committee of the Psychology Institute (CAAE: 66767317.5.0000.5561). The informed consent was obtained from the participant. The study was conducted in line with the Declaration of Helsinki 1964 and its following updates. The study was also conducted based on the case report guidelines – CARE protocol (Gagnier et al. 2013, Riley et al. 2017).

METHODS

We measured the luminance spatial contrast sensitivity for three different stimulation conditions, 1st-order and 2nd-order, with contrast modulation by white noise and pink noise carriers. The 1st-order measure is seeking the measurement of pure stimuli, enabling the identification of psychophysical spatial functions related to the physiological pathways Parvocellular (8.0cpG) and Magnocellular (0.5 and 1.0cpG) (Niemeyer et al. 2017).

The 2nd-order measures are divided into two conditions: spatial frequencies carried by white noise (interference by high-frequency components) and spatial frequencies carried by pink noise (interference amplitude inversely proportional to the spatial frequency). A critical difference between those

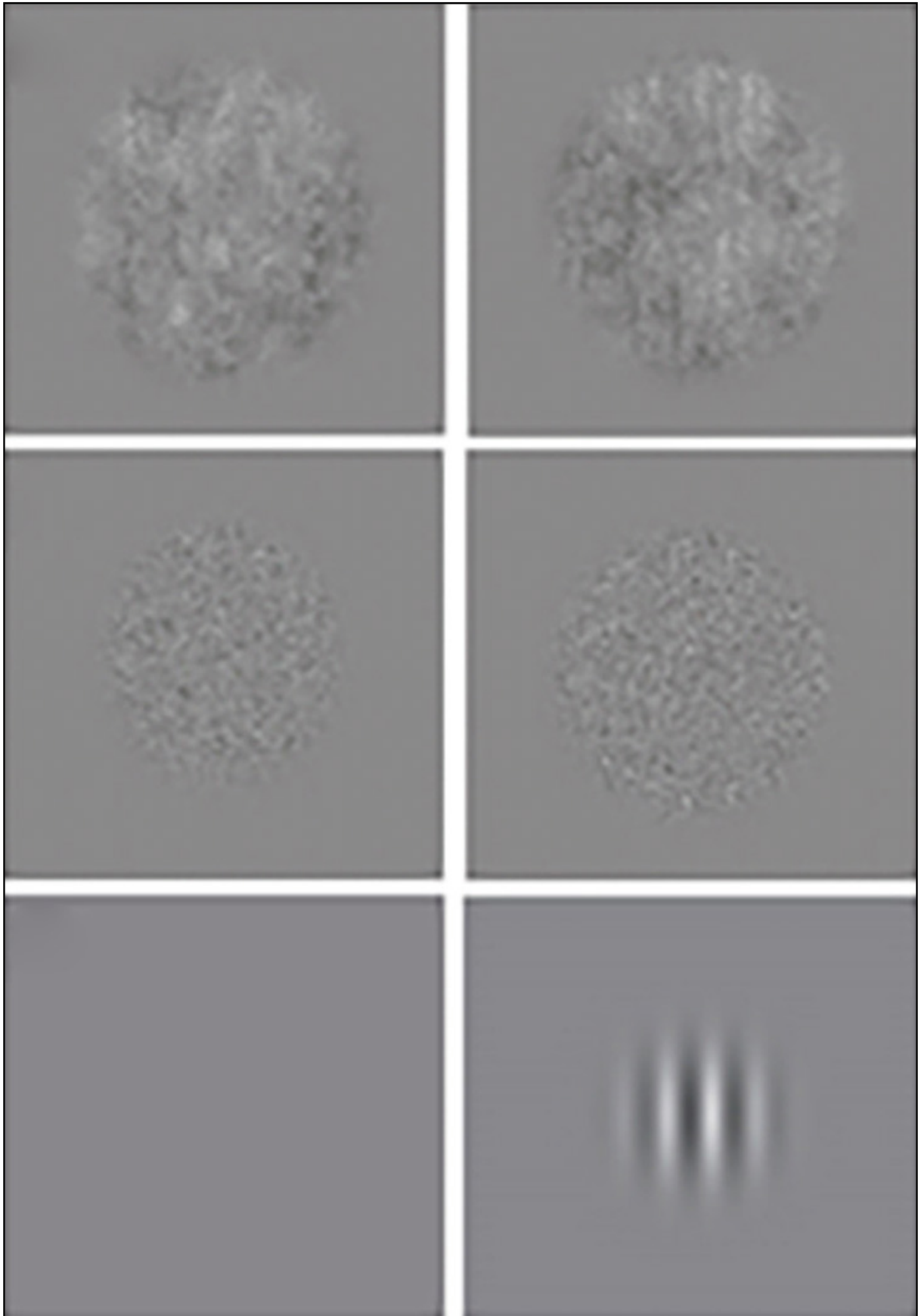


Figure 1. Sample of the stimuli presented in the experiment. In A, low spatial frequency and medium spatial frequency carried by a pink noise, respectively from left to right. In B, low spatial frequency and medium spatial frequency carried by white noise and in C the first-order contrast sensitivity luminance grating and the uniform gray background.

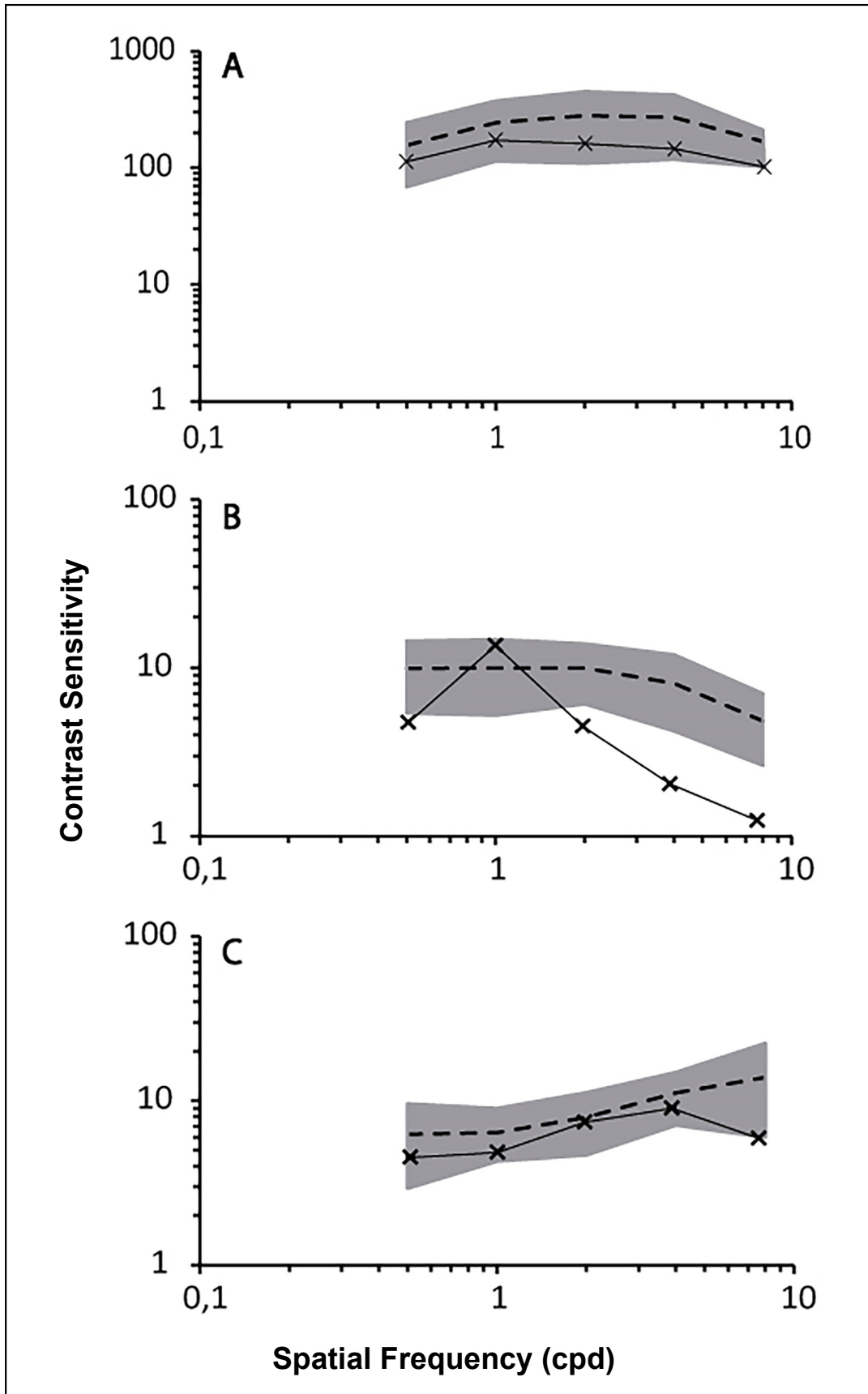


Figure 2. Contrast sensitivity function results. The gray area is the normality range, and the dashed black line is the mean contrast sensitivity for each spatial frequency. The black line with “x” marks are the result of the TS patient. In, A we have the results for the 1st-order contrast sensitivity; in B, the result for the contrast sensitivity using white noise carrier and in C, the result for the contrast sensitivity using white noise carrier. In the white noise carrier condition, almost all spatial frequencies are below the normal limits.

stimuli conditions is that 2nd-order stimuli have carriers that were set to a contrast factor above the threshold, ensuring that any 2nd-order loss in sensitivity is not simply a consequence of a less detectable carrier, which was because of a first-order loss (Spiegel et al. 2016). Different visual areas process these stimuli, with white noise modulation primarily in areas V1 and V2, while pink noise modulation is primarily in V4. We can see the difference among these three stimuli in Figure 2. All those stimuli compromised a visual angle of 6° from the test distance of 60 cm.

The spatial frequencies tested in all three stimulation conditions included low frequencies 0.5 cpd and 1.0 cpd, medium frequencies 2.0 cpd, 4.0 cpd, and high frequency 8.0 cpd (cycles by the degree of visual angle). We measured contrast sensitivity thresholds using a simple staircase psychophysical procedure, 1up:1down, with an asymmetric change in contrast, in which there was a decrease of 12.5% of contrast after a correct response and a 25% increase of contrast following a wrong response. Correct responses correspond to 74.7% of the final contrast. The tests were validated, and the normal limits were defined for the young adult population (in press), shown in the gray areas in Figure 1. The measurements of 1st-order contrast sensitivity were followed by the 2nd-order and performed on the same day, in a binocular viewing condition and a darkened room, with a resting interval of 10 minutes between measurements, amounting to a total testing time of 60 minutes.

RESULTS

The 1st-order measurement and the 2nd-order contrast sensitivity measured with the pink noise carrier were within normal limits (Figure 2A and 2C). However, for 2nd-order contrast sensitivity with white noise carrier, there was a drastic reduction in contrast sensitivity for low (0.5 and 1.0 cpd), medium (2.0 cpd), and high (8.0 cpd) spatial frequencies. Only at 4 cpd, the contrast sensitivity estimated using white noise carrier reached the normal range of the controls. These results are shown as a solid line in Figure 2.

DISCUSSION

Our case report evidenced a specific reduction in second-order contrast sensitivity carried by white noise, despite a normal first-order and second-order contrast sensitivity carried by pink noise in this TS patient. Despite being an individual measure, this is the first work that reports results of contrast sensitivity measures in this population but signals the need to further expand the functional understanding of visual information. The results found in this work point us to specific roles of the organization of visual information and

this can provide insight about the physiological processes underlying the spatial visual function.

Considering the sensory aspects of vision, the patients with Gilles de la Tourette Syndrome have been considered ophthalmologically normal, including visual acuity (Tatlipinar et al. 2001, Kovacich 2008), although, the few functional studies previously carried out identified changes in visual perimetry. According to one of those studies (Enoch et al. 1989), which used manual visual perimetry measurements, the central areas of the visual fields showed evidence of reduced sensitivity for detecting light compared with the periphery of the visual field (over 30° of the visual field). Another study, using automated measurements and performed on the central 24° of the visual field, did not identify a statistical difference between the 12 GTS patients and the 12 age-matched controls tested. However, the authors pointed to a tendency for lower sensitivity in GTS patients (Whitefield et al. 1995).

Color vision was assessed in 11 GTS patients using the Farnsworth-Munsell 100 hue, which is an ordering task of color caps, designed to evaluate the color perception performance (Melun et al. 2001). Scored data were arranged in two color-opponent red-green and blue-yellow axes and compared to healthy controls, they showed significantly higher scores (less performance in ordering color) in the blue-yellow axis. The authors concluded that those findings were due to the retinal dopaminergic mechanisms mediating color vision based on some results found in Parkinson's disease patients. However, it is difficult to consider the simplicity of this conclusion, since dopamine has an important role in the organization of the retinal circuit at the ganglion cell level, but the initial mechanisms of the ON-OFF organization occur at the level of the bipolar cells that are dominated by glycinergic and glutamatergic systems (Beaudoin et al. 2008, Brandies et al. 2008, Archibald et al. 2009).

In our study, we found contrast sensitivity to be between normal ranges for the 1st-order measurement and the 2nd-order contrast modulated and embedded in a pink noise carrier. However, a clear reduction in the wide range of spatial frequencies was measured in the 2nd-order measurement embedded in a white noise carrier. These different results could suggest different levels of spatial contrast processing impairment. The linear filters of the cell circuitry mediate the first-order contrast sensitivity in the primary visual cortex (Campbell et al. 1968). The second-order mechanisms have been recently investigated but they are more complex than the first-orders'. Modeling studies suggest linear filters are differentially combined in second-order contrast modulated stimulation. Also, recent studies have shown that white noise and pink noise carried contrast sensitivity, even if presented different mechanisms could process modulated profile. The evidence for local contrast in white-modulated carrier suggests

that both first and second-order mechanisms are stimulated, instead of only second-order mechanisms are stimulated by pink noise carriers (Schofield et al. 2003, Ellemberg et al. 2004). More recent studies have shown that stimuli using white noise carriers are particularly effective in detecting local luminance changes within images, while stimuli employing pink noise carriers are more closely associated with texture or material surface luminance changes. (Schofield et al. 2010).

Considering those outcomes, white-noise carrier contrast modulated stimuli should be processed by the neural network of V1 and V2 cortical areas whereas the pink-noise carrier contrast modulated stimuli should ideally be processed by neural networks of V4 area (Wong et al. 2001).

If we consider the presented framework for differences between white noise and pink noise carriers, our results showing reduction for that contrast sensitivity carried by white noise in 0.5, 1.0 and 2.0 cpd suggest that the non-linear mechanisms processing the visual input from V1 to V2 should be impaired considering the normal values for the first-order contrast sensitivity (processed by the linear cells in V1) and the contrast sensitivity carried by pink noise stimuli most likely processed in V4 cortical area. The specificity in the contrast sensitivity impairment we found in that patient with GTS, if replicable in a more substantial population, would support new insights regarding the visual processing network across the different cortical areas and also the role of specific neurotransmitters in different visual cortical circuitry.

CONCLUDING REMARKS

The contrast sensitivity impairment for white noise carried stimuli found in a young patient with Gilles de la Tourette syndrome supports the idea of inhibitory circuitry in the earliest stages of the cortical processing of visual information, more luminance mediated and dopaminergic and GABAergic dominated are impaired. The fact that first-order contrast sensitivity and the pink noise carried stimulus for second-order contrast processing was within normal ranges is an intriguing finding to be more profoundly addressed in future studies.

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