Neuropsychologia 48 (2010) 2602–2609

Contents lists available at ScienceDirect

Neuropsychologia

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

Auditory cortical volumes and musical ability in Williams syndrome

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ARTICLE INFO

Article history:
Received 17 November 2009
Received in revised form 26 April 2010
Accepted 1 May 2010
Available online 8 May 2010

Keywords:
Williams syndrome
Musical
Primary auditory cortex
Planum temporale
MRI

ABSTRACT

Individuals with Williams syndrome (WS) have been shown to have atypical morphology in the auditory cortex, an area associated with aspects of musicality. Some individuals with WS have demonstrated specific musical abilities, despite intellectual delays. Primary auditory cortex and planum temporale volumes were manually segmented in 25 individuals with WS and 25 control participants, and the participants also underwent testing of musical abilities. Left and right planum temporale volumes were significantly larger in the participants with WS than in controls, with no significant difference noted between groups in planum temporale asymmetry or primary auditory cortical volumes. Left planum temporale volume was significantly increased in a subgroup of the participants with WS who demonstrated specific musical strengths, as compared to the remaining WS participants, and was highly correlated with scores on a musical task. These findings suggest that differences in musical ability within WS may be in part associated with variability in the left auditory cortical region, providing further evidence of cognitive and neuroanatomical heterogeneity within this syndrome.

1. Introduction

Examining the neural substrates of musical processing in Williams syndrome (WS) offers an important opportunity to explore gene–brain-cognition relationships. Individuals with WS have a known genetic deletion that is accompanied by atypical neuroanatomy and have been characterized as possessing a fractionated cognitive profile. Their cognitive profile is characterized by relative strengths and weaknesses, including a strong affinity to music and relatively preserved musical abilities (Levitin & Bellugi, 1998; Levitin et al., 2004).

Descriptions of preserved musical skills in individuals with WS have been typically based on parental reports or the study of individuals with enhanced musical interests and/or abilities (Lenhoff, Peral, & Hickok, 2001; Levitin & Bellugi, 1998; Udwin, Yule, & Martin, 1987; von Arnim & Engel, 1964). Recent research, however, has questioned the generalizability of these findings. When compared to chronological age-matched peers, the musical abilities of individuals with WS are impaired (Deruelle, Schön, Rondan, & Mancini, 2005; Hopyan, Dennis, Weksberg, & Cytrynbaum, 2001). Similarly, although many individuals with WS display increased emotional responsiveness to music (Hopyan et al., 2001; Levitin et al., 2004), Don, Schellenberg, and Rourke (1999) noted that 15% of the participants in their study were either indifferent or displayed an intense dislike of music. Music processing has also been described as atypical in individuals with WS, with diminished awareness of the global elements of music and unusual patterns of cortical and subcortical activation in response to music stimuli compared to normal controls (Deruelle et al., 2005; Levitin et al., 2003).

The proposed musical strengths of individuals with WS have been linked to their atypical neuroanatomical profile. Specifically, a proportionally large superior temporal gyrus has been linked with their reported musical strengths (Bellugi, Mills, Jernigan, Hickok, & Galaburda, 1999). Research on normal controls has implicated the superior temporal gyrus in pitch and melodic discrimination (Peretz, 2001). This region includes both the primary auditory cortex and association auditory cortex, otherwise known as the planum temporale. The primary auditory cortex is a sensory region located within the medial portion of Heschl's gyrus within the temporal lobe (Liégeois-Chauvel, Musolino, & Chavel, 1991). It is thought to encode a range of auditory stimuli, including pitch, loudness, duration, and spatial location (McLachlan & Wilson, 2010; Zatorre & Belin, 2001) and has been shown to be enlarged in musicians (Bermudez, Lerch, Evans, & Zatorre, 2009; Pantev et al., 1998; Schneider et al., 2002; Schneider et al., 2005).

The planum temporale is a secondary, higher order auditory association area that has been linked with music processing,

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doi:10.1016/j.neuropsychologia.2010.05.007

including absolute pitch ability (Keenan, Thangaraj, Halpern, & Schlaug, 2001; Ohnishi et al., 2001; Schlaug, Jancke, Huang, & Steinmetz, 1995; Schulze, Gaab, & Schlaug, 2009; Wilson, Lusher, Wan, Dudgeon, & Reutens, 2009). It is located along the posterior and superior surface of the temporal lobe, adjacent to Heschl's gyrus and extending to the end of the Sylvian fissure (Steinmetz, Volkmann, Jancke, & Freund, 1991). Activation of the planum temporale has been reported for a variety of pitch and speech stimuli (Binder, Frost, Hammeke, Rao, & Cox, 1996; Hall & Plack, 2009), and it has been likened to a "computational hub" that is involved in many aspects of auditory and audio-motor processing (Griffiths & Warren, 2002; Warren, Wise, & Warren, 2005). Geschwind and Levitsky (1968) reported that the planum temporale was anatomically larger on the left than the right in 65% of postmortem brains, while the right planum temporale was larger in only 11% of specimens, suggesting that such anatomical asymmetries were a reflection of hemispheric functional specialization.

The surface area, volume, and asymmetry of the planum temporale have been studied in musicians who demonstrate absolute pitch perception, which is the ability to identify or reproduce a particular pitch without using a reference tone (Takeuchi & Hulse, 1993). Using surface area measurements, increased leftward asymmetry of the planum temporale was reported in musicians with absolute pitch compared to musicians without absolute pitch and non-musicians (Schlaug et al., 1995). Keenan et al. (2001) attributed this asymmetry to a smaller than average right planum temporale, rather than a larger than average left planum temporale in absolute pitch possessors.

Zatorre, Perry, Beckett, Westbury, and Evans (1998) investigated the cortical volume, rather than surface area, of the planum temporale in musicians with absolute or relative pitch, as well as controls. Individuals with relative pitch are able to make pitch judgments about musical intervals but cannot consistently identify pitches without a reference tone. The volume of the left planum temporale in the absolute pitch group was found to be significantly larger than that of non-musicians. Exaggerated leftward asymmetry was not found, however, because the right planum temporale volume was also found to be larger in the absolute pitch group, albeit not to a significant degree. In a subsequent study, Wilson et al. (2009) demonstrated volumetric asymmetry in the planum temporale of musicians with absolute pitch that reflected a smaller mean right planum temporale volume. They also showed, however, that this asymmetry varied with absolute pitch ability. Musicians with a partial form of the skill ('quasi-absolute pitch') showed similar planum temporale volumes bilaterally. Importantly, these volumetric differences were associated with different patterns of functional activation in the same musicians performing an in-scanner pitch naming task.

To our knowledge, no one has investigated the variability of musical abilities within the WS population or examined whether there are neuroanatomical differences between individuals with WS who are 'musical' and those who are 'non-musical'. In the present study, we conducted a volumetric analysis of the primary auditory cortex and the planum temporale in individuals with WS and normal controls and evaluated the musical abilities of both groups. We expected that the volumes of the primary auditory cortex and the planum temporale would be proportionally larger compared to controls because previous studies have reported that the superior temporal gyrus, which incorporates the primary auditory cortex and the planum temporale, is enhanced in individuals with WS (Chiang et al., 2007; Reiss et al., 2000; Reiss et al., 2004). We then investigated whether any of the participants with WS showed enhanced musical abilities compared to other individuals with WS or controls. Finally, given that the primary auditory cortex and planum temporale have been implicated in the ability to discriminate pitch and melodies, we expected a positive relationship between musical ability and volumes of the primary auditory cortex and planum temporale in individuals with WS who demonstrated enhanced musical abilities.

2. Materials and methods

2.1. Participants

Twenty-five individuals with WS (mean age = 18.3 years ± 7.5; range 8–41) and 29 controls (mean age = 17.5 years ± 7.6; range 8–41) were recruited to the study. The control participants were matched by chronological age, sex, and handedness. The WS diagnosis was genetically confirmed in 23 participants using fluorescent *in situ* hybridization (FISH) based on a deletion of one copy of the elastin gene. The remaining two WS participants declined FISH and were diagnosed using the clinical and medical phenotype. All controls were screened for developmental, neurological and psychiatric abnormalities. The study was approved by the relevant Human Research Ethics Committees and all participants or their guardians gave informed consent.

2.2. Stimuli

The participants were administered six subtests from the Specimen Aural Tests (SAT; Nickson & Black, 1962), which provide a measure of musical production skills. The subtests are typically used in the aural examination of training musicians in Australia. They assess rhythmic timing, as well as pitch, rhythm, and melodic reproduction. The participants were asked to clap in time to the beat of musical passages, reproduce (by clapping or singing) rhythmical passages, reproduce pitches of short melodic phrases, hum the tonic note at the end of unfinished melodic phrases, and reproduce phrases which combined melody and rhythm.

The Bentley Measures of Musical Abilities (Bentley, 1985) were also used to evaluate the participants' receptive musical skills in the areas of pitch discrimination, tonal memory, chord analysis, and rhythmic memory. The participants were asked to discriminate between two pitches, discriminate between five-note tunes and indicate which note had been changed (if any), listen to chords and indicate if the chord was composed of two, three, or four notes, and discriminate between four-beat rhythms and indicate which beat had been changed (if any).

The above tests were chosen because they were developed to assess musical skills in pediatric populations. Despite this, some of the participants with WS experienced difficulty comprehending the oral instructions or maintaining attention during testing. Complete data were obtained on 20 individuals with WS for the SAT and 17 individuals with WS for the Bentley. All 29 control participants completed both musical measures.

2.3. MRI image acquisition

MRI scans were obtained on 25 individuals with WS and 25 control participants using a 3D T_1-weighted radio-frequency spoiled gradient echo (SPGR) sequence (TE = 2.2 ms, TR = 10.5 ms, TI = 350 ms, flip angle = 20°, matrix size = 256 × 256, NEX 1, field of view = 25 cm). The images were acquired on a 1.5T Signa Echospeed Superconducting Imaging System whole-body magnetic imaging scanner (General Electric Medical Systems, Milwaukee, WI).

2.4. MRI image analysis

The images were sampled in the coronal plane with an original slice thickness of 1.5 mm × 0.9 mm × 0.9 mm (1.2 mm^3). They were then resampled to a smaller slice thickness (0.5 mm × 1 mm × 0.5 mm) in order to provide a clearer image to enhance boundary delineation during volumetric measurements. All MRI images underwent automated scalp, skull, and dura mater removal. The final images with non-brain tissues removed were registered into stereotaxic coordinate space based on the 152 subject T_1-weighted average template from the Montreal Neurological Institute using a nine parameter linear transformation (rotation, translation, and rescaling along the principal axes) and Automatic Image Registration 3.0 software (Woods, Grafton, Watson, Sicotte, & Mazziotta, 1998). Intersubject registration has been found to be necessary in studies examining morphological differences in brain structures between groups to control for differences in overall brain volume (Woods, 1996). Following registration into standard stereotaxic space, identifying names were removed from the images so that the first-named investigator was blind to group membership during structural segmentation.

Brain volume was determined by setting a threshold to separate brain from background. The absolute brain volume was calculated by dividing the volume obtained in standard space by the scale factor required for image registration into standard space. This method was also used to obtain absolute volumes for the primary auditory cortex and the planum temporale. Manual segmentation of these structures was performed using Display, an interactive mouse-driven software that allows simultaneous viewing of the coronal, sagittal, and axial images. In Display, a color is chosen and as the structure of interest is identified on each slice, the mouse is used to 'color' the identified voxels that comprise the structure. The planum temporale was observed best in the sagittal view, and then the views were verified in the axial and coronal views (see Fig. 1a). The primary auditory cortex was best viewed in