Neuropsychologia 51 (2013) 1287–1295

Contents lists available at SciVerse ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Neural correlates of visual integration in Williams syndrome: Gamma oscillation patterns in a model of impaired coherence

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ARTICLE INFO

Article history:
Received 5 November 2012
Received in revised form
4 March 2013
Accepted 27 March 2013
Available online 12 April 2013

Keywords:
Williams syndrome
Low-gamma oscillations
3D integration
Visual coherence
EEG/ERP

ABSTRACT

Williams syndrome (WS) is a clinical model of dorsal stream vulnerability and impaired visual integration. However, little is still known about the neurophysiological correlates of perceptual integration in this condition. We have used a 3D structure-from-motion (SFM) integrative task to characterize the neuronal underpinnings of 3D perception in WS and to probe whether gamma oscillatory patterns reflect changed holistic perception. Coherent faces were parametrically modulated in 3D depth (three different depth levels) to vary levels of stimulus ambiguity. We have found that the electrophysiological (EEG/ERP) correlates of such holistic percepts were distinct across groups. Independent component analysis demonstrated the presence of a novel component with a late positivity around 200 ms that was absent in controls. Source localization analysis of ERP signals showed a posterior occipital shift in WS and reduced parietal dorsal stream sources. Interestingly, low gamma-band oscillations (20–40 Hz) induced by this 3D perceptual integration task were significantly stronger and sustained during the stimulus presentation in WS whereas high gamma-band oscillations (60–90 Hz) were reduced in this clinical model of impaired visual coherence, as compared to controls.

These observations suggest that dorsal stream processing of 3D SFM stimuli has distinct neural correlates in WS and different cognitive strategies are employed by these patients to reach visual coherence. Importantly, we found evidence for the presence of different sub-bands (20–40 Hz/60–90 Hz) within the gamma range which can be dissociated concerning the respective role on the coherent percept formation, both in typical and atypical development.

1. Introduction

Williams syndrome (WS) is a clinical model of dorsal stream vulnerability and impaired visual integration. This rare genetic neurodevelopmental disorder, with a prevalence of 1 in 7500 to 20,000 live births (Stromme, Bjornstad, & Ramstad, 2002) results from a hemideletion on chromosome 7q11.23 (Bayes, Magano, Rivera, Flores, & Perez Jurado, 2003; Korenberg et al., 2000). It involves a distinct cognitive profile of relative weaknesses and strengths and is an important model of impaired visual integration and coherence (Bellugi, Lichtenberger, Jones, Lai, & George, 2000; Wang, Doherty, Rourke, & Bellugi, 1995). Accordingly, these patients exhibit a tendency to focus on parts or details of an image and consequently fail in integrating local and global levels of analysis such as in hierarchical figures (Bernardino et al., 2012). Moreover, the presence of visuospatial impairments along with motion coherence deficits has been described as the hallmark in this condition (Atkinson et al., 2006; Bellugi et al., 2000). A neural correlate for such developmental deficits has been corroborated by structural and functional imaging data showing dorsal visual pathway vulnerability (Eckert et al., 2006; Eckert et al., 2005; Jackowski et al., 2009; Meyer-Lindenberg et al., 2004; Meyer-Lindenberg, Mervis, & Berman, 2006; Mobbs et al., 2007; Reiss et al., 2004; Reiss et al., 2000). This pathway, projecting from occipital to parietal regions, plays an important role for spatial processing and has been described as subserving motion processing and 3D depth perception (Milner & Goodale, 2008). Taken together, these evidences suggest WS as a representative model of impaired visual integration and coherence associated with dorsal visual stream dysfunction.

The magnitude of visual coherence deficits has been well documented in WS by behavioural studies focusing on 2D and 3D motion coherence, requiring the integration of local signals into object percepts (Atkinson et al., 2003, 2006; Castelo-Branco

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http://dx.doi.org/10.1016/j.neuropsychologia.2013.03.020

et al., 2007; Mendes et al., 2005). Our previous behavioural study (Mendes et al., 2005) demonstrated impairments in 3D structure-from-motion (SFM) perception in WS, into a higher extent than those found in 2D motion tasks.

The perception of 3D SFM objects requires local-global integration given that the 3D shape can only be extracted from dot moving patterns by integrating motion cues over time. The object is physically nonexistent when the dots are not moving. It is, therefore, important to integrate all local perceptual features and motion cues to achieve coherent holistic perception (a form of perceptual binding because the perception of an object based on dot motion requires correlation). Functional magnetic resonance imaging (fMRI) studies have shown that dorsal parietal regions are involved in the perception of 3D SFM objects (Kriegeskorte et al., 2003; Murray, Olshausen, & Woods, 2003). Our previous EEG and fMRI results do corroborate the notion that integration across dorsal and ventral pathways is required for SFM perception (Graewe, De Weerd, Farivar, & Castelo-Branco, 2012a; Graewe et al., 2012b). 3D SFM paradigms are, therefore, of particular interest in the study of dorsal stream vulnerability based on coherent holistic perception.

This paradigm is, for that reason, suitable for the study of neurophysiological correlates of 3D visual integration in WS. There are, to our knowledge, no prior EEG/ERP studies addressing this issue, in particular in which concerns general models for holistic perception. A previous ERP study on perception of flat static photographic faces in WS did not require coherence and showed behavioural differences in a one to back face matching task (Mills et al., 2000). These results are interesting because face processing involves mainly the ventral visual stream which has been described as relatively preserved in WS. By adding 3D coherence to the paradigm we are able to address how dorsal–ventral integration helps solving 3D visual coherence.

Visual coherence and a number of cognitive processes have been related to gamma-band activity which has been interpreted as reflecting feature binding by integrating the different visual features to produce a coherent object representation (Singer & Gray, 1995). Indeed, the neural mechanisms underlying this process have not been clearly defined and different sub-bands within the gamma-band range may have distinct functional significance (Castelo-Branco, Neuenschwander, & Singer, 1998).

Our paradigm may represent a useful model to elucidate whether patterns of gamma-band oscillations (20–90 Hz) represent a neural correlate of perceptual coherence and binding, in particular, in which concerns percept formation and/or object representation (Singer, 2001; Singer & Gray, 1995). This may also provide a mechanism for clinically impaired visual coherence in neuropsychiatric disorders given the available evidence for perception related gamma-band abnormalities in pathologies of impaired coherent perception such as Autism, ADHD, Alzheimer's disease and Schizophrenia (Brown, Gruber, Boucher, Rippon, & Brock, 2005; Grice et al., 2001; Koenig et al., 2005; Lee, Williams, Breakspear, & Gordon, 2003; Uhlhaas et al., 2006; Yordanova, Banaschewski, Kolev, Woerner, & Rothenberger, 2001). Gamma-band activity is often assumed to be associated with successful performance on perceptual coherence tasks and to be reduced in neurodevelopmental disorders but this view is not consensual and, in fact, previous studies reported both increases and decreases of gamma-band oscillations in neuropsychiatric conditions (Herrmann & Demiralp, 2005; Uhlhaas & Singer, 2006). This controversy may be explained by the fact that different sub-bands within the gamma-band range are frequently reported without a detailed analysis of their respective role on the visual percept formation. Moreover, different task demands may lead to different findings which are not comparable across studies.

Here, we aimed at characterizing the neural underpinnings of 3D perception integration in a representative model of impaired visual integration and coherence associated with dorsal stream dysfunction. For this purpose, we used a 3D SFM integrative task in which the depth level was parametrically modulated. Our investigation of electrophysiological neural correlates of coherent perception in this clinical model of dorsal stream dysfunction addressed the potentially distinct functional role of different sub-bands of gamma oscillations in the construction of coherent percepts.

2. Methods

2.1. Participants

A group of 9 patients with WS aged between 15 to 37 years (mean $\pm$ SE $=21.44 \pm 2.30$) participated in this study. The WS participants were recruited from a database used in previous studies (Castelo-Branco et al., 2007; Mendes et al., 2005). All patients were diagnosed based on clinical and genetic criteria. The genetic examinations included the Fluorescence in situ hybridization (FISH) analysis, which demonstrated the hemizygous 7q11.23 deletion in all patients. Additional comprehensive genetic analysis was carried out and showed that all WS participants had similar deletion size (~1.55 Mb) and were hemizygous for GTF2IRD1 and GTF2I (Castelo-Branco et al., 2007). The parental origin of the hemideletion and the precise location of the breakpoints, have been previously characterized (Castelo-Branco et al., 2007) and are shown in Table 1 and Supplementary Fig. 1. The parents of the WS participants completed the Social Communication Questionnaire to exclude co-morbidity with Autism Spectrum Disorders (ASD) (Rutter, Bailey, & Lord, 2003). The scores were below 15, which is the positive cut-off for ASD. None of the WS participants was diagnosed with ADHD or was taking medication to control for attention and behavioural problems. All WS patients underwent a complete ophthalmologic examination performed by an experienced ophthalmologist (E.S.), including best-corrected visual acuity (Snellen optotypes), complete oculomotor examination, stereopsis evaluation using the Randot test, slit lamp examination of anterior chamber structures and fundus examination. No abnormalities that could affect vision were identified.

The control group included 8 control participants aged between 15 to 34 years (mean $\pm$ SE $=21.89 \pm 2.40$) who were matched for chronological age (Mann–Whitney U test, $p > 0.05$), gender and handedness with the WS group. In each group there were two participants who demonstrated left-hand dominance. Healthy control participants had no history of psychiatric and neurologic pathologies and were not taking medication for depression. They had normal or corrected-to-normal vision and were naïve regarding the testing procedures.

The participants included in the study received the Portuguese adapted version of the Wechsler Intelligence Scale for Children—3rd edition (WISC-III) (Wechsler, 2003) or the Wechsler Adult Intelligence Scale—3rd edition (WAIS-III) (Wechsler, 2008), according to the participant's age. One control participant was unavailable to complete the IQ assessment.

The demographic characteristics of the patient and control groups are summarized in Table 2.

Written informed consent was obtained from parents of participants or, when appropriate, the participants themselves. The study was conducted according to the declaration of Helsinki and was approved by the local Ethics Committee of the Faculty of Medicine of Coimbra.

Table 1
Detailed genetic characterization of WS patients. Deletion size, specific break point and parental origin are reported.

Subject	Deletion size (Mb)	Break point	Parental origin
WS_1	1.55	B-block, between NCF1 and GTF2IRD2	Mother
WS_2	1.55	B-block before NCF1 starts	Father
WS_3	1.55	B-block—inside GTF2I between GTF2I and NCF1	Father
WS_4	1.55	B-block—inside GTF21RD2*	Father
WS_5	1.55	B-block—inside GTF21RD2*	Mother
WS_6	1.55	B-block before NCF1 starts	Unknown
WS_7	1.55	B-block before NCF1 starts	Mother
WS_8	1.55	B-block, between NCF1 and GTF21RD2	Mother
WS_9	1.55	B-block—inside GTF2I or between GTF2I and NCF1	Mother