Abnormal Electrical Brain Responses to Pitch in Congenital Amusia

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Congenital amusia is a lifelong disability that prevents afflicted individuals from enjoying music as ordinary people do. The deficit is limited to music and cannot be explained by prior brain lesion, hearing loss, or any cognitive or socioaffective disturbance. Recent behavioral results suggest that this disorder is critically dependent on fine-grained pitch discrimination. Here, we present novel electrophysiological evidence that this disorder can be traced down to a right-lateralized N2-P3 response elicited by pitch changes. This abnormal brain response begins as early as 200 milliseconds after tone onset and may serve as a marker of an anomaly in music acquisition.

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Music is ubiquitous. In all cultures, humans have produced and enjoyed music. Yet, some individuals have extreme difficulties appreciating and producing music, despite their efforts to do so.[1–3] It is estimated that 4% of people are afflicted with this disorder, termed *congenital amusia* (or tone deafness).[4] This disorder is akin to other developmental disorders, such as dysphasia and dyslexia, and is thought to result from an inborn deficiency in fine-grained pitch discrimination.[5,6] The neural correlates of this deficit are currently unknown. The goal of this study was to narrow down the neural origin of the anomaly.

Knowing that the deficit experienced by amusic individuals is fine grained and selective to the pitch dimension,[5] the temporal neocortex is the most likely location for uncovering a neural anomaly. Indeed, both lesion and neuroimaging data are consistent in implicating the secondary auditory cortex in processing relationships between pitch elements as they change over

time,[7] especially the right auditory cortex if the changes are small.[8]

Various methods can be used to uncover a possible anomaly in the auditory cortex. In this study, we used the event-related potential (ERP) analysis of the electroencephalographic method because the *oddball* paradigm, which is commonly used in ERP studies, closely resembles the behavioral conditions we used previously to document the pitch deficit in amusic individuals.[5] In that prior behavioral study, amusic and control adult subjects were presented with monotonic and isochronous sequences of five tones (ie, with constant pitch and intertone interval). Their task was to detect when the fourth tone was displaced in pitch or time. In the *oddball* paradigm, the task is similar. Subjects are required to detect a deviant tone in a sequence of repetitive standard tones. Typically, the deviance lies along the pitch dimension and elicits brain potentials that are proportional to the size of the pitch change, even in the absence of attention.[9] Thus, the *oddball* paradigm is ideally suited to demonstrate the temporal brain dynamics of the pitch deficit experienced by amusic individuals. To this aim, amusic and control adult subjects performed a pitch change detection task while their ERPs were recorded online with a dense electrode array.

Subjects and Methods

Eight amusic adults (all participants of previous studies[1,5]; 2 men; mean age, 58 years; mean education, 17 years) and 10 matched control subjects who had no musical education and no musical impairment (2 men; mean age, 59 years; mean education, 17 years) were selected. They were considered as amusic (or not) from their scores on the Montreal Battery of Evaluation of Amusia.[10] The battery involves 6 tests (180 trials) that assess various music processing components (see Peretz and colleagues[10] for more information). Each amusic subject tested here obtained a composite score (between 51 and 71%) that was 2 standard deviations less than the mean for control subjects (mean score, 88.6%; standard deviation, 5.4; chance level being 50%). Their disorder is also specific to music. For example, the amusic subjects scored 63.4% on auditory memory for tunes (without lyrics), whereas they reached 90% on auditory memory for lyrics of the same songs. Control subjects performed significantly better on tunes with 85% correct ($p < 0.001$; see also Peretz and Hyde[2]) but did not score higher on lyrics with 88% correct.

Amusic and control subjects were presented with the same stimuli as was used in our prior study.[5] In the "standard" sequence, all 5 tones were 100 milliseconds long, played at a pitch level of C6 (1,047Hz), and synthesized in a piano timbre with an intertone-onset interval of 350 milliseconds. In half the sequences, the fourth tone was displaced upward or downward in pitch by one of five pitch distances. These ranged from 25 to 300 cents (where 100 cents corresponds to 1 semitone). Trials were randomized and mixed with half the sequences that contained no change (ie, the standard sequence); participants were informed about the nature and

the position in the sequence where a change could occur. They also received 40 practice trials. The session comprised 600 sequences (300 standards, 30 of each of 10 altered sequences). Participants were asked to press a "yes" button whenever they detected a change and a "no" button when they were unable to detect a change. They were further requested to blink at the end of each sequence, to focus on their hands, and to remain relaxed. They were tested individually with the stimuli presented bilaterally through headphones in a quiet room at an intensity level of 70dB sound pressure level (SPL)-A.

The electroencephalogram was recorded (bandpass, 0.15–50Hz; sampling rate, 256Hz; impedance, <5kΩ) via an InstEP amplifier (InstEP, Ottawa, Canada) from 60-tin electrodes. The reference electrode was placed on the tip of the nose. Bipolar electrode pairs monitored horizontal and vertical electrooculograms. Offline, the electroencephalograph contaminated by eye and movement artifacts was corrected, filtered (bandpass, 0.5–25Hz, 24dB/octave), and divided into epochs of 1,000 milliseconds including a 100-millisecond baseline before the target note (with Neuroscan, Computermedics, El Paso, TX). The resulting ERPs obtained for each target, regardless of performance, were quantified by computing mean amplitude values in selected latency regions relative to baseline at Cz. The amplitudes were determined as an average of 40 milliseconds centered at the grand-average peaks and the latencies as the time point of maximal potential. Scalp topography was assessed at AFz, Fz, FCz, Cz, CPz, Pz, POz, Oz, and FC5, FC3, C5, C3, FC4, C4, FC6, C6.

Results

All measurements were subjected to analyses of variance with repeated measures. The original degrees of freedom for all analyses are reported throughout the article. Type I errors associated with inhomogeneity of variance were controlled by decreasing the degrees of freedom using the Greenhouse–Geisser epsilon, and the probability estimates are based on these reduced degrees of freedom. Post hoc tests were conducted by Fisher's least-significant difference comparisons.

As found previously,[5] the amusic subjects detect large pitch changes as accurately and as quickly as unimpaired subjects but exhibit difficulties at small distances. As shown in Figure 1, they can barely detect changes of 50 and 25 cents. This performance highlights the fine-grained nature of the pitch disorder; it is supported by a significant interaction between Group and pitch Distance, with $F(4,64) = 5.52$ and 5.57, $p < 0.001$, for accuracy and response times, respectively.

This pitch deficit can be seen in the brain responses (Fig 2) where all major ERP components but N1 differentiate amusic from control subjects. N1 was similar in the two groups ($F[1,16] = 1.5$, not significant; there was no interaction between Group and Pitch distance, $F < 1$, for both amplitude and latency), although its generators are slightly more posterior in the
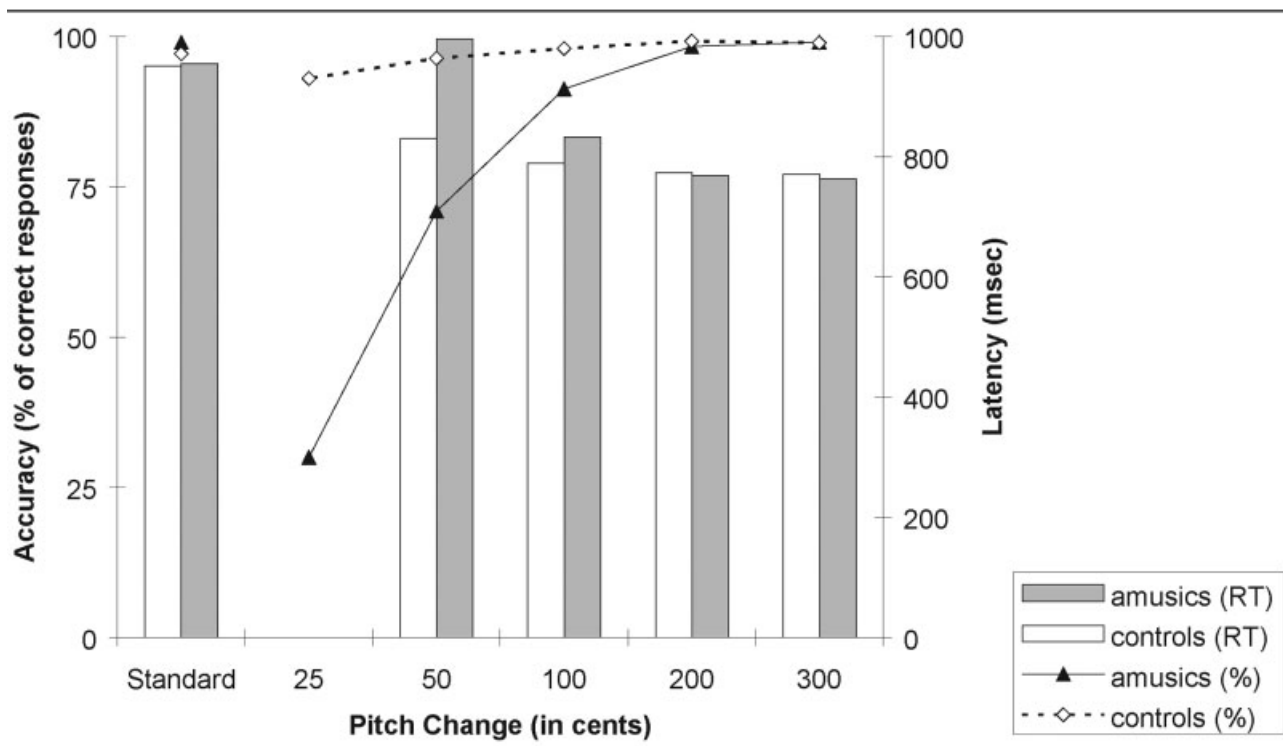

Fig 1. Mean percentages of correct responses and mean latencies response times (RT) of the correct responses obtained by amusic and control subjects as a function of the size of the pitch change. Standard refers to the no-change condition. The mean RTs for the 25-cent conditions are not reported because there were too few measures in amusic subjects.
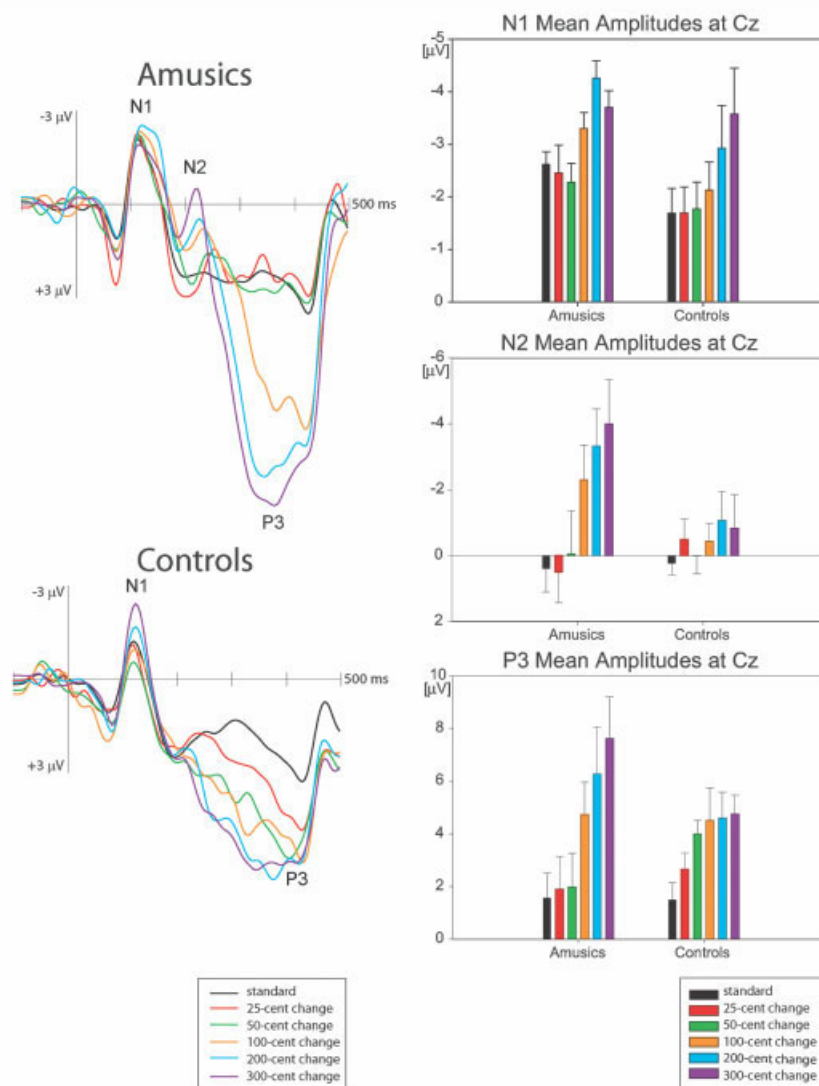
Fig 2. Grand-average standard (black) and pitch-change ERPs (shown in color) at central electrode (Cz) in amusic and control subjects.

amusic brain as shown by Brain Electrical Source Analysis[11] (see Fig 3). The divergent ERP components emerge later, starting with N2 (culminating at 215 milliseconds) that is present in amusic subjects only and in the subsequent P3.

Although P3 peaks at about the same time in both groups (around 400 milliseconds, $t[16] = 1.45$, not significant; see Fig 2), P3 is markedly different in amplitude, with a significant Group $\times$ pitch Distance interaction; $F[5, 80] = 3.7$; $p < 0.01$). For large pitch distances, P3 is enhanced in amusic compared with control subjects, with 7.6 and 4.7μV, respectively ($p < 0.01$). In contrast, for the pitch changes of 25 and 50 cents, the P3 is smaller in amusic subjects ($p < 0.05$), whereas it is similar for standards (1.5μV in each group). Finally, both groups exhibit a clear laterality effect by obtaining much larger P3 responses over

the right (FC4, C4, FC6, C6) than left electrodes (FC5, FC3, C5, C3; $t[7] = 2.45$, $p < 0.05$, and $t[9] = 4.50$, $p < 0.002$ for amusic and control subjects, respectively). However, the P3 was more strongly lateralized to the right side and also more posterior and superior in control subjects (the interaction among Group, pitch Distance, and Electrodes yielding $F[45,720] = 3.07$; $p < 0.001$).

Discussion
The remarkable finding in this study is that the pitch deficit in amusic subjects can be traced down to their brain responses. The amusic brain does not respond to pitch deviances smaller than one semitone, whereas a normal brain does so reliably. In contrast, the amusic brain "overreacts" to large pitch changes by eliciting an N2 (that is not present in normal brains) and a P3 that
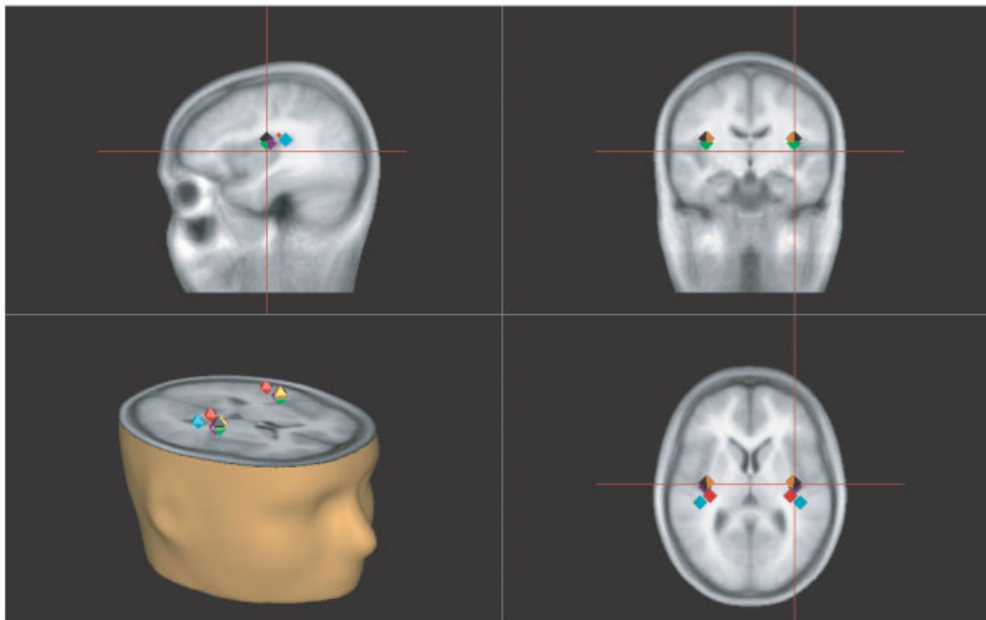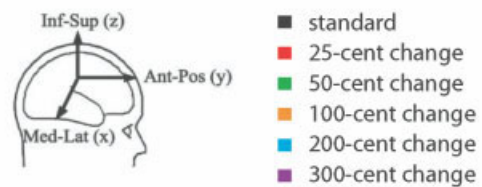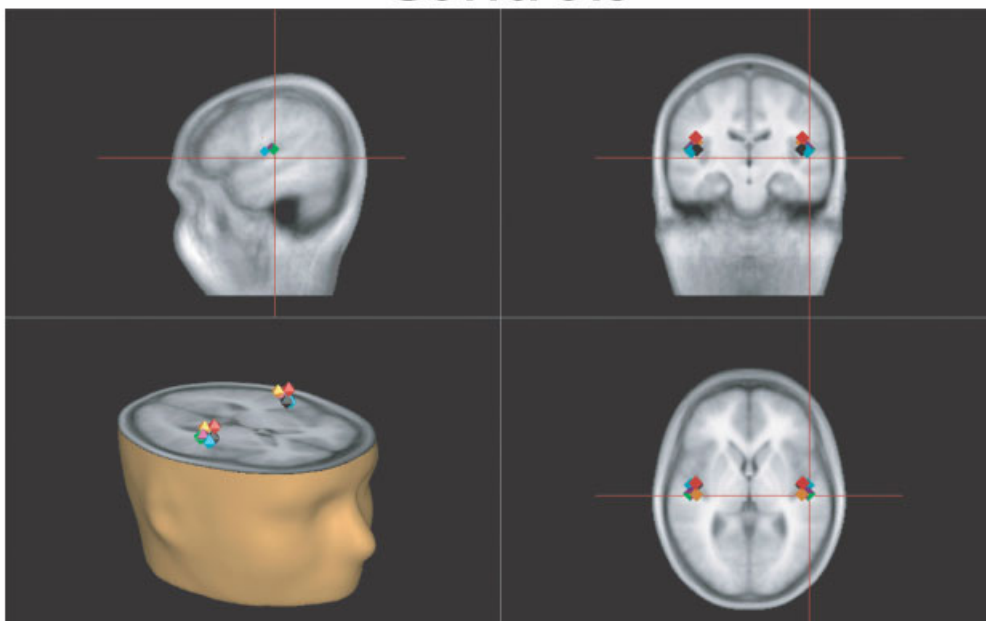
Fig 3. Regional source models of N1 to the largest pitch changes in amusic (top) and control (bottom) subjects. The BESA brain image was generated by averaging the Talairach-transformed magnetic resonance images of 24 adults. There was an interaction between Group and Spatial coordinates (mediotemporal [x], anteroposterior [y], and inferior-superior [z]), with $F(2,32) = 5.65$, $p < 0.01$, indicating that the N1 sources were more posterior in amusic than in control subjects on the z axis.

is almost twice as large as that observed in control subjects' brains. This altered pattern of electrical activity does not appear to arise from an anomalous functioning of the auditory cortex, but rather to show difficulties that occur later along the auditory pathway.

Contrary to expectations, the electrical activity of the auditory cortex of amusic individuals appears intact. Despite a slight difference in N1 generator loci across the two groups, the N1 voltage distribution over the scalp is consistent with a localization of the generators in the secondary auditory cortex.[12] Moreover, our N1 results are in line with preliminary magnetic resonance imaging and functional magnetic resonance imaging data[13–15] suggesting that the neural anomaly in congenital amusia lies outside the auditory cortex.

Support for this conclusion arises from the observation of an enhanced N2-P3 complex in amusic individuals. Unfortunately, lesion and depth electrode studies indicate that the activity indexed by the surface N2-P3 is widespread, probably involving multiple generators in the neorcortical[16] and subcortical regions.[17] Future research will provide insight into which of these neural networks determines the condition of congenital amusia. In the meantime, the N2-P3 brain response can serve as a noninvasive marker of a pitch deficit, which, in turn, may aid to diagnose problems in music acquisition.

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