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Impairments in musical abilities reflected in the auditory brainstem: evidence from congenital amusia

Alexandre Lehmann,[1,2,3] Erika Skoe,[4,5,6] Patricia Moreau,[1,2] Isabelle Peretz[1,2] and Nina Kraus[7,8,9,10]

[1]International Laboratory for Brain, Music and Sound Research (BRAMS), Center for Research on Brain, Language and Music (CRBLM), Pavillon 1420, Montreal, QC H3C 3J7, Canada
[2]Department of Psychology, University of Montreal, Montreal, QC, Canada
[3]Department of Otolaryngology Head & Neck Surgery, McGill University, Montreal, QC, Canada
[4]Department of Speech, Language and Hearing Sciences, University of Connecticut, Storrs, CT, USA
[5]Department of Psychology Affiliate, University of Connecticut, Storrs, CT, USA
[6]Cognitive Science Affiliate, University of Connecticut, Storrs, CT, USA
[7]Auditory Neuroscience Laboratory, Northwestern University, Evanston, IL, USA
[8]Department of Communication Sciences, Northwestern University, Evanston, IL, USA
[9]Department of Neurobiology and Physiology, Northwestern University, Evanston, IL, USA
[10]Department of Otolaryngology, Northwestern University, Evanston, IL, USA

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Abstract

Congenital amusia is a neurogenetic condition, characterized by a deficit in music perception and production, not explained by hearing loss, brain damage or lack of exposure to music. Despite inferior musical performance, amusics exhibit normal auditory cortical responses, with abnormal neural correlates suggested to lie beyond auditory cortices. Here we show, using auditory brainstem responses to complex sounds in humans, that fine-grained automatic processing of sounds is impoverished in amusia. Compared with matched non-musician controls, spectral amplitude was decreased in amusics for higher harmonic components of the auditory brainstem response. We also found a delayed response to the early transient aspects of the auditory stimulus in amusics. Neural measures of spectral amplitude and response timing correlated with participants' behavioral assessments of music processing. We demonstrate, for the first time, that amusia affects how complex acoustic signals are processed in the auditory brainstem. This neural signature of amusia mirrors what is observed in musicians, such that the aspects of the auditory brainstem responses that are enhanced in musicians are degraded in amusics. By showing that gradients of music abilities are reflected in the auditory brainstem, our findings have implications not only for current models of amusia but also for auditory functioning in general.

Introduction

Congenital amusia is a disorder affecting 2.5% of the population, characterized by a deficit in music perception and production. The deficits cannot be explained by hearing loss, frank brain lesions, intellectual deficiencies or lack of exposure to music (Stewart, 2011; Peretz, 2013). Despite their inferior performance on musical tasks, particularly those involving fine-grained pitch discrimination (e.g. Peretz *et al.*, 2002), amusics exhibit normal pre-attentive auditory cortical responses to pitch changes. Specifically, early components of cortical event-related potentials (MMN and N200) to eighth-tone pitch deviations are normal, whereas the later P300/600 component, associated with conscious detection of pitch deviations, is absent (Moreau *et al.*, 2009; Peretz *et al.*, 2009). Anatomical anomalies, such as increased cortical thickness in the right temporal and inferior frontal gyrus (Hyde *et al.*, 2007) and reduced arcuate fasciculus connectivity (Loui *et al.*, 2009) have linked musical impairments in congenital amusia to a disturbed fronto-temporal network of cortical regions implicated in musical processing (Hyde *et al.*, 2011).

However, recent evidence suggests that early auditory cortical responses – indexed by the magnetoencephalography component N100 m – are diminished in amusics (Albouy *et al.*, 2013; see also Omigie *et al.*, 2013). Yet to date, there is no evidence of subcortical anomalies in congenital amusia – (Cousineau *et al.*, 2015). Current research on subcortical responses shows a relationship between musical training and expertise and sound processing at the brainstem (reviewed by Kraus & Chandrasekaran, 2010; Strait & Kraus, 2014), suggesting that musical impairments might likewise affect complex auditory brainstem responses (cABRs). Musicians, both young and old, show enhanced encoding of harmonics compared with non-musicians (Musacchia *et al.*, 2008; Strait *et al.*, 2011; Parbery-Clark *et al.*, 2012; Skoe & Kraus, 2013) as well as earlier responses to the onset and temporally dynamic components of sound (Musacchia *et al.*, 2007; Strait *et al.*, 2014) compared with non-musicians. This observed enhancement correlates with the extent

Correspondence: Dr I. Peretz, [1]BRAMS, as above.
E-mail: isabelle.peretz@umontreal.ca

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and onset of musical experience (Musacchia *et al.*, 2007; Wong *et al.*, 2007) and with music aptitude across musically trained and untrained individuals (Strait *et al.*, 2011). The corticofugal system, a network of efferent fibers linking cortical to subcortical auditory structures, is also stronger in musicians (reviewed by Perrot & Collet, 2014), suggesting that the corticofugal system plays a role in mediating music-related subcortical plasticity (Kraus & Chandrasekaran, 2010).

Here we investigated whether congenital amusia is associated with subcortical anomalies. Because cABRs are enhanced in musicians, we predicted that musical disorders would also exert an effect on those responses, through a cortical anomaly that has led over time to impaired cABRs via top-down, corticofugal influences (Rebuschat *et al.*, 2012). To test this possibility, we recorded cABRs in congenital amusic adults and non-musician controls. We expected that group differences would parallel those observed between non-musicians and musicians. In other words we expected that the components of the brainstem response that are enhanced in musicians to be weaker in amusics. As is the case for musicians, we also predicted a relationship between the degree of manifestation of the disorder and the temporal and spectral characteristics of the subcortical response.

Methods

The experimental procedures conformed to the World Medical Association's *Declaration of Helsinki* and were approved by the Research Ethics Committee of the Faculty for Arts and Sciences of the University of Montreal.

Participants

Ten congenital amusics and 11 controls gave informed consent to participate in the experiment. Participants were categorized as amusic if their composite score on the Montreal Battery of Evaluation of Amusia (MBEA) was more than two standard deviations below controls (Peretz *et al.*, 2003). The MBEA is the primary diagnostic tool for amusia; it is a normed test consisting of six tests using the same pool of 30 novel musical melodies. Each test is a two-alternative forced choice that assesses the functioning of the various processing components involved in Western tonal music, including melody, rhythm, meter and memory. Table 1 shows MBEA global score, audiometry and demographic information for the two groups.

All participants were submitted to an audiometric evaluation and click-evoked ABR testing to assess their hearing. To be included in the study, participants were required to have age-appropriate hearing thresholds ≤ 40 dB normal hearing level at 2 kHz, ≤ 60 dB at 4, 6 and 8 kHz, and no more than 20 dB difference between ears at any two frequencies. Furthermore, a visible, above baseline wave V was required in the click ABR. Data from one control participant were excluded because of a noisy electroencephalogram (EEG) recording. Results are presented from the ten congenital amusics (three males) and the remaining ten matched control participants (one male). Both groups had minimal musical training, with an average of < 1.5 years.

EEG stimuli and recording parameters

cABRs were recorded to a click sound (100-μs square wave) and a 40-ms speech syllable /da/. The speech sound, created with a Klatt-based synthesizer, has been used extensively in previous cABR studies from Kraus and colleagues (e.g. Skoe *et al.*, 2015). This stimulus has a fundamental frequency (F0) that rises linearly from 103 to 121 Hz with voicing beginning at 5 ms and onset noise burst occurring during the first 10 ms.

Brainstem EEG recordings were collected while click and speech were presented binaurally at 70 dB SPL through ER-2 insert earphones (Etymotic Research, Elk Grove Village, IL, USA) driven by a programmable hardware signal processor (Tucker Davis Technology, Alachua, FL, USA) controlled by a custom stimulation program in MATLAB (The Mathworks, Natick, MA, USA). Stimuli were calibrated with an SE SoundPro DL 1/3 octave level meter (Quest Technologies, London, UK) using a 2-CC ear coupler (Quest electronics, WI, USA) with appropriate rates, i.e. impulse for click and fast rate for the speech syllable, using the A-weighting frequency curve. Six thousand responses to each stimulus were collected. Stimuli were presented in alternating polarities (Skoe & Kraus, 2010), using a repetition rate of 20 Hz for clicks and 11.1 Hz for the syllables, corresponding to a stimulus-onset asynchrony of 50 and 90 ms, respectively.

A vertical montage of five active sintered Ag/AgCl electrodes was used to record neurophysiological responses (central vertex, left and right earlobes, two ground electrodes on the central forehead). Active electrodes contain the first amplifier stage within the electrode cover (BioSemi, Amsterdam, the Netherlands), and provide impedance transformation on the electrode to prevent interference currents from generating significant impedance-dependent nuisance voltages. We therefore did not control electrode impedances but rather kept direct-current offset close to zero during electrode placement. Reference-free electrode signals were amplified with a BioSemiActiveTwo amplifier (BioSemi), sampled at 16 384 Hz, and stored for offline analysis using BioSemi ActiView software. During testing, subjects sat comfortably in a reclining chair inside a faradized soundproof room. To maintain relaxation and prevent drowsiness, subjects were instructed to watch a self-selected subtitled movie without soundtrack.

Analyses

Pure-tone audiometry

Pure-tone audiometric thresholds were grouped in three frequency bands (Low: 0.5, 1 kHz, Mid: 2, 3, 4 kHz; High: 6, 8 kHz). To

TABLE 1. Participant characteristics

	MBEA	Audiometry (dB HL)			Click-ABR	Demography	
Group	Global Score (%)	Low	Mid	High	Wave V latency (ms)	Age (years)	Musical education (years)
Control	92 (3)	18.8 (13.3)	19.1 (12.6)	32.9 (14.1)	6.25 (0.55)	64.3 (5.1)	1.3 (1.6)
Amusic	63 (6)	13.1 (8.1)	21.2 (13.1)	31.3 (14.3)	6.39 (0.36)	64.8 (5.6)	0.9 (1.0)

Means and standard deviations (in parentheses) are reported for the Control and Amusic groups. Pure-tone audiometric thresholds were averaged across three frequency bands (Low: 0.5, 1 kHz; Mid: 2, 3, 4 kHz; High: 6, 8 kHz).

confirm that the groups were matched, we then performed a 3 × 2 × 2 repeated-measures analysis of variance (ANOVA) with frequency (Low, Mid, High) and ear (L, R) as within-subject factors and group (Amusic, Control) as between-subject factors and used a Greenhouse – Geisser correction.

Auditory brainstem response

Analysis of the brainstem EEG was conducted using custom software in MATLAB, as well as EEGLAB (Delorme & Makeig, 2004) and the Brainstem Toolbox (Skoe & Kraus, 2010). Responses were processed off-line by referencing to the average recording from the earlobes. They were then filtered from 100 to 1000 Hz (Butterworth filter, 12 dB per octave) to isolate the subcortical component of the EEG from the more low-frequency cortical component (Chandrasekaran & Kraus, 2010; Skoe & Kraus, 2010). The recordings were subsequently epoched with an interval of −10 to 90 ms for the /da/ sound and from −5 to 15 ms for the click. Trials with activity exceeding ±35 μV were considered artifacts and were excluded from the average. Across all participants, peak latencies were corrected to account for the delay introduced by the insert tubes and other equipment within the signal delivery chain. Separate averages were obtained for each stimulus polarity.

Added and subtracted responses to alternating polarities were computed to analyse both low- and high-frequency components of the neural response, respectively. Adding responses to alternating polarities maximizes low-frequency components of the response, including phase-locking to the (low-frequency) stimulus envelope; it also minimizes the cochlear microphonic and stimulus artifact (Skoe & Kraus, 2010). Subtracting emphasizes higher frequency components of the response but may accentuate artifact contamination (Aiken & Picton, 2008; Skoe & Kraus, 2010). Each individual subtracted waveform was visually inspected for both stimulus and cochlear microphonic artifacts and only subjects deemed by two raters to not have artifact contamination were included in the upper frequency analysis (>400 Hz) (six amusics and six matched controls). The stimulus and cochlear microphonic artifacts can be differentiated from the cABR by their earlier time signature.

Click responses were collected to assess the integrity of peripheral auditory pathway and to ensure that wave V latency, a commonly used audiological index (Hood, 1998), was matched between groups. All latency analyses were performed on the added response waveforms. Latency values were first extracted using a peak-picking algorithm and then refined based on observation (Skoe & Kraus, 2010).

Analysis of the responses to the /da/ stimulus followed published reports using similar stimuli and recording parameters (Russo *et al.*, 2004). The primary dependent measures were: peak latency in the temporal domain and response amplitude encompassing frequencies of interest in the spectral domain. For the latency analysis, we first identified the prominent positive-going peaks in the grand average waveform created by averaging all subjects independent of group membership (Fig. 1B, seven peaks total). Collapsing across groups, the average latencies of the seven peaks were: (1) 6.89, (2) 10.58, (3) 15.08, (4) 21.85, (5) 30.63, (6) 38.88 and (7) 47.85 ms. Peak 1 corresponds to the response to the onset of sound, peaks 2 and 3 correspond to the transition between the stop-burst and the onset of voicing, peaks 4–6 are the dominant peaks within the frequency-following response (FFR) and correspond to phase-locking to the fundamental frequency and its harmonics, and peak 7 reflects the offset response. The latencies of these seven peaks in the grand average were then used as the basis for performing an automated peak detection procedure on the individual waveforms to find the local maximum within ±1 ms of the average latency for that peak. Following the application of the automated routine, the latencies were refined based on visual inspection. If visual observation revealed that the amplitude of the peak was not above the amplitude of the pre-stimulus period, it was coded as ‘not reliable, nr’ and excluded from analysis. For peak 1, reliability was 100% in the control group and 90% in the Amusic group. For peak 2, reliability was 90% for the control group and 80% for the

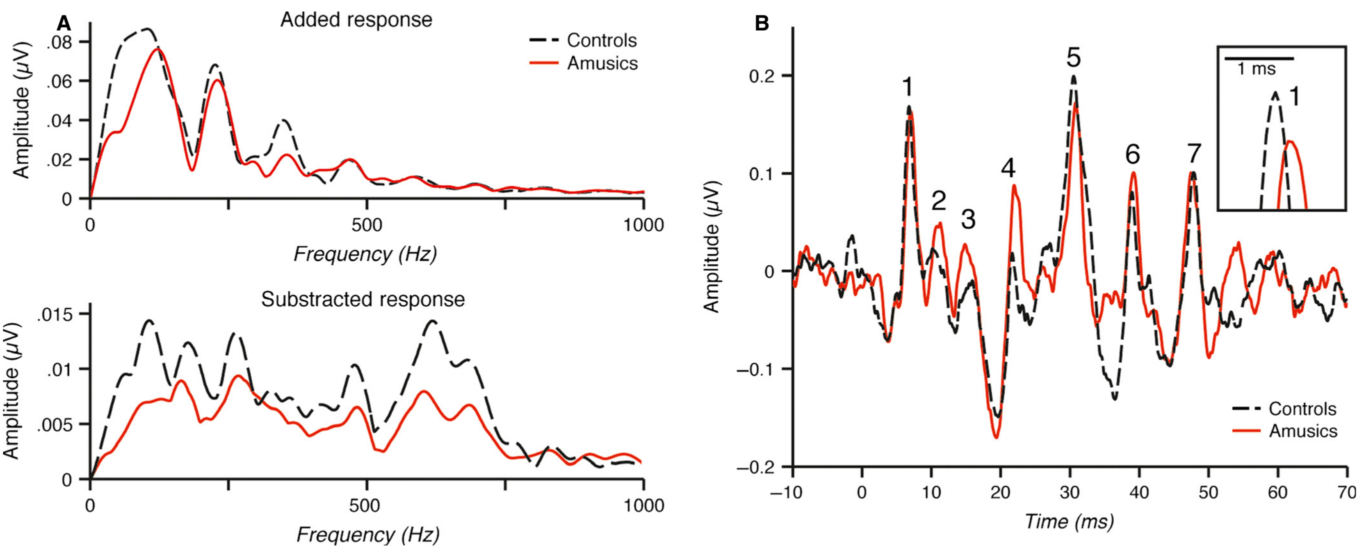

FIG. 1. Grand-average auditory brainstem response to complex sound /da/ (cABR). (A) Frequency domain. Amusics (solid) have weaker encoding of higher harmonics than controls (dashed), as illustrated in the fast Fourier transform (FFT) of the grand average FFRs obtained by adding (top panel) and subtracting (bottom panel) responses to alternating stimulus polarities. In the visual depiction of the data, the spectral maxima occur at slightly different frequencies in the grand-average waveform for the two groups, although this is an artifact of the averaging process and does not reflect systematic differences between the groups. (B) Time domain. Amusics (solid) have slower response onset latencies (peaks 1–3) than controls (dashed). Subpanel shows a magnified view of peak 1.

Amusic group. The remaining peaks had 100% reliability in both groups.

To increase statistical power for this limited dataset, two composite values were computed to reflect different time regions of the response: 'onset response' (peaks 1–3, occurring between 7 and 20 ms) and 'FFR-offset response' (peaks 4–7, occurring between 20 and 50 ms). To derive these composite measures for each individual, the latency of each peak was first normalized by subtracting the value of the average latency for that peak and then averaging the normalized latencies across peaks 1–3 for the onset index and peaks 4–7 for the FFR-offset index. If the peak was 'nr', it was not factored into the average calculation. The composite measures do not reflect the raw latencies but instead indicate the extent (in ms) to which a given individual deviates from the average, with a positive value indicating that the response is delayed from the average and a negative value indicating that the response is earlier than the average.

Amusic and control groups were compared on these composite measures using a repeated-measures ANOVA with time region (onset vs. FFR-offset) as the within-subject factor and group as the between-subject factor.

Spectral encoding was analysed using a zero-padded Fourier analysis of the FFR (22–45 ms). Average spectral amplitude was calculated for six frequency ranges: fundamental frequency (F0, 103–121 Hz) as well as four 100-Hz-wide bins centered relative to the harmonics of F0, including H2 (230 Hz), H3 (350 Hz), H4 (475 Hz) and H5 (620 Hz). Following published reports using similar stimuli and population demographics (Anderson *et al.*, 2012b, 2013a), spectral amplitudes around F0, H2 and H3 were assessed using added-polarity responses whereas H4 and H5 amplitudes were evaluated using subtracted-polarity responses. Because the number of participants differs between the added and subtracted polarity response measures, an ANOVA was not used here. Instead, for each of the five spectral measures, amusic and control populations were compared using a two-tailed paired Student test (*t*-test). To control for family-wise error, the Holm–Bonferroni method (Holm, 1979) was used to adjust *P*-values.

Pearson correlation coefficients were computed between the neural measures and age, education and the global MBEA scores. A significance level of 5% was used for all statistical tests.

Group matching

Amusics and controls were matched for age and musical education (Table 1). Mean age and years of musical education did not differ between groups ($t_{18} = 0.21$, $P = 0.84$; $t_{18} = 0.68$, $P = 0.51$, respectively). Groups were matched on pure tone audiometry: there was no main effect of group ($F_{1,18} = 0.11$, $P = 0.75$) or of ear ($F_{1,18} = 0.51$, $P = 0.82$), nor significant interactions. Average latency of click-evoked wave V was comparable between groups ($t_{18} = 0.67$, $P = 0.51$).

Results

Diminished high-frequency responses in amusics

Spectral amplitude around the fundamental frequency (F0) and the first harmonic (H2) did not differ between amusics and controls (Fig. 2A: F0 $t_{18} = 0.59$, Holm–Bonferroni adjusted *P*-value = 1; H2 $t_{18} = 0.65$, adjusted-$P = 1$). In contrast, for harmonic ranges above H2, amusics had smaller spectral amplitudes (Fig. 2A; H3: $t_{18} = 3.09$, adjusted-$P = 0.024$; H4 $t_{10} = 2.92$, adjusted-$P = 0.045$; H5: $t_{10} = 4.27$, adjusted-$P = 0.005$).

Delayed brainstem responses in amusics

For the composite latency measures, there was a significant interaction between time region and group ($F_{1,18} = 12.38$, $P = 0.002$) but no main effect of time ($F_{1,18} = 0.00$, $P = 0.93$) nor main effect of group ($F_{1,18} = 0.72$, $P = 0.40$) (Fig. 2B). Post-hoc analyses revealed that the amusic group was delayed by 0.64 ms relative to the control group for the onset peaks ($t_{18} = 2.492$, $P = 0.023$) but that the latency of the later peaks (FFR offset) was more comparable ($t_{18} = -0.764$, $P = 0.455$).

Correlations between brainstem responses and musical ability

Musical ability assessed via the MBEA correlated with brainstem physiology (Table 2), such that higher behavioral scores mapped to greater harmonic amplitude and faster onset responses (Fig. 2C). MBEA global score correlated positively with the spectral amplitude measured at harmonics H3 and H5 ($r = 0.55$, $P = 0.013$ for H3; $r = 0.77$, $P = 0.003$ for H5). MBEA global score correlated negatively with the onset peaks ($r = -0.461$, $P = 0.041$).

Discussion

We show that fine-grained processing of sound acoustics, as captured by cABR, differs from the normal range in congenial amusia. We find decreased spectral encoding and slower onset responses in amusics compared with matched controls. In addition to differences between groups, these neural variables correlated with musical ability, with harmonic coding being weaker and responses becoming more delayed with an increasing severity of amusia (Fig. 2A and B). This neural profile of amusia mirrors what has been observed in musicians, such that the aspects of sound encoding that are enhanced in trained musicians (Musacchia *et al.*, 2007, 2008) appear to be depressed in amusics compared with non-musician controls. Taken together, the results suggest that gradients of musical ability are reflected in the cABR.

Top-down origin of the cABR correlates of amusia

What is the origin of these cABR correlates of amusia? Given that amusics were audiometrically matched to controls, this minimizes the possibility that the group differences are the result of peripheral factors, and instead favors a central explanation. If the cABR profile is indeed central in origin, it could either pre-date the well-described cortical differences observed in amusia (Peretz *et al.*, 2002; Loui *et al.*, 2009; Hyde *et al.*, 2011) or emerge as the result of the congenital cortical anomalies. Given the mature age of our population (average age is 64 years), we are not in a position to assess whether the brainstem anomalies we observe here are the cause or consequence of amusia. However, we can provide a speculative explanation for how these abnormalities might emerge.

Within the auditory system, cortical and subcortical structures are highly interconnected and interact in a bottom-up and top-down fashion via afferent and corticofugal pathways. The auditory brainstem processes the fast aspects of sound (e.g. onsets and offsets), through an interactive circuit that involves peripheral, cortical and subcortical auditory, as well as non-auditory, centers. The corticofugal pathway system contains a massive array of efferent fibers that project from deep layers of the auditory cortex. Through this efferent circuitry, cortical structures can exert their influence on subcortical structures and the cochlea, to fine-tune how behaviorally relevant signals are processed (Suga *et al.*, 2000; Suga & Ma,

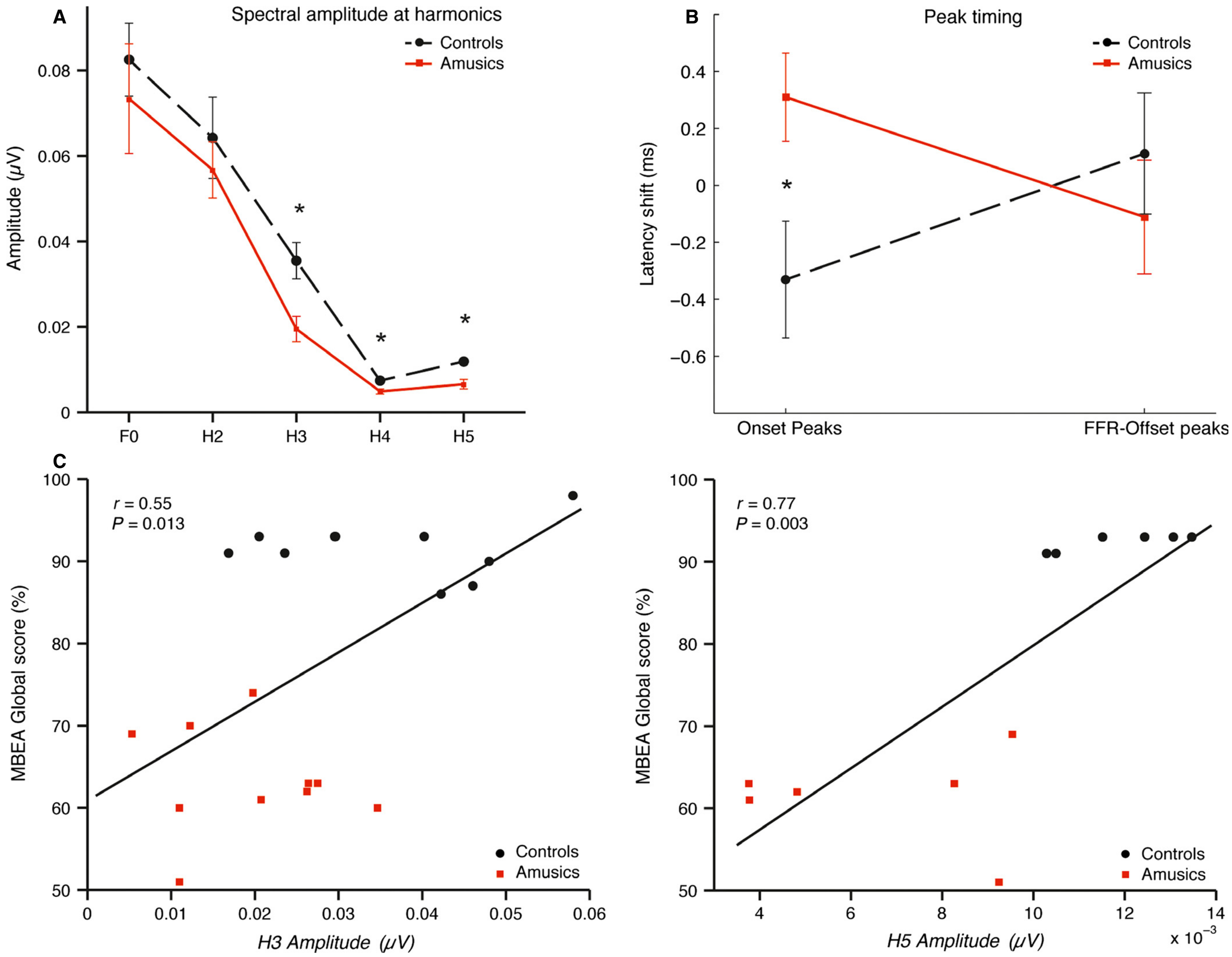

FIG. 2. Brainstem encoding is diminished in congenital amusics. (A) Mean spectral amplitudes around the fundamental frequency (F0) and the second to fifth harmonics (H2, H3, H4, H5) are shown for the amusic (squares solid line) and control (circles dashed line) groups. Error bars represent 1 SEM. (B) Latency shift (relative to grand average) of the response onset peaks and offset peaks (Onset and FFR-Offset) are shown for the amusic (squares solid line) and control (circles dashed line) groups. Error bars represent 1 SEM. (C) Mean spectral amplitudes of the third and fifth harmonics correlate with musical ability as assessed by the MBEA global score (amusics are shown as squares and controls as circles). $^*P < 0.05$.

TABLE 2. Correlations among dependent variables

Brain behavior	F0	H2	H3	H4	H5	Onset peaks	FFR-Offset peaks
Age	$r = -0.29$ $P = 0.214$	$r = 0.25$ $P = 0.283$	$r = -0.38$ $P = 0.097$	$r = -0.51$ $P = 0.091$	$r = 0.22$ $P = 0.493$	$r = -0.153$ $P = 0.518$	$r = 0.158$ $P = 0.507$
Education	$r = -0.08$ $P = 0.724$	$r = -0.38$ $P = 0.103$	$r = -0.29$ $P = 0.213$	$r = 0.06$ $P = 0.845$	$r = 0.34$ $P = 0.273$	$r = 0.197$ $P = 0.406$	$r = 0.054$ $P = 0.820$
MBEA global	$r = 0.04$ $P = 0.862$	$r = 0.02$ $P = 0.942$	**$r = 0.55$** **$P = 0.013$**	$r = 0.52$ $P = 0.081$	**$r = 0.77$** **$P = 0.003$**	**$r = -0.461$** **$P = 0.041$**	$r = 0.121$ $P = 0.612$

Significant correlations are shown in bold type.

2003). If the cortical auditory processing centers are compromised, this could interfere with normal corticofugal feedback to ultimately negatively affect how auditory signals are processed in the brainstem. Indeed, there is evidence indicating that experience-dependent plastic changes can be observed in the cortical areas before they can be seen in the auditory brainstem in rodents (Lu *et al.*, 2014). In the case of amusia, we propose that cABR anomalies may result from the impoverished fronto-temporal connectivity found in this population (Loui *et al.*, 2009; Hyde *et al.*, 2011), which over a lifetime has compromised subcortical auditory processing through faulty top-down feedback, impacting specific aspects of sound processing in the brainstem.

It is interesting to note that the subcortical anomalies found in the auditory brainstem responses in amusia correspond to the components that are most sensitive to musical experience, namely harmonic encoding and response timing (Skoe & Kraus, 2013; reviewed by

Strait & Kraus, 2014). These aspects may be particularly sensitive to regular experience with music. While amusics are not musically deprived, they certainly have impoverished musical experiences by refraining from engaging in musical activities such as singing and dancing. Another, not mutually exclusive explanation is that our findings are the result of impaired top-down attentional monitoring (originating from the attentional hubs located in the frontal lobes). There is substantial evidence that backward propagation from the inferior frontal gyrus to the auditory cortex is dysfunctional in amusics (Hyde *et al.*, 2011; Albouy *et al.*, 2013). This poor fronto-temporal connectivity may compromise normal shaping of auditory responses in both the auditory cortex and the brainstem. Likewise, dyslexic participants show a comparable cABR profile to the amusia group, which has been suggested to result from a similar top-down mechanism (Banai *et al.*, 2009; Chandrasekaran & Kraus, 2012; Kraus & Nicol, 2014).

Domain generality of auditory brainstem anomalous response

This study used a speech stimulus to probe subcortical processing in amusia. Our results are consistent with prior findings showing mild impairments in amusia for processing speech stimuli. A mild deficit in processing intonation has been documented in both non-tonal and tonal language-speaking amusics (Patel *et al.*, 2008; Hutchins & Peretz, 2012; Liu *et al.*, 2012). This issue of domain transfer in amusia, however, deserves further attention and could be addressed using directly comparable speech and music stimuli (e.g. Musacchia *et al.*, 2007). Studying cABR in tone-language amusic populations may allow vocal and musical features to be more directly contrasted. Domain-transfer effects may reflect that music requires more precision than speech in the processing of timing and periodicity. This precision may drive experience-dependent plasticity in subcortical networks that process such features and that overlap across domains (Patel, 2011, 2014). The mechanism that enhances precision of auditory brainstem processing may be less well tuned in non-musicians than in musicians and even less so in amusics.

A subcortical deficit to be remediated?

Subcortical processing can be altered by short-term training (Song *et al.*, 2008; Carcagno & Plack, 2011; Anderson *et al.*, 2013b; Tierney *et al.*, 2013). Relevant to the current study are data showing that short-term training can improve subcortical response timing in children undergoing musical training (Tierney *et al.*, 2013; Kraus *et al.*, 2014) and older adults who have participated in auditory training (Anderson *et al.*, 2013b). This raises the question of whether similar training paradigms might prove beneficial in amusia. Attempts of musical rehabilitation either through music exposure or vocal training in amusia have shown little to no improvement (Anderson *et al.*, 2012a; Mignault-Goulet *et al.*, 2012), suggesting that training might not be sufficient to overcome lifelong cortical changes that led to the subcortical deficit in the first place.

Limitations and future directions

We contrasted two groups of participants who were differentiated based on their musical abilities (MBEA scores). In each group, there was dense clustering of MBEA scores, with a clear separation between the groups. Expanding the dataset to include a wider range of performance that samples the full continuum of musical scores is necessary to better understand how fine gradients of musical abilities are reflected in the auditory brainstem.

This study focused exclusively on subcortical processing of sound. To further elucidate the link between cortical and subcortical correlates of congenital amusia, future studies should take advantage of methodological advances that allow cortical and subcortical activity to be recorded simultaneously (S. Nozaradan, M. Schönwiesner, L. Caron-Durocher & A. Lehmann, unpublished data; Krizman *et al.*, 2014).

The present study opens the door to a more systematic evaluation of auditory brainstem processing of complex sounds in congenital amusia in children and young adults, using a cross-sectional or longitudinal design. This would help to reveal whether subcortical anomalies manifest differently at different points in an amusic's life. By tracing how brainstem function changes as a function of both age and experience, the mechanisms underlying our reported effects can be better delineated.

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Abbreviations

ANOVA, analysis of variance; cABR, complex auditory brainstem response; EEG, electroencephalogram; FFR, frequency-following response; MBEA, Montreal Battery of Evaluation of Amusia.

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