Aversion, awareness, and attraction: investigating claims of hyperacusis in the Williams syndrome phenotype

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Background: Williams syndrome (WS), a neurodevelopmental disorder, is characterized by pervasive cognitive deficits alongside a relative sparing of auditory perception and cognition. A frequent characteristic of the phenotype is adverse reactions to, and/or fascination with, certain sounds. Previously published reports indicate that people with WS experience hyperacusis, yet careful examination reveals that the term ‘hyperacusis’ has been used indiscriminately in the literature to describe quite different auditory abnormalities. Method: In an effort to clarify and document the incidence of auditory abnormalities in and among people with WS we collected data from parents of people with WS (n = 118) and comparison groups of people with Down syndrome, autism, and normal controls. Results: Our findings revealed four phenomenologically separate auditory abnormalities, all of which were significantly more prevalent in WS than the three comparison groups. Among people with WS, we found relatively few reports of true hyperacusis (lowered threshold for soft sounds) or auditory fascinations/fixations, whereas 80% reported fearfulness to idiosyncratically particular sounds, and 91% reported lowered uncomfortable loudness levels, or ‘odynacusis.’ Conclusions: Our results confirm anecdotal reports of an unusual auditory phenotype in WS, and provide an important foundation for understanding the nature of auditory experience and pathology in WS. We conclude by reviewing the ways in which the present findings extend and complement recent neuroanatomical and neurophysiological findings on auditory function in people with WS. Keywords: Hyperacusis, odyacusis, allodynia, Williams syndrome, Williams–Beuren syndrome, loudness thresholds, odynacusis.

Williams syndrome (WS, also known as Williams–Beuren syndrome) is a neurodevelopmental disorder occurring in approximately 1 in 20,000 live births, and is characterized by marked deficits in cognitive function, coupled with relative sparing of music and language skills (Bellugi, Lichtenberger, Jones, Lai, & St. George, 2000; Levitin & Bellugi, 1998; Mervis, Morris, Bertrand, & Robinson, 1999). People with WS are reputed to suffer from hyperacusis (sometimes referred to in the literature by a synonym ‘oxyacusis’), a heightened sensitivity to all or only certain sounds (Hagerman, 1999; Klein, Armstrong, Greer, & Brown, 1990; Martin, Snodgrass, & Cohen, 1984; Nigam & Samuel, 1994; Udwin & Yule, 1991). In the present study, we sought to clarify and quantify the incidence of hyperacusis and other auditory disorders in WS, and to determine if people with WS experience hyperacusis more often than members of other groups, including control groups of people with other neurodevelopmental disorders. We also sought to characterize the types of sounds and contexts in which people with WS (and members of comparison groups) experience auditory disorders.

WS is known to be caused by the hemizygous deletion of approximately 17 genes on chromosome 7 band 7q11.23 (Francke, 1999; Korenberg et al., 2000). A positive diagnosis of WS is determined either by genetic testing (the fluorescent in situ hybridization, or FISH test) or by clinical evaluation (Jarrold, Baddeley, & Hewes, 1998; American Academy of Pediatrics Committee on Genetics, 2001). Because the genetic deletion is known in WS, and the phenotypic manifestations are relatively well defined and stable, WS presents researchers with a unique opportunity to uncover the neurobiological basis of complex cognitive behaviors, and in particular, to begin to draw out the links between genes, neurodevelopment, cognition, and behavior.

Phenotypic manifestations of WS include low IQ, ranging from 40–100 (mean ~61, s.d. 11; Howlin, Davies, & Udwin, 1998; Mervis et al., 1999), although a marker of WS is the presence of peaks and valleys in cognitive function. People with WS typically present deficits in key cognitive domains including conceptual reasoning (Bellugi, Klima, & Wang, 1996), problem solving, arithmetic and spatial cognition (Bellugi et al., 2000), coupled with relative sparing in four domains: social drive (Doyle, Bellugi, Korenberg & Graham, 2003; Tager-Flusberg, Sullivan, Boshart, Guttmann, & Levine, 1996; Udwin & Yule, 1991), face processing (Bellugi & Wang, 1999; Pezzini, Vicari, Volterra, Milani, & Ossella, 1999), language (Mervis et al., 1999; Rossen, Klima, Bellugi, Bihrlle, & Jones, 1996), and music (Brochard, Drake, & Robicon, 2003; Don, Schellenberg, & Rourke, 1999; Levitin & Bellugi, 1998, 1999). People with WS tend to spend more time than others...
listening to music and show heightened emotional responses to music (Don et al., 1999; Levitin & Bellugi, 1999; Levitin et al., in press). Their short-term memory for auditorily presented rhythmic sequences appears to be a relative strength, and when they make mistakes in replicating rhythmic sequences, their mistakes tend to be more musical and semantically congruent than those of mental-age matched controls (Levitin & Bellugi, 1998).

Three prior studies used questionnaires to probe the auditory experiences of people with WS. Udwin's (1990) survey of people with WS (but no control group) was mostly concerned with occupations, living arrangements, social relationships, etc. One item asked about their history of hyperacusis and found that of 119 adults surveyed, 110 (92%) reported hyperacusis, and 93% of these (78% of the total group) remained hyperacusic as adults.

Don et al. (1999) administered a questionnaire to 19 people with WS aged 8–13, and a comparison group of typically developing normal children aged 5–12 to investigate differences in musical backgrounds and behaviors. They found that 100% of the WS group reported a history of hyperacusis, compared to 10% of the control group. Seventy-five percent of the people with WS in their sample reported an unusual liking for certain sounds compared to 5% of the control group.

Klein et al. (1990) administered a questionnaire to the parents of 65 people with WS and a control group of typically developing normal children. The questionnaire was designed to obtain information about the prevalence of hyperacusis and otitis media, the specific sounds that were offending, and reactions to them. Ninety-five percent of the WS and 12% of the control group reported to suffer from hyperacusis at some time in their lives, with a drop to 83% and 3% respectively reported to be currently suffering from hyperacusis.

One impediment to a clear interpretation is that across various studies, the term ‘hyperacusis’ has been employed rather indiscriminately to describe several distinct auditory abnormalities (Anari, Axelson, Eliasson, & Magnnsson, 1999; Baguley, 2003; Katznell & Segal, 2001; Kalfa et al., 2002; Marriage & Barnes, 1995; Nigam & Samuel, 1994; Phillips & Carr, 1998). ‘Hyperacusis’ is defined medically as an ‘abnormal sensitivity to sound’ (Dirckx, 2001; Venes, Thomas, & Taber, 2001) where ‘sensitivity’ is taken to mean lowered hearing thresholds, that is, an ability to hear soft sounds that others cannot. Yet lingering behind the apparent precision of this single term are reports of people with WS who experience fear of sounds that others don’t find fearful, who report that some sounds are too loud even when others don’t find them to be so, and an unusual attraction to or fascination with certain sounds (Einfeld, Tonge, & Floria, 1997; Klein et al., 1990; Levitin & Bellugi, 1999; Marriage, 1995; Udwin, 1990).

It is important to note here that lowered hearing thresholds – thresholds of detectability – are not phenomenologically the same as lowered pain thresholds, and moreover, that such disturbances of loudness perception need to be distinguished from the ‘annoyance’ that sounds may provoke in individuals (Phillips & Carr, 1998; Stansfeld, 1992). As Phillips and Carr (1998) note, a disturbance in loudness perception or a symptom of noise sensitivity refers to a predisposition toward perceiving noisy events. On the other hand, annoyance is an affective or attitudinal factor that refers to the extent to which noisy events are evaluated unfavorably (Phillips & Carr, 1998; Stansfeld, 1992; Taylor, 1984). The notion that reports of sound discomfort may involve sensory, attentional, and affective systems is consistent with well-established theories of pain in general (Melzack & Katz, 1984; Phillips & Carr, 1998).

Because all of these reported symptoms probably stem from different underlying physiological correlates and aetiologies (Phillips & Carr, 1998), it is important to be precise with terms so as not to lead to confusion. Klein et al. (1990) and Rosenhall, Nordin, Sandström, Ahlsen, and Gillberg (1999) both conflate hyperacusis and lowered pain thresholds, whereas Hopyan, Dennins, Weksberg, and Cytrynbaum (2001) use the term to mean simply ‘an abnormally strong affective response to certain categories of sound.’

In the present study, therefore, we sought to extend and improve these earlier studies in four key respects:

(1) The Klein et al. study used a forced-choice paradigm, listing sample offending sounds; this could have biased the results, so we employed a free-response open-ended questionnaire.

(2) No comparison groups of other developmentally disabled populations were included in any previous study; a first reasonable null hypothesis would be that the observed auditory anomalies are in some way related to neurodevelopmental impairment or to developmental delay. We included people from two neurodevelopmentally impaired groups, Autism and Down syndrome, as well as age-matched controls.

(3) We sought to disentangle the phenomenologically different reports of auditory abnormalities, to differentially label them and provide estimates of their occurrence in each population.

(4) We sought to obtain additional qualitative information to provide a richer and more detailed picture of the phenomenology of auditory abnormalities in WS and other neurodevelopmentally disabled populations.

Methods

Participants

Participants were the parents or caregivers of people with WS, autism (AUT) and Down syndrome (DNS), as well as an adult group of typically developing normal
control participants (CTL) who were instructed to consult with their parents in filling out the questionnaire. IQs for the people WS, AUT and DNS were assessed using the WAIS-R or the WISC-III, as appropriate depending on the age of the participants.

The parents of WS participants \( (n = 118) \) were solicited from the Williams Syndrome Association of America, from professional and parental conferences on WS in North America, and from ongoing research studies in our laboratories. The diagnosis of WS was confirmed using accepted procedures mentioned above, either the FISH test or the WS Diagnostic Score Sheet (American Academy of Pediatrics Committee on Genetics, 2001). Of 149 people with WS that we originally recruited, 118 were positively diagnosed by the above criteria and thus retained in the present report. The mean full scale IQ of our retained sample was 66 (s.d. 11).

Parents of DNS participants \( (n = 40) \) were solicited from ongoing studies at the Laboratory for Cognitive Neuroscience at the Salk Institute in San Diego, California. The diagnosis of DNS was positively confirmed by genetic testing for trisomy 21. Mean full scale IQ was 56 (s.d. 9.1).

Parents of AUT participants \( (n = 30) \) were solicited from the Developmental Neuropsychology Laboratory at the Alliant International University in San Diego, California. All AUT participants were positively diagnosed by trained neuropsychologists prior to their participation in the study using a standardized diagnostic battery that included the Autistic Diagnostic Interview-Revised (ADI), Autistic Diagnostic Observation Schedule (ADOS), and Childhood Autism Rating Scale (CARS). Mean full scale IQ was 74.5 (s.d. 27.8).

CTL participants \( (n = 118) \) were obtained from an undergraduate psychology class at San Diego State University in California. They were instructed to consult with their parents in completing this questionnaire and were reminded that the questions referred to their childhood history, not their present experience.

The age and gender distribution of the participants by diagnosis are shown in Table 1. An ANOVA confirmed that there were no statistically significant differences in age between groups \( (F(3,302) = 2.1, \text{n.s.}) \). All questionnaires were administered in the same way to each parent group.

### Materials

In order to avoid any suggestibility or bias in parental responses, we created a questionnaire that simply asked, in free-response format, about the childhood history of unusual reactions to sounds, the types of sounds that elicited these reactions, and other behaviors related to fear of or fascination with sound. In a further effort to reduce response bias, we did not explicitly mention any particular sounds that might cause these symptoms, and left this open in free-response format. In addition, we asked parents to provide the age of onset of any unusual auditory perceptions or reactions. In pilot testing, parents seemed to remember most clearly the first manifestation of auditory aversions, compared to the other behaviors. (The other behaviors might have been noticed only gradually rather than defined by a single salient incident.) Therefore, we asked two follow-up questions about auditory aversions: the age of onset, and whether or not the symptom had changed (improved or worsened) with time.

### Coding

Two data coders, blind to group membership and hypotheses, tabulated the results and organized the data into categories of auditory dysfunction. Both coders, working separately, constructed four categories: reports of lowered hearing thresholds (an ability to hear soft sounds that others can’t), lowered uncomfortable loudness levels (discomfort owing to sounds seeming too loud), aversion to certain sounds, and attraction to certain sounds. Interrater agreement was .91, and disagreements were resolved by a third coder.

### Results

Based on the categories that emerged in data coding, we distinguished four nominal categories of abnormal reactions to sound. We employ the following descriptive terms, making no assumptions at this stage about correlations or conditional probabilities among them:

- **True hyperacusis**: lowered hearing thresholds, that is, detectability thresholds for soft sounds (after Dirckx, 2001; Venes et al., 2001).
- **Odynacusis**: a lowered pain threshold for loud sounds, also known as lowered uncomfortable loudness levels or LULLs in the literature (Phillips & Carr, 1998).
- **Auditory allodynia**: a substantial aversion to or fear of certain sounds not normally found aversive. Note that this describes responses to sounds that are not regarded as too loud to the child. The feelings of pain elicited by certain sounds appear to have something in common with allodynia, a pathological state typically following tissue or nerve damage in which patients feel pain from stimuli that are not normally perceived as painful. (We first introduced this term in Levitin et al., 2003. These symptoms have sometimes been referred to in the literature as ‘phonophobia,’ but that term, like ‘hyperacusis’ also has a history of misuse, and consequently we opted for a new term without prior ambiguous associations.)
- **Auditory fascinations**: a substantial attraction to or fascination with certain sounds.

### Table 1 Age and gender distribution of the participants in this study

<table>
<thead>
<tr>
<th></th>
<th>AUT</th>
<th>Control (CTL)</th>
<th>DNS</th>
<th>WS</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>30</td>
<td>118</td>
<td>40</td>
<td>118</td>
</tr>
<tr>
<td>Mean</td>
<td>18.2</td>
<td>20.9</td>
<td>17.2</td>
<td>20.4</td>
</tr>
<tr>
<td>age (s.d.)</td>
<td>(7.7)</td>
<td>(7.4)</td>
<td>(9.2)</td>
<td>(10.4)</td>
</tr>
<tr>
<td>Male</td>
<td>24</td>
<td>28</td>
<td>20</td>
<td>61</td>
</tr>
<tr>
<td>Female</td>
<td>6</td>
<td>90</td>
<td>20</td>
<td>57</td>
</tr>
</tbody>
</table>
Parents of people with WS reported the highest incidence of each of the four auditory conditions under investigation compared to the other groups. These intergroup differences were statistically significant (by Z-tests for proportions, adjusted for multiple comparisons, for true hyperacusis, \( p < .03 \), for all others, \( p < .001 \)). The results for all behaviors cross-tabulated by group are shown in Table 2.

**True hyperacusis**

The WS group was the only group that reported lowered auditory thresholds (what we refer to as ‘true hyperacusis’), with an incidence rate of 4.7% in our sample. Typical responses by parents of people with WS on the questionnaire included reports that their children could literally hear a pin drop on the other side of the room, or that they can ‘hear sounds long before we do – fire engines, dogs barking from far away, etc.’

**Odynacusis (or ‘LULLs’)**

This was reported to occur in 79.8% of the sample of people with WS, compared to 33% of the people with DNS and AUT, and only 4% of the CTL sample. Typical were reports of children covering their one or both ears when a car radio was playing, or at a playground. There was no obvious difference between groups in the types of sounds reported to cause odynacusis.

**Auditory alldynia (or auditory aversions)**

Aversion to particular sounds that are not normally considered to be aversive were reported by 90.6% of the parents of people with WS, compared to roughly 27% of the AUT, 7% of the DNS and 2% of the CTL groups. We found significant intergroup differences for the age of onset of auditory aversions (by planned linear contrast comparisons, \( F (3, 115) = 11.6, p < .001 \)) with onset in WS occurring significantly earlier than in other groups (Table 3). There were no other intergroup differences. Mean age of onset (and s.d.) was as follows: AUT = 3.3 (1.1); CTL = 2.8 (1.7); DNS = 2.3 (1.6); WS = 1.1 (1.4).

Among those respondents who reported a history of auditory aversions, we found that changes in this symptom were significantly more likely to have occurred among the people with WS than other groups (by \( t \)-test, for all pair-wise comparisons, \( p < .01 \) adjusted for multiple comparisons), and in particular, that the symptoms of auditory aversions among WS tend to decrease over time. Among those parents who reported a change, 95% noted a decrease in symptoms, and 5% noted an increase in symptoms. There were no changes over time reported from among the DNS group. Only 3 members each of the AUT and CTL group reported a change, and this was also a decrease of symptoms over time. Unlike the 5% of the WS group, no respondents among the comparison groups reported that symptoms had increased over time. There was no significant relation between IQ and symptoms within or across groups (by nominal logistic regression).

The types of sounds that were reported to cause aversive reactions were similar for all groups, and included sounds such as water running, toilets flushing, vacuum cleaners, fans, laughter, and babies crying. Some children were reported to cover their ears in response to such sounds, but their behaviors made it clear to the parents that it was not because the sounds were too loud (in which case we would have coded them as odynacusis) but because the sounds were somehow intrinsically frightening to the child.

We analyzed the types of sounds that cause adverse reactions in our sample of people with WS, and found reports similar to those found by Klein et al. (1990), with fireworks and engines being cited as the most common irritants (39% and 30% respectively), followed by thunder (28%), and vacuum cleaners (22%). Note that among the sounds reported as distressing are some that many young children find frightening (fireworks, thunder, balloon popping) and others that seem innocuous to most children but that the parents we surveyed reported were particularly aversive (vacuum, blender, applause). To qualify for inclusion in this category, however, the reaction to the sound had to be, in the parents’ judgment, extreme given the stimulus. For example, many children don’t like thunder, but relatively few over the age of six react by violent and inconsolable screaming, or by being terrified in anticipation of the noise (as were reported by the parents we surveyed).

### Table 2

Percentage of participants in each group for whom parents reported the auditory perceptions indicated. Williams individuals are significantly different from all other groups (\( p < .03 \)) on all measures

<table>
<thead>
<tr>
<th>Symptom</th>
<th>AUT</th>
<th>CTL</th>
<th>DNS</th>
<th>WS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperacusis</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.7</td>
</tr>
<tr>
<td>Odynacusis</td>
<td>33.3</td>
<td>3.9</td>
<td>32.5</td>
<td>79.8</td>
</tr>
<tr>
<td>Auditory aversion</td>
<td>26.7</td>
<td>2.3</td>
<td>6.8</td>
<td>90.6</td>
</tr>
<tr>
<td>Auditory fascinations</td>
<td>0</td>
<td>.8</td>
<td>0</td>
<td>9.3</td>
</tr>
</tbody>
</table>
In an effort to classify the sounds that cause distress in people with WS, we employed a classification system based on the spectral and spectro-temporal properties of the sounds. The resulting four categories of sound, and the percentage of parents of people with WS who endorsed those sounds as frightening to their children, are as follows:

1. **broad-band, continuous sounds**, e.g., blender, vacuum, lawnmower, airplane, buzzer, cheering crowd, and vehicle engine (53%);
2. **broad-band percussive (sudden onset) sounds**, e.g., fireworks, balloon pop, fire alarm (pulsed *eh-eh-eh* type, not the frequency sweeping type), thunder, lightening, and door slam (69%);
3. **narrow-band continuous sounds**, e.g., dentist equipment, air brakes, power saw, and power drill (32%);
4. **human/animal sounds** (typically, though not exclusively, distress sounds), e.g., baby cries, screams, yelling, dog barking, operatic singing, sirens (frequency sweeping type), coughing, and sneezing (14%).

These category differences were found to be statistically significant (by Z-test for correlated proportions, \( p < .05 \) for all comparisons).

Several unusual sounds were reported as causing extreme discomfort in the children. Two respondents with WS each listed reverberation from a gymnasium or open stairway, air brakes, and the whistle from a tea kettle (one child found this latter sound utterly intolerable). One respondent each listed the following as causing great distress: cicadas, unbalanced washing machine, slamming toilet seat, cow, cough, sneeze, clearing throat, a truck passing our car, coffee maker, shaving cream being sprayed, operatic soprano or violin, turning on a kitchen faucet, THX surround sound in theater (but not normal movie theater sound), champagne cork, and saxophonist Kenny G.

The types of sounds causing distress within the AUT and DNS groups were generally limited to motor-like sounds and high frequency noises. Exceptions included one respondent each within the AUT group reporting distress caused by church choirs, circus noises (but not crowd noises in general), the high-pitched whine of a television picture tube, and the push button on restroom hand dryers. One DNS child was distressed by sneezing, one by Muzak, and one by the sound of the ocean. Only one CTL subject reported distress to an unusual sound, and this was to paper-crackling.

**Auditory fascinations**

Among parents of people with WS, 9% reported that their children had a fascination with certain sounds. Neither of the neurodevelopmentally impaired groups reported auditory fascinations, and only one member of the control group (.8%) reported an auditory fascination. In every case of a fascination, all parents reported that their child had previously been afraid of the object of fascination. In other words, every *fascination* began as an *aversion*.

The types of sounds that were the object of auditory fascinations were more likely to be broad-band noises (such as humming, buzzing, motor noises and thunder, categories 1 and 2 above) than other sounds (\( z = 2.32, p < .02 \)), although there was one report of a child with WS who had a fixation on steel drums that lasted for about six months and then disappeared.

Our own direct interviews with people with WS revealed that many of them additionally had a particular interest and affinity for special effects sounds such as found in Loony Tunes (Stalling, 1990) and Hanna-Barbera cartoons (Hanna-Barbera, 1994), and musical sound effects, such as those found in Spike Jones records (Jones, 1999). The following give some of the flavor or phenomenology of these auditory fascinations. One parent reported that her child

> ‘loves the sound of the humming of bees, and he is very gentle, so he’ll cradle one or more bees in the palm of his hand, and then hold it up to his ear, smiling. He said, “they sound so pretty, I like to hear it, and it sounds funny.”’

Another reported:

> ‘Our son loved the sound of the electric razor so much that when he cried, his mother would turn on the electric razor and he would stop crying. He yearned and begged for a leaf blower. It used to bother him, although then he became fascinated with it. He asked for a leaf blower for Xmas. He loved it and carries it everywhere. He goes around the neighborhood, and the neighbors love it, because he collects their leaves in his leaf blower, even though it used to bother him to hear it. In contrast, he never liked my blow dryer, he hates it.’

The attractions that people with WS feel toward sounds frequently go far beyond merely wanting to hear the sound, and extend to fascinations with the sources of the sounds – the objects themselves. Numerous reports told of children who wanted to see pictures of the object, cut pictures out of magazines and collected them, and wanted to learn as much as they could about the objects and their categories. For example, several children had learned to recognize specific cars coming from a distance, much the same way one might recognize specific voices of people. Other children would caress the objects of their auditory fascinations or try to surround themselves by them, even when the objects were not making noise.

**Association among symptoms**

One might ask the extent to which the presence of any one of these four symptoms was associated with any of the others. Because it was found in the
previous section that auditory fascinations in all cases grew out of auditory aversions, fascinations were not included in the following analyses. Two by two contingency tables for presence vs. absence of a given symptom were created to examine the co-occurrence of symptoms, and Yule’s Q was used to measure the strength of association. For the people with WS in our study, there was no significant association between hyperacusis and odynacusis, with only 2.5% of participants experiencing both; because no other experimental group reported hyperacusis this test was not performed for them. We found a significant association between reports of odynacusis and auditory aversions in the WS group, with 79% of participants experiencing both symptoms (Yule’s $Q = .95$, $p < .001$); no other pairwise associations of symptoms were significant. According to the parents, 3% of people with WS in our study reported experiencing all three of the symptoms (ns) and no one in the other participant groups did. In all three comparison groups, odynacusis and auditory aversions were also significantly associated ($Q = .97$, $p < .001$): 7.5% of DNS, 13.3% of AUT, and 1.7% of CTLs were reported to suffer from both odynacusis and auditory aversions. No other comparisons were significant.

One girl with WS was reported to be sensitive to the sound of a particular make of vacuum cleaner, but not to others, forming something of a hybrid case of hyperacusis and an auditory fascination. The vacuum that she was sensitive to she could hear from several houses away. We asked her how she felt when she heard the sound and she said ‘the sound gets inside my head and reverberates.’

**Discussion**

To our knowledge, the present study is the first to systematically distinguish among several different auditory anomalies in WS that have been somewhat indiscriminately termed ‘hyperacusis’ in the literature. We found that the incidence of true hyperacusis – the ability to hear sounds too soft for most people to hear – was less than 5% in WS, and we found no occurrences in the other populations.

While present in people with AUT and DNS (33% each), odynacusis was more than twice as likely to be found in people with WS (91%). Termed ‘recruitment’ when the pain is due to outer hair cell damage, the origin of this is not yet known in WS and will require further research. One logical possibility is that lowered uncomfortable loudness levels (LULLs) are the result of a shift in the range of hearing, and if this were true, odynacusis and hyperacusis would be strongly associated. Previous studies of typical developing people have found no such association (Anari et al., 1999), and neither did the present investigation, although this was perhaps due to the relatively low incidence of true hyperacusis observed. Rosenhall et al. (1999) observed an 18% prevalence of odynacusis in their sample of people with Autism, roughly half the number we observed here.

It has been widely reported that people with WS have a heightened, non-habituating fear of certain sound classes. This has been incorrectly referred to as ‘hyperacusis’ in many reports and elsewhere (Levitin et al., 2003) we proposed to use the term auditory allodynia. Our finding of an incidence of 90.6% among people with WS is consistent with previous reports of 94–95% (Klein et al., 1990; Martin et al., 1984). Klein et al. had reported that these symptoms decreased slightly in severity with age, and we found even stronger support for this developmental course, with 95% of respondents reporting a decrease in symptoms with age. Whether this decrease in auditory aversions over time is the result of a physiological change or of an increased coping ability is currently undetermined, and may well reflect an interaction of physiological and environmental factors.

Whereas it is not uncommon in all populations to find an aversion to loud or startling sounds, or to sounds that signal danger (such as sirens, babies crying, people screaming), responses to sounds by people with WS can be atypical in the magnitude of the reaction, and in the types of sounds which the individual finds aversive. One child in our study covered her ears and cried to her mother that the birds outside were ‘hollering’ at her. One 17-year-old girl reported extreme distress from the sound of a vacuum cleaner in another room, explaining that ‘the sound reverberates in my head.’ Many typically developing people are known to be uncomfortable at hearing fingernails scratching on a chalkboard. For some people with WS, an entire panoply of sounds appears to create a similar reaction.

We found that 8% of people with WS experienced auditory fascinations, with virtually no other reports in the comparison groups.

**Neurobiological considerations**

It is reasonable to ask if hyperacusis, odynacusis, auditory aversions and auditory fascinations in WS are based on peripheral auditory pathology or on higher-level cognitive or emotional abnormalities. Mechanical abnormalities in the middle ear, secondary to the elastin deficit in WS, could cause hyperacusis (Gordon, 1986), although the weight of evidence argues for a central rather than peripheral explanation. Most people with WS who exhibit these symptoms exhibit normal audiological exam results (Hickok et al., 1995), and there is no evidence of systematic peripheral auditory system abnormalities in WS.

One possible explanation for the odynacusis is an abnormal or compressed loudness function, that is, an increased perception of loudness in response to
small intensity changes (termed ‘recruitment’ when the etiology is outer hair cell damage). However, Hickok et al. (1995) found no evidence of an abnormal loudness growth function. Another possibility is that people with WS are unable to tune out extraneous sounds and attend only to pertinent auditory information. Speech discrimination testing of the child’s ability to discriminate words in quiet and in the presence of noise were actually above age expectation for 1/3 of the children with WS assessed (Hickok et al., 1995). These findings suggest heightened awareness and abnormalities in central auditory processing.

People with WS showed morphology, distribution, sequence, and latency of evoked response potential (ERP) components similar to typically developing normal controls (Bellugi, Bihrlle, Doherty, Neville, & Damasio, 1989; Bellugi, Bihrlle, Neville, Jernigan, & Doherty, 1990; Hickok et al., 1995). However, in tests of the auditory recovery cycle, people with WS showed a marked increase in the amplitude of the N100 and P200 responses at faster repetition rates, suggesting that the refractory period for neurons responding to sound is shorter in WS, and indicating hyperexcitability. This effect occurred only in temporal cortex, and only to auditory stimuli (refractory periods in the visual modality are equivalent in people with WS and typically developing controls). The authors concluded that auditory processing in people with WS, in addition to being mediated by hyperexcitability, is carried out by different neural systems than in normals (Bellugi et al., 1990), and emphasized that the effect is apparently confined to the auditory domain.

The shortened auditory recovery cycle in WS, as indexed by ERPs, confirms that the hyperexcitability is at the cortical level, not at the level of the peripheral auditory system. We speculate that hyperexcitability of auditory neurons could account for both the symptoms of hyperacusis and odynacusis. Hyperexcitable neurons would tend to fire in response to lower input levels than normal. If pain is experienced as the consequence of temporal summation (integration under the area of a curve defined by neural firing rates, Price, Hu, Dubner, & Gracely, 1977) then broad-band noisy sounds would be more likely to evoke aversion (since they consist of a greater range of frequencies than other sounds). Accordingly, one of the goals of the present study was to discover if broad-band sounds were more likely to cause aversion and attraction than other types of sounds, and this was indeed found to be the case.

Cytoarchitectonic studies in people with WS have found that auditory cell-packing density and neuronal size (in area 41) were abnormal (Galaburda & Bellugi, 2000; Holinger, Galaburda, McMenamin, & Sherman, 2002; Holinger et al., submitted). People with WS had an excess of mid and large cells in layers II in both cerebral hemispheres, and in layer VI in the left hemisphere. There was a hemisphere by diagnosis interaction between the brains of people with WS and controls in cell-packing density in layer IV, and in neuronal size in layer III. Larger than normal pyramidal neurons were found bilaterally in layer II, in left layer III and VI and were interpreted as being consistent with a hypothesis of increased connectivity in the auditory cortex of people with WS. This hyperconnectivity may be related to the relative sparing of language, music, and other auditory function, and could account for some of the unusual reactions to auditory stimuli documented in the present study.

Taken together, the ERP, structural MRI and cytoarchitectonic findings suggest the possibility that the brains of people with WS are organized differently than normals, at both a micro and a macro level. The first functional neuroimaging study of people with WS (Levitin et al., 2003) further substantiated this claim by uncovering significantly greater activation of amygdaloid regions in people with WS as well as widespread and diffuse cortical activations in response to music and noise. This points to a possible neuroanatomical basis for the four unusual auditory behaviors observed in the present study. These results thus provide neuroscientific confirmation of the claims of people with WS that sounds hold special emotional meaning to them. The pattern and levels of activations observed suggest the anatomical underpinnings of the unusual auditory profiles reported by the parents of people with WS in this study. In particular, reports of hyperacusis, odynacusis and auditory aversions may be related to hyperexcitability of auditory cortex neurons coupled with widespread cortical activation (and supporting the temporal summation theory of pain), whereas auditory fascinations may be related to the recruitment of emotional centers of the brain in response to particular auditory stimuli.

**Phenomenology**

A flavor of what it is like to have or live with WS emerged from the questionnaires. Many people with WS were reported to sit for hours enchanted by certain sounds, or to learn to name cars and vacuum cleaners by their make and model numbers, based solely on the acoustic information. There were no similar reports from the comparison groups. During a testing session with us for a study of music cognition (Levitin & Bellugi, 1998), one young adult spontaneously said that he loved the sound of vacuum cleaners. His parents reported that he owned 18 vacuum cleaners, and that this was the only present he ever wanted for his birthday or for Christmas. At Halloween he dressed up like a vacuum cleaner, and he had taped the sounds of vacuum cleaners and would play the tape at night for himself. While administering a test of timbre discrimination to him in which we had digitally recorded twelve different vacuum cleaners (Levitin, Bellugi, & Cole, in preparation), he not only obtained a perfect score, but
discussed each sound after presentation. Addressing the young (female) experimenter he cooed ‘Ooooh, isn’t that beautiful?’ holding his hand on his heart. ‘That’s a Hoover!’ After another trial he remarked, ‘That’s a Kirby, I don’t like that one as much.’ At the conclusion of testing, he flirtatiously said to the experimenter, ‘My, you have a very interesting vacuum cleaner collection – I’d sure love to come over to your house and see them sometime!’

Caveats

As Udwin (1990) noted for her questionnaire study of people with WS, several caveats apply in the present study as well. The data presented here are subject to the limitations of parental recall and subjectivity, and they are based on a somewhat self-selected sample of families of people with WS, nearly all of whom are members of either the Williams Syndrome Foundation of America or the Williams Syndrome Association of North America. At present, these two organizations are the only registries of affected people in North America, and hence the primary way that we had to contact families with WS. People with WS tend to be more verbally and emotionally expressive, more loquacious, than the comparison groups and this could have biased our findings – it may be that the parents of children with WS are more aware of their sound fears and fascinations precisely because their children are more likely to communicate them through facial expression and language (two areas of preserved skill) than are children with autism or Down syndrome. Indeed, the reports we received from parents of people with WS were far more rich in detail than the reports we received from any other group.

Conclusions

The results of this study indicate that people with WS present four unusual behaviors of auditory perception: hyperacusis, odynacusis, auditory aversions, and auditory fascinations. The hyperacusis might be characterized as an early awareness of sounds that are either too soft for others to hear or simply inconsequential to others. Both odynacusis and auditory allodynia create distress/discomfort in people with WS, and together constitute aversion. Finally, we documented that people with WS may show an intense fascination for or attraction to certain classes of sounds, often the same sounds of which they were frightened at a younger age. Thus, the concepts of aversion, awareness and attraction seem to characterize the auditory anomalies observed in WS, and may help to describe the WS phenotype, although we note that reports of true hyperacusis were significantly less common than of aversions and attractions.

The present study contributes significantly to a clinical and conceptual understanding of auditory abnormalities in WS. Because the genotypes in WS, DNS and AUT are clearly defined, the study of these distinct populations offers an unprecedented opportunity to link genes, brain, and behavior. This effort is greatly facilitated by the ability to document such striking phenotypic differences as exist in auditory function among the groups. Although the precise mechanisms underlying the four auditory anomalies in WS remain unknown, the present paper documents the existence of abnormalities in auditory perception which previous reports had confounded. Ongoing work in our laboratories focuses on the functional and structural neuroanatomical components of these disorders, with the goal of eventually understanding how genes, brain, and cognition are linked. People with WS may provide important clues to the neurogenetic basis of cognition, perception, and complex behaviors.

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