Brain and Cognition 121 (2018) 24–37

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Attentional rather than sensory differences characterize auditory processing in Williams syndrome

Magdalene Jacobs[a], Elisabeth M. Dykens[b,c], Alexandra P. Key[a,c,*]

[a] Department of Hearing and Speech Sciences, Vanderbilt University Medical Center, United States
[b] Department of Psychology and Human Development, Vanderbilt University, United States
[c] Vanderbilt Kennedy Center for Research on Human Development, United States

ABSTRACT

Individuals with Williams Syndrome (WS) exhibit an atypical auditory profile. Across two experiments, we used event-related potentials (ERPs) in a three-stimulus auditory oddball task to examine early sensory (P1, N1, P2) and later cognitive (P3a, P3b) stages of cortical auditory processing in adults with WS and age-matched typical peers. In Study 1, piano chords served as standard, target, and novel stimuli; whereas, in Study 2, a variety of non-piano sounds comprised the novel stimuli. Across both experiments, there were no group differences in the earliest stages of sensory encoding (P1, N1), along with evidence for atypically large P2 responses in participants with WS. Persons with WS exhibited larger than typical P3a responses when the novel stimuli were perceptually distinct from the standard and the target stimuli (Study 2), but not when task-relevant and -irrelevant stimuli were perceptually similar (Study 1). Further, the WS group demonstrated reduced goal-directed attention (attenuated P3b response). These group differences in ERPs were not directly related to IQ. Our results in the context of an active discrimination task point to a more complex profile of auditory processing in persons with WS than previously reported, with group differences emerging during the later stages of stimulus categorization and evaluation, but not within early stimulus detection and feature encoding.

1. Introduction

Williams syndrome (WS) is a neurodevelopmental disorder caused by a microdeletion of ~28 genes on chromosome 7q11.23 (Ewart et al., 1993) and has an estimated prevalence of 1:7500 (Strømme, Bjømstad, & Ramstad, 2002). It is associated with mild to moderate intellectual disability and a unique behavioral cognitive profile, such that individuals with WS typically exhibit visuospatial difficulties alongside relative strengths in expressive and receptive language ability (Bellugi, Wang, & Jernigan, 1994; Martens, Wilson, & Reutens, 2008; Mervis et al., 2000). Additionally, individuals with WS demonstrate a distinct auditory profile characterized by high levels of auditory attraction and aversion, including auditory fascinations (Don, Schellenberg, & Rourke 1999; Einfeld, Tonge, & Florio, 1997; Levitin, Cole, Lincoln, & Bellugi, 2005), phonophobia (Elsabbagh, Cohen, Cohen, Rosen, & Karmiloff-Smith, 2011; Gothelf, Farber, Raveh, Apter, & Attias, 2006; Klein, Armstrong, Greer, & Brown, 1990), and a strong engagement with music (Don et al., 1999; Dykens, Rosner, Ly, & Sagun, 2005; Hopyan, Dennis, Weksberg, & Cytrynbaum, 2001; Levitin & Bellugi, 1998; Levitin et al., 2004).

The auditory profile of WS has been described as "hypersensitive" to sound (Bellugi, Lichtenberger, Jones, Lai, & George, 2000; Neville, Mills, & Bellugi, 1994), arising from psychoacoustic, perceptual, and emotional factors (Blomberg, Rosander, & Andersson, 2006; Dykens et al., 2005; Levitin et al., 2005). Additionally, studies frequently cite high rates of hyperacusis in WS, defined as increased sensitivity to specific frequency and volume characteristics, resulting in decreased tolerance to environmental noises (Bellugi & Morris, 1995; Lenhoff, Wang, Greenberg, & Bellugi, 1997; Levitin et al., 2005). More recently, however, researchers posit that the auditory behaviors in this population are likely related to differential reactivity to sound, independent of any peripheral auditory pathology. Thus, the WS auditory profile could be characterized as "hypersensitive" or "hyperreactive" (Gallo, Klein-Tasman, Gaffrey, & Curran, 2008; Levitin et al., 2005). The sounds that persons with WS commonly find aversive are comprised of broadband frequencies and high intensities (Gothelf et al., 2006; Klein et al., 1990), such as fireworks, thunder, and electric machines. Conversely, individuals with WS also spend more time listening to music than typical peers (Don et al., 1999; Levitin & Bellugi, 1998), suggesting that sound complexity and overall intensity may not explain the full range of

* Corresponding author at: Vanderbilt Kennedy Center, 230 Appleton Place, Peabody Box 74, Vanderbilt University Medical Center, Nashville, TN 37203, United States.
E-mail address: sasha.key@vanderbilt.edu (A.P. Key).

https://doi.org/10.1016/j.bandc.2018.01.005
Received 3 March 2017; Received in revised form 21 December 2017; Accepted 4 January 2018

auditory behaviors in WS.

Structural neuroimaging studies in WS have reported an overall reduction in brain volume but relative sparing of the auditory cortex, superior temporal gyrus, amygdala, and orbitofrontal cortex (Campbell et al., 2009; Chiang et al., 2007; Martens, Reutens, & Wilson, 2010; Meyer-Lindenberg, Mervis, & Berman, 2006). Functional neuroimaging results revealed that individuals with WS activate an atypically diffuse network of cortical regions in response to musical stimuli: in addition to the auditory cortex, increased activation has been reported in the amygdala, cerebellum, brainstem, and occipital regions (Levitin et al., 2003; Thornton-Wells et al., 2010). These results suggest that increased reactivity to auditory stimuli on the behavioral level may be associated with the atypical interactions between the auditory cortex and other neural systems.

While these studies provided evidence of potentially altered brain responses to sound in WS, the low temporal resolution of fMRI is not sufficient to determine if auditory preferences in WS can be attributed to sensory hypersensitivity or to attention-related processes. In the current study, we aimed to examine the relative contribution of these information processing stages through the use of event-related potentials (ERPs). ERPs offer the needed temporal resolution and may capture subtle differences in sensory and/or cognitive processes that are not always observable in behavior (Molfese, Molfese, & Kelly, 2001).

Previous ERP studies of auditory processing in WS have focused primarily on the obligatory, stimulus-driven responses (measured by the P1, N1, and P2 components) that reflect the initial cortical processing of stimulus physical characteristics. In typical adults, these responses occur sequentially in time, at approximately 50 (P1), 100 (N1) and 200 (P2) ms after stimulus onset, with maximum amplitudes over fronto-central scalp regions (see Key, Dove, & Maguire, 2005 for review). The P1 reflects general level of arousal, as well as attention to auditory input and suppression of unattended information (Herrmann & Knight, 2001; Key et al., 2005). The N1 is associated with stimulus detection and preliminary discriminatory processing (Hink, Hillyard, & Benson, 1978; Näätänen, Gaillard, & Mäntysalo, 1978). The P2 indexes stimulus encoding and classification (Picton & Hillyard, 1974). While primarily associated with the sensory stages of information processing, these ERP responses are also subject to the top-down effects of attention, with larger amplitudes observed for the attended than ignored stimuli (Hillyard, Hink, Schwent, & Picton, 1973; Knight, Hillyard, Woods, & Neville, 1981; Ritter, Simson, & Vaughan, 1988).

The majority of published auditory ERP studies have used word-level stimuli to examine auditory responses in WS as a part of the broader focus on language processing. ERPs elicited by individual words in a sentence were characterized by atypically large P1 and P2 responses, as well as by reduced N1 amplitudes (Bellugi, Lichtenberger, Mills, Galaburda, & Korenberg, 1999; Mills et al., 2013; Pinheiro, Galdo-Álvarez, Rauber, Sampaio, Niznikiewicz, & Gonçalves, 2011). More recently, a similar pattern was reported in a study using passive exposure to non-linguistic tonal stimuli (Zarchi et al., 2015). These P1-N1-P2 results have been interpreted to indicate auditory hypersensitivity in WS (Bellugi et al., 1999; Zarchi et al., 2015). Investigation of the auditory N1-P2 complex in WS reported atypically large amplitudes to tonal stimuli presented at shorter interstimulus intervals (e.g., 200 ms), but no significant difference from typical subjects was observed when using longer (e.g., 1000 ms) intervals (Neville, Holcomb, & Mills, 1989). This timing-dependent effect suggests that individuals with WS may exhibit less refractory or "more excitable" responses to auditory stimuli than typical controls (Bellugi, Bihrle, Neville, Jernigan, & Doherty, 1992; Neville et al., 1989).

In addition to the reported differences in early, sensory/perceptual stages of auditory processing, the auditory profile in WS may also reflect atypical later stimulus evaluation processes. This possibility has not been extensively explored in the auditory ERP literature on this population, even though individuals with WS often display behavioral characteristics of ADHD (Leyfer, Woodruff-Borden, Klein-Tasman, Fricke, & Mervis, 2006) and experience difficulties disengaging attention from both social (e.g., faces; Karmiloff-Smith, Scerif, & Ansari, 2003; Riby & Hancock, 2009; Riby et al., 2011) and nonsocial stimuli (geometric shapes and tones; Lincoln, Lai, & Jones, 2002).

In ERP studies, attentional resource engagement during stimulus evaluation is indexed by the P3a and P3b responses elicited in an oddball paradigm (Polich, 2007), in which an infrequent "target" or "novel" stimulus is presented among more frequent "standard" trials. The P3a has a fronto-central scalp maximum and occurs starting approximately 250 ms after stimulus onset (Squires, Squires, & Hillyard, 1975). The P3a is elicited by infrequent task-irrelevant distractors and thought to reflect involuntary, transient allocation of attention to novel stimuli (i.e., orienting response; Picton, Champagne, & Kellett, 1992; Polich & Comerchero, 2003). The P3b has a centro-parietal distribution, is typically observed within 300–500 ms post-stimulus onset or later (Polich, 2007) when participants actively search for and detect the "target" stimulus. The P3b is interpreted as an index of voluntary attention and working memory processes needed to carry out ongoing stimulus evaluation and relevant target detection (Polich, 2007; Rugg & Coles, 1995).

To date, few ERP studies examined these higher-order attentional resource allocation processes in WS. In the visual domain, reduced P3b amplitudes and increased or delayed P3a responses have been reported in persons with WS compared to typical controls (Greer, Hamilton, McMullon, Riby, & Riby, 2017; Key & Dykens, 2011, 2016). Only a single ERP study has directly examined auditory attention in individuals with WS. Using a timbre discrimination task, Lense, Gordon, Key, and Dykens (2012) reported that persons with WS were able to detect the rare target stimulus (piano chord) among frequent distractors (cello and trumpet notes), as suggested by a larger parietal P3b response (P300 in the authors' notation) within the 300–500 ms time window. However, the response to the target stimulus was lower in amplitude in participants with WS versus typical controls, suggesting group differences in the difficulty of focusing attention on the target presented among diverse distractors. The authors did not report analyses of early sensory responses.

The current study investigated auditory processing in WS from early sensory encoding to later attentional modulation. In a series of two studies, we used a three-stimulus oddball task to examine different stages of auditory processing in adults with WS and typical peers. The inclusion of a rare, task-irrelevant novel sound in addition to the target stimulus allowed to evaluate both bottom-up attention orienting to novel stimuli as well as top-down goal-directed attention to target stimuli (Bidet-Caulet, Bottemanne, Fonteneau, Giard, & Bertrand, 2015; Joos, Gilles, Van de Heyning, De Ridder, & Vanneste, 2014; Polich, 2007). Early sensory responses are also reliably elicited during this procedure (cf. Donkers et al., 2015; Javitt, 2015).

If the auditory profile of individuals with WS is driven by the atypical hyperresponsiveness to the sensory features of the stimuli, group differences were expected in the amplitude of the obligatory fronto-central P1-N1-P2 responses. If auditory processing in WS is characterized by extended attentional evaluation of the stimuli, it would be reflected by larger than typical fronto-central P3a and centro-parietal P3b responses to novel and target stimuli, respectively.

2. Method

2.1. Study 1: Participants

Nineteen adults with WS (9 females; age $M = 24$ years, $SD = 5.7$, range: 17–34 years) were recruited from a residential summer music camp. Four subjects with WS were left-handed, and the rest were right-handed as indexed by the Edinburgh Handedness Inventory (Oldfield, 1971), $M = 0.56$, $SD = 0.67$. Handedness data were not available for one subject. The mean IQ for the group was 66.42, $SD = 16.03$ (KBIT-2; Kaufman & Kaufman, 2004).