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# Atypical hemispheric asymmetry in the perception of negative human vocalizations in individuals with Williams syndrome

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ABSTRACT

Williams syndrome is a neurological condition associated with high levels of auditory reactivity and emotional expression combined with impaired perception of prosody. Yet, little is currently known about the neural organization of affective auditory processing in individuals with this disorder. The current study examines auditory emotion processing in individuals with Williams syndrome. Hemispheric organization for positive and negative human non-linguistic sound processing was compared in participants with and without the disorder using a dichotic listening paradigm. While controls exhibited an expected right cerebral hemisphere advantage for processing negative sounds, those with Williams syndrome showed the opposite pattern. No differences between the groups emerged for the positive stimuli. The results suggest aberrant processing of negative auditory information in Williams syndrome.


## 1. Introduction

Williams syndrome (WS) is a multisystem neurogenetic disorder caused by a hemizygous deletion of 25–30 genes on chromosome 7q11.23 (Ewart et al., 1993; Korenberg et al., 2000). It is manifested by a wide range of clinical symptoms, which includes distinct facial features and a complex profile of cognitive and behavioral characteristics, most notably hyper-sociability (see Järvinen-Pasley et al., 2008; Meyer-Lindenberg, Mervis, & Berman, 2006). Individuals with WS tend to have IQs between 40 and 90 (Searcy et al., 2004), with better performance in verbal as compared with performance tasks (e.g., Howlin, Davies, & Udwin, 1998). Moreover, in general, individuals with WS show higher levels of performance in tasks pertaining to social as compared to non-social information processing (Bellugi, Lichtenberger, Jones, Lai, & St. George, 2000; Martens, Wilson, & Reuters, 2008). The deficits in visual–spatial functions have been linked to dorsal stream dysfunction (e.g., Atkinson, Braddick, Anker, Curran, & Wattam-Bell, 2003), whereas the relatively better processing of, e.g., language functions reflect relatively less affected ventral stream function (e.g., Gothelf et al., 2008).

A notable aspect of the WS phenotype is an unusual profile of auditory processing. Individuals with WS show a high affinity to music and musical activities (Dykens, Rosner, Ly, & Sagun, 2005; Levitin, Cole, Chiles, et al., 2005). WS is also usually accompanied by hyperacusis to moderate intensity sounds, reflecting highly selective and specific sound aversions and attractions (Gothelf, Farber, Raveh, Apter, & Attias, 2006; Levitin, Cole, Lincoln, & Bellugi, 2005). Moreover, Individuals with WS are often described as very expressive, with strong abilities to socially engage the listeners through increased use of prosodic effects (Reilly, Losh, Bellugi, & Wulfeck, 2004). For example, while individuals with WS have been found to perform similarly to matched TD controls on an experimental battery involving affective prosody imitation, their spontaneous speech is characterized by increased emotionality and higher as well as wider pitch range (Setter, Stojanovik, Van Ewjik, & Moreland, 2007). A growing body of research has specifically examined receptive prosodic processing skills in individuals with WS. For example, Plesa-Skwerer, Faja, Schofield, Verbalis, and Tager-Flusberg (2006) used The Diagnostic Analysis of Nonverbal Accuracy test (DANVA2; Nowicki & Duke, 1994) to evaluate recognition of happy, sad, angry, and fearful prosodic expressions.

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Individuals with WS exhibited poorer performance than chronological age (CA)-matched typically developing (TD) controls with all but the happy expressions. Thus, while individuals with WS exhibit greater than typical use of emotional speech effects, they have difficulties in processing such information in the speech of others.

Structural magnetic resonance imaging (MRI) evidence on the neurobiological underpinnings of auditory function in WS show that such individuals have smaller left planum temporale (part of the auditory association cortex) relative to controls (Eckert et al., 2006). Conversely, larger volumes of the ventral–orbital prefrontal region have been associated with greater use of social-affective language in individuals with WS (Gothelf et al., 2008). While cytoarchitectonic evidence has shown relative preservation in cell packing density and cell size in the primary auditory cortex in individuals with WS relative to TD controls, interesting between-group differences with implications for laterality have been reported (Holinger et al., 2005). In areas associated with language function, asymmetries in neuronal packing density were found in controls, whereas they were lacking in the brains of individuals with WS. Moreover, an excessively large layer of neurons in an area receiving projections from the amygdala suggested that the auditory cortex may be more limbically connected in WS than in controls. This may underlie the heightened emotional reactivity to certain sounds in individuals with WS.

The current study is aimed at addressing the question of why individuals with WS are "hypersocial" in terms of affect production (e.g., Järvinen-Pasley et al., 2008) but impaired at affect perception. We evaluated perceptual asymmetries for the processing of positive and negative affective vocalizations in individuals with WS relative to TD controls. Thus, in the current study, the dichotic listening (DL) technique was used as a preliminary step for elucidating the hemispheric asymmetries for the processing of affective vocalizations in individuals with WS.

The DL technique is a reliable method for examining hemispheric lateralization by presenting different information simultaneously to both ears. Based upon the differential temporal resolution of the left hemisphere (LH) and the right hemisphere (RH), verbal non-emotional material is typically preferentially processed through the right ear (RE, to the LH), whereas words with emotional content are preferentially processed through the left ear (LE, to the RH) reflecting each hemisphere's specialization (Bryden, 1988; Schirmer & Kotz, 2006; Voyer & Flight, 2001). The main principle underlying this procedure is that when the brain is presented with more information than can be processed the two hemispheres integrate the information received into a single percept (Hugdahl, 2000; Kimura, 1961). The DL method exploits the contralateral neural organization of the auditory pathways: that is the connection between the RE and the LH, and between the LE and the RH. The ipsilateral pathways can also transmit sensory information, albeit less efficiently. Resulting data is termed an ear asymmetry, or an index of which ear (and hence hemisphere) holds an advantage over the other in its readiness to analyze the incoming material. Thus, when an individual reports hearing the material presented to the LE, increased activation of the RH may be inferred, and likewise, attention to the message presented to the RE implicates LH activation.

The general issue to be examined in present study concerns whether individuals with WS have differential difficulty perceiving emotional information when linguistic (but not semantic) content is removed. Non-linguistic human vocalizations with either negative or positive emotional meaning, such as giggles and grunts, will be used as stimuli. A more specific hypothesis tests whether negative emotional information is particularly challenging for people with WS to perceive. This hypothesis is motivated by the Plesa-Skwerer et al.'s (2006) findings of adequate performance by individuals with WS on accurate recognition of happy prosodic information. In addition, two recent functional MRI (fMRI) studies indicate that WS individuals have reduced amygdala and orbitofrontal cortex (OFC) activation in response to negative face stimuli as compared to TD controls (Meyer-Lindenberg et al., 2005). Additionally, combined event-related potentials (ERPs) and fMRI evidence show that brain responses to negative facial expressions are attenuated in WS, while neural activity to positive facial expressions is enhanced (Haas et al., 2009). These data raise the possibility that the valence-specific neural activation patterns observed in the visual domain may also apply to the auditory domain.

The valence-specific hypotheses described below are consistent with the existing DL literature (e.g., Pollak, Holt, & Wismer Fries, 2004), and are based upon electroencephalographic (EEG) evidence indicating individual differences in affectivity within the TD population such that, prominent activity over the LH frontal regions is associated with positive emotional states, whereas prominent activity over the RH frontal areas is associated with negative affective states (Davidson, 2004). Further, evidence from typical adults shows that the direct communications between the anterior prefrontal cortex and the posterior regions associated with perception are mediated by the amygdala (Amaral, Price, Pitkänen, & Carmichael, 1992). These communications between the anterior and posterior affective areas are reciprocal, in that augmented activation in one area is associated with an attenuated activity of the other (e.g., Davidson & Hugdahl, 1996). Specifically, we hypothesized that the TD controls would show the normative pattern of perceptual asymmetries (e.g., Pollak et al., 2004): for positive stimuli presented to the LE a LE advantage was predicted, reflecting the RH posterior system activation; positive stimuli presented to the RE were hypothesized to activate the left anterior system, implicating a RE advantage. No ear advantage was predicted for the negative stimuli presented to the LE, as this represented the only condition implicating both anterior and posterior activation within the same hemisphere; for negative stimuli presented to the RE a LH advantage was predicted. Finally, the presentation of neutral information to either RE or LE was predicted to activate neither anterior nor posterior emotion areas. We predicted that individuals with WS would exhibit similar processing of positively valenced auditory information to the TD controls, but reduced RH efficiency at processing negative auditory information. The rationale was that neurobiological data point to reduced leftward asymmetry in WS (Holinger et al., 2005), and decreased neural responses to negative visual stimuli in such individuals relative to TD controls (Haas et al., 2009; Meyer-Lindenberg et al., 2005). At the same time, neural activity in response to positive face stimuli is preserved or even enhanced in individuals with WS relative to TD controls (Haas et al., 2009).

## 2. Method

### 2.1. Participants

Eighteen individuals with WS (8 males) were recruited through a multicenter program based at the Salk Institute. Only right-handed participants were included in the study, and handedness was established on the basis of the hand that the individuals used for writing. For all participants, genetic diagnosis of WS was established using fluorescence in situ hybridization (FISH) probes for elastin (ELN), a gene invariably associated with the WS microdeletion (Ewart et al., 1993). In addition, all participants exhibited the medical and clinical features of the WS phenotype, including cognitive, behavioral, and physical features (Bellugi et al., 2000). Eighteen right-handed TD individuals (9 males) were matched to those with WS for CA. The participants were screened for the level of education, and those with more than 2 years of college-level education were excluded from this study. Each participant was screened for current and past psychiatric and/or neurological problems, and only those deemed clinically asymptomatic were included in the study. A small DD comparison group of five individuals with a learning and intellectual disability of unknown origin was included (3 males). As right-handedness was a prerequisite for being included in this study, the recruitment of the DD participants proved difficult, as a large proportion of our available population was left-handed (cf. Grouios, Sakadami, Poderi, & Alevriadou, 1999). Although the small sample size precluded