

Original Article

The left dorsal stream causally mediates the tone labeling in absolute pitch

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Absolute pitch (AP) refers to the ability to effortlessly identify given pitches without any reference. Correlative evidence suggests that the left posterior dorsolateral prefrontal cortex (DLPFC) is responsible for the process underlying pitch labeling in AP. Here, we measured the sight-reading performance of right-handed AP possessors and matched controls under cathodal and sham transcranial direct current stimulation of the left DLPFC. The participants were instructed to report notations as accurately and as fast as possible by playing with their right hand on a piano. The notations were simultaneously presented with distracting auditory stimuli that either matched or mismatched them in different semitone degrees. Unlike the controls, AP possessors revealed an interference effect in that they responded slower in mismatching conditions than in the matching one. Under cathodal stimulation, this interference effect disappeared. These findings confirm that the pitch-labeling process underlying AP occurs automatically and is largely nonsuppressible when triggered by tone exposure. The improvement of the AP possessors' sight-reading performances in response to the suppression of the left DLPFC using cathodal stimulation confirms a causal relationship between this brain structure and pitch labeling.

Keywords: cathodal tDCS; Stroop; interference; sight-reading; musicians

Introduction

Absolute pitch (AP) is the ability to effortlessly identify the chroma of a tone without the aid of any reference pitch.^{1,2} This ability is sparsely distributed in the population (<1%),³ yet it bears phylogenetic and ontogenetic significance.⁴ There is considerable scientific consensus on its acquisition, namely that AP emerges from an interplay of a certain genetic predisposition and specific environmental inputs and learning factors (i.e., music engagement and language exposure) that operate within a sensitive period during childhood development.^{5–12} By contrast, lesser consensus exists on the exact mechanisms and involved brain structures driving AP. One brain structure frequently reported to contribute to AP is the planum temporale (PT),^{13–19} a region

that covers the superior temporal plane posterior to the Heschl's gyrus and is involved in language and higher auditory functions.^{20–23} In AP possessors, the PT is likely responsible for a higher resolution in the pitch perception of categories; in other words, the encoding of tones within narrower long-term stored categories.^{11,19,24,25} Neuroimaging studies have found an increased leftward asymmetry of the PT,^{15–17} possibly underlying this so-called categorical pitch perception in AP.^{13,14} In the right brain hemisphere, this structure, together with a network comprising the Heschl's gyrus and some nonauditory structures, was found to have an impact on AP perception.²⁶ Another brain structure reported to be related to AP is the left posterior dorsolateral prefrontal cortex (DLPFC). This area drives conditional associative learning and memory.^{27–32}

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In the context of AP, the posterior DLPFC may be responsible for the process underlying the association between categorized pitches and verbal labels or other abstract or sensorimotor codes;^{33–35} in other words, the pitch-labeling process. Neuroimaging studies revealed that AP possessors exhibit comparatively thinner cortical thickness there³⁶ and selectively recruit this particular brain region during mere tone listening.³⁴ In the same study, musicians without AP recruited this region while performing an interval-labeling task. However, they additionally recruited the right inferior frontal gyrus (IFG),³⁴ an area involved in working memory (WM) retrieval.^{37,38} Conversely, AP possessors did not show this additional activation while performing the same task. This lack of IFG involvement suggests that AP underlies an automatic pitch-labeling process, functioning without the use of WM resources. A series of experiments using electroencephalography (EEG) confirmed this interpretation and provided corroborative evidence for the specificity of the pitch-labeling process underlying AP. In auditory oddball or labeling tasks, AP possessors displayed absent, reduced, or accelerated specific electrophysiological responses pertaining to the P3 complex,^{39–44} reflecting a more efficient and parsimonious tone processing in AP. Further event-related EEG components representing hierarchically higher cognitive processes were found to be specific and linked to the labeling performance of AP possessors.⁴⁵

The purpose of the present study was to investigate the causal role of the left DLPFC in the pitch-labeling process underlying AP by applying a cathodal-sham transcranial direct current stimulation (tDCS) protocol. Cathodal tDCS suppresses cortical excitability of the targeted region, diminishing its underlying function.⁴⁶ Given that the pitch-labeling process in genuine AP occurs automatically and thus is rather nonsuppressible,^{25,44,47–52} a modulation in the pitch-labeling performance as a result of cathodal stimulation of the left DLPFC would reveal its causal impact on AP. During cathodal and sham stimulation, participants with AP and matched control participants without AP were instructed to sight-read, reporting the presenting notations as accurately and fast as possible by playing with their right hand on a piano. Sight-reading, the practice of reading and immediately performing notations on an instrument or by singing, is

an activity that musicians with and without AP easily master. Simultaneously, auditory stimuli were presented during the task that either matched with the notations or mismatched with them. However, these tones were irrelevant to the task. This experimental setup corresponded to a so-called Stroop paradigm.^{53,54} The Stroop paradigm measures the interference in performances resulting from conflicting asymmetrical processes, namely between overlearned automatically running and more effortful processes. The classical Stroop experiments revealed the robust finding of worsened color-naming performance when participants were challenged to name depicted colors of color names semantically standing for different colors.^{53,54} In the case of the classical Stroop task, the interference is due to the fact that reading is virtually overlearned among literate people, making the execution of the less familiar practice, namely color naming, demanding when simultaneously suppressing the decoding of target words. Meanwhile, this Stroop principle was extended to capture interference effects across multiple domains,⁵⁴ including music cognition,^{55–57} but also to verify the authenticity of conditions, such as synesthesia^{58–60} and AP,^{44,47,51} both of which are characterized by nonsuppressible uncommon additional experiences that are inaccessible to outsiders.

In accordance with the Stroop paradigm,^{53,54} we expected that only AP possessors reveal an interference in the mismatching trials, resulting from the distraction in performing the actual sight-reading task owing to the unique pitch-labeling process automatically triggered by tone exposure. Thus, this interference is expected to be reflected as a performance drop in the sight-reading activity. Furthermore, we expected this drop to diminish when suppressing the left DLPFC using cathodal stimulation. Should the automatic pitch-labeling process be driven by the left DLPFC, then suppressing its cortical excitability is expected to diminish its function, leading to less interference with the sight-reading activity and, therefore, to an improvement in performing this task.

Material and methods

Participants

A sample of 36 healthy musicians participated in this study, of which half were AP possessors (13 females) and the others were non-AP (NAP)

Table 1. Characteristics and data on the musical background of the two samples

	AP	NAP
Age (years)	27.83 (10.14)	33.56 (8.23)
Cognitive capability (IQ scores)	123.33 (11.25)	122.05 (13.20)
Age at commencement of musical practice (years)	5.36 (1.55)	6.67 (2.47)
Duration of musical training (years)	22.47 (9.95)	26.61 (7.3)
Advanced Measures of Music Audition test (raw scores)	65.33 (7.34)	64.33 (8.56)
Tonal (raw scores)	31.89 (4.27)	31.89 (4.33)
Rhythm (raw scores)	33.44 (3.42)	32.44 (4.57)

Listed are the means with the standard deviations in parentheses. All independent-samples *t*-test calculated for each variable revealed the values of $P > 0.05$. AP, absolute pitch; NAP, nonabsolute pitch (each $N = 18$).

control participants (12 females). All participants were right-handed, as determined using the Annett Handedness Inventory⁶¹ and the Edinburgh Handedness Inventory.⁶² The two samples were comparable regarding age ($t_{34} = 1.86$, $P = 0.07$, $d = 0.62$), the distribution of the sexes ($\chi^2_1 = 0.13$, $P = 0.72$), general cognitive capability ($t_{34} = 0.2$, $P = 0.84$, $d = 0.10$) as measured by a standard German intelligence screening test (“Kurztest für allgemeine Intelligenz”),⁶³ and musical aptitude (tonal: $t_{34} < 0.01$, $P = 1$, $d < 0.01$; rhythm: $t_{34} = 0.74$, $P = 0.46$, $d = 0.25$; total: $t_{33,23} = 0.09$, $P = 0.71$, $d = 0.13$) as evaluated using the Advanced Measures of Music Audition test.⁶⁴ Both AP and NAP participants commenced their musical training at a comparable age range ($t_{34} = 1.90$, $P = 0.07$, $d = 0.63$) and trained for a comparable number of years ($t_{34} = 1.09$, $P = 0.29$, $d = 0.47$). Six participants of the AP sample and seven of the NAP sample professionally played the piano as their first instrument. This distribution (binary categorization of a “pianist” versus a “non-pianist”) did not differ between the two samples ($\chi^2_1 = 0.12$, $P = 0.72$). However, all participants were skilled at playing the piano, as this instrument was taught during music education as part of their professional degree program. The values on characteristics and musical background are reported in Table 1. All participants gave written informed consent to a protocol that was approved by the Cantonal Institutional Review Board of Zurich.

AP verification

AP was confirmed using an established pitch-labeling test previously used in multiple studies on AP.^{43,65–67} In this test, the participants were instructed to immediately write down the accordant tonal label of corresponding sine tones (A4

tuned at 440 Hz) presented to them. Hundred and eight tones covering three octaves from A3 to A5 were presented in a pseudorandomized order. Each tone was presented three times, the same tones were never presented successively, and each tone had a duration of 1 second. The interstimulus interval was 4 s and filled with Brownian noise. Accuracy was evaluated by summing the number of correct responses. However, the participants were not asked to identify the octaves of the presented tones. AP possessors performed (% correct responses) considerably better (mean correct: 69.5, SD = 21.5) than NAP participants (mean correct: 9.36, SD = 6.9; $t_{20,46} = 11.29$, $P < 3.04 \times 10^{-10}$, $d = 3.59$). NAP participants did not perform better than chance level (8.3%; $t_{17} = 0.65$, $P = 0.53$). The individual scores are depicted in Figure 1.

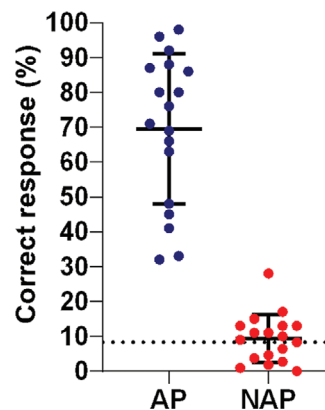


Figure 1. The pitch-labeling performance. Depicted are the individual scores (%) achieved by the participants with absolute pitch (AP, blue dots; $N = 18$) and participants without absolute pitch (NAP, red dots; $N = 18$) from the pitch-labeling test. The plotted values are the means with standard deviations. The dotted line represents the baseline at 8.3%.

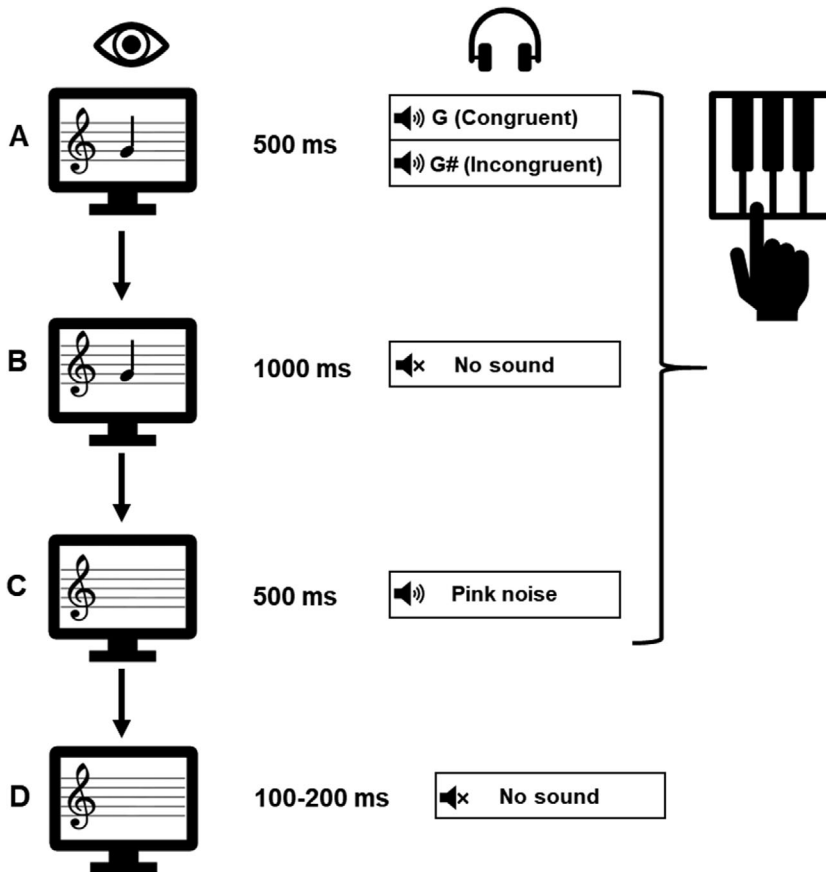


Figure 2. A schematic representation of the task. Each trial began with a bimodal stimulus that lasted for 500 ms (A), comprising a notation (e.g., G) presented on a monitor and a piano tone presented via headphones. The piano tone was either congruent (e.g., G) or incongruent (e.g., G \sharp) with the notation. The visual counterpart lasted for an additional 1000 ms (B), followed by pink noise for a duration of 500 milliseconds. The next trial followed after a duration jittered between 100 and 200 milliseconds (D). The participants were instructed to report the notation as quickly and accurately as possible by sight-reading, specifically by playing with their right hand on a piano. Responses were allowed and recorded for a duration of <2 s after stimulus onset (A–C).

Experimental task and stimulus material

The involvement of the left DLPFC in AP ability was investigated by letting both participant samples perform a modified Stroop task under a tDCS protocol. In this task, the participants were exposed to a stream of bimodal musical stimuli, comprising visually presented notations in combination with auditorily presented tones. The participants were instructed to sight-read and report the presenting notations as accurately and fast as possible by playing an electronic piano (Yamaha Electronic Piano, P-60S) with their right hand. During the experiment, the participants positioned their right hand over the piano keys, covering the C4 scale in order to be able to respond promptly.

The piano did not deliver auditory feedback but recorded the response behavior. The bimodal musical stimuli were randomly presented in different matching conditions. In half of the trials, the tones correctly corresponded to the notations (congruent), whereas in the other half, they did not (incongruent). The incongruent trials mismatched in six different conditions, deviating between tones and notations in ± 1 , ± 2 , and ± 3 semitones. Each of the six incongruent conditions had an occurrence probability of 0.083. The set of presented notations comprised the C scale of the 12 subsequent notes ranging from C4 to B4. The set of presented auditory stimuli were piano tones corresponding to the particular tones of the C scale (C4 tuned at

Table 2. Accuracy scores achieved in the modified Stroop task

Matching	AP		NAP	
	Sham	Cathodal	Sham	Cathodal
-3	0.99 (0.03)	0.98 (0.05)	0.98 (0.04)	0.97 (0.05)
-2	0.98 (0.03)	1.00 (0.01)	1.00 (0.01)	0.98 (0.03)
-1	0.99 (0.02)	0.99 (0.01)	0.99 (0.02)	0.99 (0.02)
0	0.99 (0.02)	0.99 (0.02)	0.99 (0.01)	0.99 (0.02)
1	0.99 (0.02)	0.98 (0.04)	0.97 (0.04)	0.98 (0.02)
2	0.98 (0.05)	0.97 (0.07)	0.99 (0.02)	0.99 (0.02)
3	0.99 (0.02)	0.99 (0.03)	0.99 (0.02)	0.97 (0.05)

The mean accuracy score (correct responses/total trials) is listed for each condition for both samples (AP, absolute pitch; NAP, nonabsolute pitch; each $N = 18$). The standard deviations are listed in parentheses. Matching units are in semitones. Negative numbers indicate “flat” (i.e., lower) deviations, and positive numbers indicate “sharp” (i.e., higher) deviations.

262 Hz), including the extension of the three successive “deviating” semitones at the scale edges in both directions (A3, B3-flat, B3, and C5, C5-sharp, D5). The tones were professionally recorded with an acoustic piano (the University of Iowa Electronic Music Studios, <http://theremin.music.uiowa.edu/MISpiano.html>) and were trimmed later, resulting in lengths of 500 milliseconds. In the task, the notations were presented 1000 ms longer than the tones, resulting in a duration of 1500 milliseconds. Afterward, pink noise followed for a duration of 500 milliseconds. Per trial, responses were allowed and recorded for a duration of <2 s after stimulus onset. The intertrial interval varied randomly between 100 and 200 milliseconds. The tones were delivered via

Sennheiser HD 205 headphones at the sound pressure level of 75 dB, and the notations were shown in the center of a PC monitor mounted on top of the electronic piano. The procedure of one trial is illustrated in Figure 2. Stimulus presentation, as well as behavior collection (via Musical Instrument Digital Interface), was controlled by the Presentation software (Neurobehavioral System, Version 18.2).

The tDCS protocol

After the participants performed a practice block of 20 trials, the tDCS equipment was applied to them. The participants underwent two subsequent experimental blocks, namely one with the tDCS technique turned on, inhibiting the left DLPFC (cathodal stimulation), and one with it turned off (sham stimulation). The order of the blocks was randomized across participants, and the participants were kept unaware of the respective stimulation condition to avoid confounding effects of expectation and order. Each block lasted 10 min and consisted of 288 trials, of which half were congruent and the other half incongruent. Regarding the incongruent trials, each combination (12 notations paired with tones mismatching in six particular degrees) was presented twice, resulting in 144 trials in total. Regarding the congruent trials, each combination (12 notations paired with matching tones) was presented 12 times, also resulting in 144 trials in total.

The current intensity of 1.5 mA was transferred by a saline-soaked pair of surface sponge electrodes and delivered by a battery-driven constant current stimulator (NeuroConn GmnH, Ilmenau, Germany). The sponges were stitched to an

Table 3. Reaction times achieved in the modified Stroop task

Matching	AP		NAP	
	Sham	Cathodal	Sham	Cathodal
-3	655 (632–756)***	668 (615–725)**	648 (601–751)	656 (616–718)
-2	669 (618–725)***	661 (608–709)***	653 (598–746)	655 (607–716)
-1	667 (620–763)***	662 (614–719)**	641 (617–732)*	660 (614–736)
0	651 (601–701)***	655 (597–694)***	629 (597–744)*	653 (607–718)
1	662 (622–730)***	662 (624–740)**	631 (595–755)*	654 (602–723)
2	663 (614–739)***	661 (601–730)**	640 (608–721)*	654 (616–726)
3	666 (632–752)***	665 (611–768)**	644 (609–768)*	656 (626–709)

The median reaction time (ms) is listed for each condition for both samples (AP, absolute pitch; NAP, non-absolute pitch, each $N = 18$). The lower and upper quartiles are listed in parentheses. Matching units are in semitones. Negative numbers indicate “flat” (i.e., lower) deviations, and positive numbers indicate “sharp” (i.e., higher) deviations.

* $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$, as revealed by the Shapiro–Wilk test.

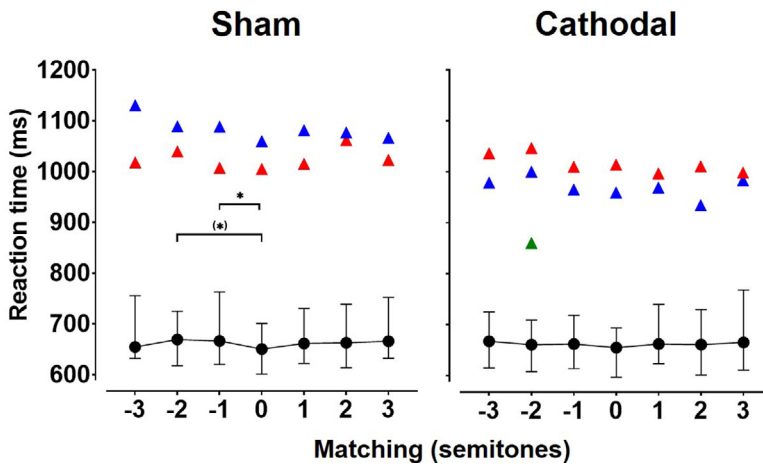


Figure 3. Reaction times achieved by AP possessors in the modified Stroop task. The plotted values are the medians together with the IQRs for each matching and stimulation condition. The colored triangles represent outliers. Each color (i.e., blue, red, and green) refers to a single participant. Negative semitones indicate “flat” (i.e., lower) deviations, and positive semitones indicate “sharp” (i.e., higher) deviations. Bonferroni-adjusted $*P < 0.05$; $(*)P = 0.054$ without outliers, otherwise P value is < 0.05 .

electroencephalogram cap based on the international 10–20 system to ensure the same placement for all participants. This specific current intensity was chosen based on documentation on the time course of the tDCS aftereffect and on previous tDCS studies investigating the DLPFC.^{68,69} For cathodal stimulation, the current was applied for 9 min, including fade-in/out phases of 10 s, respectively. The stimulation and the task were initiated simultaneously. In the sham condition, stimulation was applied for 30 s, including fade-in/out phases of 10

s, respectively, so that the subjects experienced the initial tingling associated with the onset of stimulation. Between the two blocks, a break of 30 min was held to ensure an unaffected sham session.⁴⁶ The left DLPFC was targeted by placing the (cathodal) electrode with a surface of 4×8 cm into a sponge on the scalp at the coordinate F3 according to the international 10–20 system. This localization method was successfully conducted in previous studies,^{69–74} and was confirmed as an appropriate approach by neuronavigational techniques.⁷⁵ As a

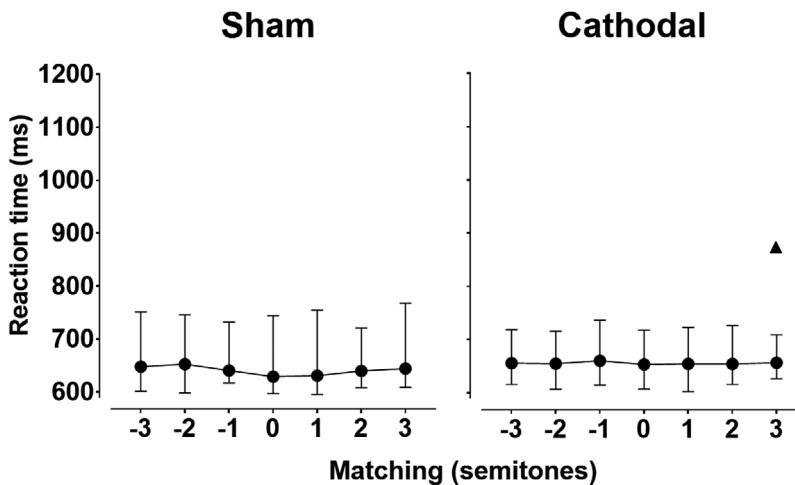


Figure 4. Reaction times achieved by the control participants in the modified Stroop task. Plotted are the medians together with the IQRs for each matching and stimulation condition. The triangle represents an outlier. Negative semitones indicate “flat” (i.e., lower) deviations, and positive semitones indicate “sharp” (i.e., higher) deviations.

reference, an (anodal) electrode with a larger surface of 10×10 cm was placed on the right parietal area, fixating the corners of the sponge at the coordinates Cz, C4, POZ, and P8 according to the international 10–20 system. This larger surface size was used to minimize current density over the parietal cortex.

Data analysis

For each participant, the median reaction times (RT) and accuracy scores were obtained from each matching and stimulation condition. During the entire study, only 13 missing responses occurred, which were omitted. The RT and accuracy values were imported into the SPSS® software (IBM SPSS Statistics, IBM Corp., Armonk, NY) for statistical analyses. The accuracy scores were not further subjected to inferential statistics due to an obvious ceiling effect (Table 2). Given that the values of the RTs were largely not normally distributed (Table 3), as assessed by the Shapiro–Wilk test, nonparametric procedures were performed to determine the effects of interest. Values outside of the interquartile range (IQR) \pm the IQR multiplied by 1.5 were considered outliers. For each group (i.e., AP and NAP) and stimulation condition (i.e., sham and cathodal), Friedman tests with matching as within-factor (i.e., seven levels: 0, ± 1 , ± 2 , and ± 3 semitones) were run. Significant results were followed up with pairwise comparisons using Wilcoxon signed-rank tests. The Bonferroni procedure was applied to correct for multiple comparisons (corrected $\alpha' < 0.05/21 = 0.0024$). The impact of the interaction between the within-factors “stimulation” and “matching” on the RT was estimated using generalized estimating equations (GEE) with gamma as distribution and log as link function together with an unstructured working correlation matrix. Effect size measures were calculated, namely the Cohen’s *d* for the *t*-tests, Kendall’s coefficient of concordance (*W*) for the Friedman tests, and the rank-biserial correlation coefficient (*r*) for the Wilcoxon signed-rank tests.

Results

The accuracy scores and RT values achieved at each condition by both samples are listed in Tables 2 and 3.

Three AP participants were identified as outliers, of which two stood out systematically across all matching and stimulation conditions. In the

NAP sample, one outlier was detected. Overall, the outliers did not skew the results. The RT values, including outliers, are depicted in Figures 3 and 4.

In the AP sample, the Friedman test revealed a significant effect of matching in the sham ($\chi^2_6 = 20.44$, $P = 0.002$, $W = 0.19$) but not in the cathodal condition ($\chi^2_6 = 11.63$, $P = 0.07$, $W = 0.11$). This effect remained after removing the outliers (sham: $\chi^2_6 = 18.95$, $P = 0.004$, $W = 0.21$; cathodal: $\chi^2_6 = 11.84$, $P = 0.07$, $W = 0.13$). In the sham condition, post hoc Wilcoxon signed-rank tests revealed significant differences in two congruent-incongruent pairs (-2 : $z = -3.42$, Bonferroni-adjusted $P = 0.013$, $r = -0.57$; -1 : $z = -3.47$, Bonferroni-adjusted $P = 0.012$, $r = -0.59$) and in one pair after removing the outliers (-1 : $z = -3.12$, Bonferroni-adjusted $P = 0.037$, $r = -0.57$). The GEE analysis revealed a significant effect of the interaction between “matching” and “stimulation” on the RT (Wald $\chi^2_6 = 16.95$, $P = 0.009$) even after removing the outliers (Wald $\chi^2_6 = 27.71$, $P < 0.001$).

In the NAP sample, the Friedman test did not reveal any significant effects of matching on the RT (sham: $\chi^2_6 = 2.17$, $P = 0.903$, $W = 0.02$; cathodal: $\chi^2_6 = 6.34$, $P = 0.386$, $W = 0.06$) even after removing the outlier (sham: $\chi^2_6 = 4.15$, $P = 0.657$, $W = 0.04$; cathodal: $\chi^2_6 = 5.01$, $P = 0.543$, $W = 0.05$). The GEE analysis did not reveal any interaction effect between “matching” and “stimulation” on the RT (Wald $\chi^2_6 = 1.246$, $P = 0.975$) even after removing the outlier (Wald $\chi^2_6 = 0.82$, $P = 0.992$).

Discussion

In this study, we investigated the causal role of the left DLPFC in the pitch-labeling process underlying AP by using a customized Stroop task in the context of a cathodal-sham tDCS protocol. Whereas the previous studies on AP using Stroop tasks recorded the participants’ responses vocally^{44,47,51} or per button click,⁷⁶ our experimental setup allowed a more natural behavior, namely the responding by performing on an actual piano, constituting a highly familiar situation incorporated in a musician’s everyday life.

Stroop and tDCS findings

The nearly perfect accuracy scores achieved in the modified Stroop task by both possessors and

nonpossessors of AP ensure that the notations have properly been internalized and that the sight-reading activity has conscientiously been executed. This compliance appears nontrivial due to the large range and variation of stimulus–response commands provided during the task. Whereas the previous Stroop studies on AP included only a handful of stimuli with two matching conditions (i.e., congruent and incongruent),^{25,44,47,51,76} our task explored an entire scale (i.e., 12 notations and 12 particular piano key responses) with matching and mismatching conditions, systematically covering three double-sided levels of deviation (± 1 , ± 2 , and ± 3 semitones).

Despite the participants' high performance, an interference was still detectable under the sham condition in the RT of AP possessors. This interference was reflected in that AP possessors responded slower to notations with mismatching tones than to notations with matching tones. This effect was centered within narrow deviations in the flat direction (i.e., -2 and -1). This finding suggests that the impact of distraction on pitch labeling increases as a function of the difficulty in pitch categorization. Furthermore, this finding implies a certain asymmetrical proneness that may underlie AP, mirroring, in this case, the observation of usual “undershooting” when singing out-of-tune.⁷⁷ Consistent with this presumption are findings showing that some aging AP possessors undergo a distortion in pitch perception that are mostly biased toward one direction.^{78,79}

Under cathodal stimulation, the interference effect shown by the AP possessors disappeared. More precisely, the suppression of cortical excitability of the left DLPFC led to a better sight-reading performance in AP possessors, suggesting less interference and thus that at least some of the irrelevant tones became more suppressible for them. By contrast, the control participants showed no variation in the RT as a function of the matching condition. In line with previous Stroop and other interference studies on AP,^{25,44,47,49–52,80} these results confirm that the pitch-labeling process is largely nonsuppressible when triggered by tone exposure, interfering with the conflicting task of sight-reading. The fact that our matched control musician sample without AP did not show this interference pattern further suggests that automaticity in the context of pitch labeling is unique for AP.

The modulation of the task performance as a function of the tDCS stimulation of the left DLPFC indicated, at least to some extent, a causal relationship between this specific brain region and the pitch-labeling process. However, other brain structures may likely be involved in this process as well or may perhaps even be indispensable in this regard. Correlative evidence strongly suggests that the PT is another crucial brain structure for AP.^{15–17,25,26,66,81} The PT is anatomically connected via the arcuate fasciculus with the DLPFC⁸² and, in AP possessors, the left PT functionally interacts with the left DLPFC already at rest.⁶⁶ However, the PT was rather reported to specifically be responsible for early AP-related encoding processes, such as categorical pitch perception.^{11,19,24,25} But, its causal contribution to AP as a whole or to pitch labeling as a subprocess has not been established yet. A few lesion cases of AP possessors have been documented, but in their entirety so far, they have been inconclusive in this regard. A few patients were able to retain their AP ability after undergoing left or right temporal lobectomy.^{83–86} Others either lost their AP ability or underwent a severe “sharp”-aligned distortion after left or right hemispheric strokes.^{87,88} In order to advance our understanding of the mechanisms and the involved brain structures driving AP, future studies using techniques in the field of neuromodulation should be conducted, particularly undertaking the PT next for a more systematic investigation on its causal impact on AP.

Pitch labeling: a case for the dorsal stream function

Previous studies on AP yielded results that are not readily reconcilable with the so-called dual-stream models of auditory cortical processing. These models propose that auditory cortical processing pathways are organized dually, namely ventrally (i.e., the ventral or “what” stream) and dorsally (i.e., the dorsal or “where” stream).^{89,90} Whereas the ventral stream processes the identification of nonspatial auditory properties, the dorsal processing stream integrates spatial sensorimotor information, ultimately associating auditory properties with spatial codes and motor commands.^{89–91} In relation to AP, some research has identified the ventral processing stream within the temporal lobe,^{92,93} while others have loosely assigned the dorsal stream function to the left DLPFC and related them to the

pitch-labeling process.^{34–36,66,82} In two previous studies from our research group, we provided evidence for a correlation between the pitch-labeling performance and the functional and structural connectivity within the left dorsal pathway in AP possessors.^{66,82} Here, we extended these findings, providing causal evidence of the left DLPFC on the pitch labeling. On this basis, we argue more strongly that the pitch-labeling process underlies the dorsal stream function. Our first argument concerns the dorsal location of the assigned brain structure itself that not only drives the pitch-labeling process in AP, as revealed by the present findings and previous studies,^{34,36,66,82} but also bears an associative–integrative function in NAP musicians, nonmusicians, and even monkeys while learning or performing certain association tasks.^{27–32,35} Further in line with the dorsal stream function concerns the “where” dimension of pitch labeling. In the human mind, the linkage between space and pitch is profoundly incorporated, apparent not only in our musical notations based on a vertical mapping system but also in our usage of the word “height” to describe both space and pitch. Intercultural research revealed that pitch labels are internally represented in a systematic spatial order and that the availability of space–pitch mapping may even be of prelinguistic nature.^{94–98} In some rare cases (e.g., pitch–space synesthesia), this order may even reach explicitness, consisting of particularly unique pitch–location pairs.^{99,100} Finally, in line with the dorsal stream function is the coactivation of motor commands during pitch labeling. There is evidence that AP possessors not only rely on verbal information during pitch labeling but also on sensorimotor codes (e.g., specific vocalization or fingering unambiguously coupled to specific tone responses).³³ Consistent with this framework and our findings, AP possessors show an interference when vocally imitating mistuned tones¹⁰¹ and a stronger left hemispheric activation during the processing of auditory feedback for vocal motor control.¹⁰²

Conclusions

By applying a cathodal-sham tDCS protocol, we provided, for the first time, causal evidence that the left DLPFC drives the pitch-labeling process underlying AP. Furthermore, the findings yielded from our customized piano-playing Stroop task support automaticity as a unique feature of AP,

confirming a unique pitch-processing mode virtually nonreliant on cognitive load. Altogether, these findings substantiate previous functional studies showing that AP possessors selectively recruit the left DLPFC during tone exposure and label tones without relying on WM resources,³⁴ as discussed with reference to reduced or absent P3 responses and lack of activation in the IFG.^{34,39–44}

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Competing interests

The authors declare no competing interests.

References

1. Baggaley, J. 1974. Measurement of absolute pitch. *Psychol. Music* **2**: 11–17.
2. Takeuchi, A.H. & S.H. Hulse. 1993. Absolute pitch. *Psychol. Bull.* **113**: 345–361.
3. Gregersen, P.K., E. Kowalsky, N. Kohn, *et al.* 1999. Absolute pitch: prevalence, ethnic variation, and estimation of the genetic component. *Am. J. Hum. Genet.* **65**: 911–913.
4. Levitin, D.J. & S.E. Rogers. 2005. Absolute pitch: perception, coding, and controversies. *Trends Cogn. Sci.* **9**: 26–33.
5. Theusch, E., A. Basu & J. Gitschier. 2009. Genome-wide study of families with absolute pitch reveals linkage to 8q24.21 and locus heterogeneity. *Am. J. Hum. Genet.* **85**: 112–119.
6. Baharloo, S., S.K. Service, N. Risch, *et al.* 2000. Familial aggregation of absolute pitch. *Am. J. Hum. Genet.* **67**: 755–758.
7. Baharloo, S., P.A. Johnston, S.K. Service, *et al.* 1998. Absolute pitch: an approach for identification of genetic and nongenetic components. *Am. J. Hum. Genet.* **62**: 224–231.
8. Deursch, D., T. Henthorn & M. Dolson. 2004. Speech patterns heard early in life influence later perception of the Tritone Paradox. *Music Percept.* **21**: 357–372.
9. Deutsch, D., T. Henthorn & M. Dolson. 2004. Absolute pitch, speech, and tone language: some experiments and a proposed framework. *Music Percept.* **21**: 339–356.
10. Deutsch, D., T. Henthorn, E. Marvin, *et al.* 2006. Absolute pitch among American and Chinese conservatory students: prevalence differences, and evidence for a speech-related critical period. *J. Acoust. Soc. Am.* **119**: 719.
11. Zatorre, R.J. 2003. Absolute pitch: a model for understanding the influence of genes and development on neural and cognitive function. *Nat. Neurosci.* **6**: 692–695.
12. Russo, F.A., D.L. Windel & L.L. Cuddy. 2003. Learning the “Special Note”: evidence for a critical period for absolute pitch acquisition. *Music Percept.* **21**: 119–127.
13. Loui, P., H.C. Li, A. Hohmann, *et al.* 2010. Enhanced cortical connectivity in absolute pitch musicians: a model

- for local hyperconnectivity. *J. Cogn. Neurosci.* **23**: 1015–1026.
14. Jäncke, L., N. Langer & J. Hänggi. 2012. Diminished whole-brain but enhanced peri-sylvian connectivity in absolute pitch musicians. *J. Cogn. Neurosci.* **24**: 1447–1461.
 15. Wilson, S.J., D. Lusher, C.Y. Wan, *et al.* 2009. The neurocognitive components of pitch processing: insights from absolute pitch. *Cereb. Cortex* **19**: 724–732.
 16. Keenan, J.P., V. Thangaraj, A.R. Halpern, *et al.* 2001. Absolute pitch and planum temporale. *Neuroimage* **14**: 1402–1408.
 17. Schlaug, G., L. Jäncke, Y. Huang, *et al.* 1995. *In vivo* evidence of structural brain asymmetry in musicians. *Science* **267**: 699LP–701.
 18. Burkhard, A., J. Hänggi, S. Elmer, *et al.* 2020. The importance of the fibre tracts connecting the planum temporale in absolute pitch possessors. *Neuroimage* **211**: 116590.
 19. Schulze, K., N. Gaab & G. Schlaug. 2009. Perceiving pitch absolutely: comparing absolute and relative pitch possessors in a pitch memory task. *BMC Neurosci.* **10**: 106.
 20. Griffiths, T.D. & J.D. Warren. 2002. The planum temporale as a computational hub. *Trends Neurosci.* **25**: 348–353.
 21. Meyer, M., S. Elmer & L. Jäncke. 2012. Musical expertise induces neuroplasticity of the planum temporale. *Ann. N.Y. Acad. Sci.* **1252**: 116–123.
 22. Elmer, S., J. Hänggi, M. Meyer, *et al.* 2013. Increased cortical surface area of the left planum temporale in musicians facilitates the categorization of phonetic and temporal speech sounds. *Cortex* **49**: 2812–2821.
 23. Elmer, S., J. Hänggi & L. Jäncke. 2016. Interhemispheric transcallosal connectivity between the left and right planum temporale predicts musicianship, performance in temporal speech processing, and functional specialization. *Brain Struct. Funct.* **221**: 331–344.
 24. Siegel, J.A. 1974. Sensory and verbal coding strategies in subjects with absolute pitch. *J. Exp. Psychol.* **103**: 37–44.
 25. Schulze, K., K. Mueller & S. Koelsch. 2013. Auditory stroop and absolute pitch: an fMRI study. *Hum. Brain Mapp.* **34**: 1579–1590.
 26. Wengenroth, M., M. Blatow, A. Heinecke, *et al.* 2013. Increased volume and function of right auditory cortex as a marker for absolute pitch. *Cereb. Cortex* **24**: 1127–1137.
 27. Petrides, M. 1990. Nonspatial conditional learning impaired in patients with unilateral frontal but not unilateral temporal lobe excisions. *Neuropsychologia* **28**: 137–149.
 28. Petrides, M., B. Alivisatos, A.C. Evans, *et al.* 1993. Dissociation of human mid-dorsolateral from posterior dorsolateral frontal cortex in memory processing. *Proc. Natl. Acad. Sci. USA* **90**: 873LP–877.
 29. Petrides, M. 1985. Deficits in non-spatial conditional associative learning after periaruate lesions in the monkey. *Behav. Brain Res.* **16**: 95–101.
 30. Petrides, M. 1997. Visuo-motor conditional associative learning after frontal and temporal lesions in the human brain. *Neuropsychologia* **35**: 989–997.
 31. Boettiger, C.A. & M. D'Esposito. 2005. Frontal networks for learning and executing arbitrary stimulus-response associations. *J. Neurosci.* **25**: 2723–2732.
 32. Lepage, M., M. Brodeur & P. Bourgooin. 2003. Prefrontal cortex contribution to associative recognition memory in humans: an event-related functional magnetic resonance imaging study. *Neurosci. Lett.* **346**: 73–76.
 33. Zatorre, R.J. & C. Beckett. 1989. Multiple coding strategies in the retention of musical tones by possessors of absolute pitch. *Mem. Cognit.* **17**: 582–589.
 34. Zatorre, R.J., D.W. Perry, C.A. Beckett, *et al.* 1998. Functional anatomy of musical processing in listeners with absolute pitch and relative pitch. *Proc. Natl. Acad. Sci. USA* **95**: 3172–3177.
 35. Bermudez, P. & R.J. Zatorre. 2005. Conditional associative memory for musical stimuli in nonmusicians: implications for absolute pitch. *J. Neurosci.* **25**: 7718LP–7723.
 36. Bermudez, P., J.P. Lerch, A.C. Evans, *et al.* 2009. Neuroanatomical correlates of musicianship as revealed by cortical thickness and voxel-based morphometry. *Cereb. Cortex* **19**: 1583–1596.
 37. Zatorre, R.J., A.C. Evans & E. Meyer. 1994. Neural mechanisms underlying melodic perception and memory for pitch. *J. Neurosci.* **14**: 1908LP–1919.
 38. Henson, R.N.A., T. Shallice & R.J. Dolan. 1999. Right prefrontal cortex and episodic memory retrieval: a functional MRI test of the monitoring hypothesis. *Brain* **122**: 1367–1381.
 39. Klein, M., M. Coles & E. Donchin. 1984. People with absolute pitch process tones without producing a P300. *Science* **223**: 1306LP–1309.
 40. Crummer, G.C., J.P. Walton, J.W. Wayman, *et al.* 1994. Neural processing of musical timbre by musicians, nonmusicians, and musicians possessing absolute pitch. *J. Acoust. Soc. Am.* **95**: 2720–2727.
 41. Wayman, J.W., R.D. Frisina, J.P. Walton, *et al.* 1992. Effects of musical training and absolute pitch ability on event-related activity in response to sine tones. *J. Acoust. Soc. Am.* **91**: 3527–3531.
 42. Hantz, E.C., G.C. Crummer, J.W. Wayman, *et al.* 1992. Effects of musical training and absolute pitch on the neural processing of melodic intervals: a P3 event-related potential study. *Music Percept.* **10**: 25LP–42.
 43. Rogenmoser, L., S. Elmer & L. Jäncke. 2015. Absolute pitch: evidence for early cognitive facilitation during passive listening as revealed by reduced P3a amplitudes. *J. Cogn. Neurosci.* **27**: 623–637.
 44. Itoh, K., S. Suwazono, H. Arao, *et al.* 2005. Electrophysiological correlates of absolute pitch and relative pitch. *Cereb. Cortex* **15**: 760–769.
 45. Elmer, S., S. Sollberger, M. Meyer, *et al.* 2013. An empirical reevaluation of absolute pitch: behavioral and electrophysiological measurements. *J. Cogn. Neurosci.* **25**: 1736–1753.
 46. Nitsche, M.A. & W. Paulus. 2000. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J. Physiol.* **527**: 633–639.
 47. Akiva-Kabiri, L. & A. Henik. 2012. A unique asymmetrical Stroop effect in absolute pitch possessors. *Exp. Psychol.* **59**: 272–278.

48. Ziv, N. & S. Radin. 2014. Absolute and relative pitch: global versus local processing of chords. *Adv. Cogn. Psychol.* **10**: 15–25.
49. Miyazaki, K. & A. Rakowski. 2002. Recognition of notated melodies by possessors and nonpossessors of absolute pitch. *Percept. Psychophys.* **64**: 1337–1345.
50. Miyazaki, K. 1993. Absolute pitch as an inability: identification of musical intervals in a tonal context. *Music Percept.* **11**: 55LP–71.
51. Miyazaki, K. 2000. Interaction in musical-pitch naming and syllable naming: an experiment on a Stroop-like effect in hearing. In *Integrated Human Brain Science: Theory, Method, Application (Music)*. Nakada, T., Ed.: 412–423. Amsterdam: Elsevier.
52. Hsieh, I.H. & K. Saberi. 2008. Language-selective interference with long-term memory for musical pitch. *Acta Acust.* **94**: 588–593.
53. Stroop, J.R. 1935. Studies of interference in serial verbal reactions. *J. Exp. Psychol.* **18**: 643–662.
54. MacLeod, C.M. 1991. Half a century of research on the Stroop effect: an integrative review. *Psychol. Bull.* **109**: 163–203.
55. Zakay, D. & J. Glicksohn. 1985. Stimulus congruity and S-R compatibility as determinants of interference in a Stroop-like task. *Rev. Canad. Psychol.* **39**: 414–423.
56. Grégoire, L., P. Perruchet & B. Poulin-Charronnat. 2013. The musical Stroop effect: opening a new avenue to research on automatisms. *Exp. Psychol.* **60**: 269–278.
57. Stewart, L., V. Walsh & U. Frith. 2004. Reading music modifies spatial mapping in pianists. *Percept. Psychophys.* **66**: 183–195.
58. Beeli, G., M. Esslen & L. Jäncke. 2005. When coloured sounds taste sweet. *Nature* **434**: 38.
59. Ward, J., B. Huckstep & E. Tsakanikos. 2006. Sound-colour synaesthesia: to what extent does it use cross-modal mechanisms common to us all? *Cortex* **42**: 264–280.
60. Itoh, K., H. Sakata, H. Igarashi, *et al.* 2019. Automaticity of pitch class-color synesthesia as revealed by a Stroop-like effect. *Conscious. Cogn.* **71**: 86–91.
61. Annett, M. 1970. A classification of hand preference by association analysis. *Br. J. Psychol.* **61**: 303–321.
62. Oldfield, R.C. 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* **9**: 97–113.
63. Lehrl, S. 1993. Geistige Leistungsfähigkeit: Theorie und Messung der biologischen Intelligenz mit dem Kurztest KAI.
64. Gordon, E. 1989. *Manual for the Advanced Measures of Music Audiation*.
65. Oechslin, M.S., M. Meyer & L. Jäncke. 2010. Absolute pitch—functional evidence of speech-relevant auditory acuity. *Cereb. Cortex* **20**: 447–455.
66. Elmer, S., L. Rogenmoser, J. Kühnis, *et al.* 2015. Bridging the gap between perceptual and cognitive perspectives on absolute pitch. *J. Neurosci.* **35**: 366–371.
67. Jäncke, L., L. Rogenmoser, M. Meyer, *et al.* 2012. Pre-attentive modulation of brain responses to tones in coloured-hearing synesthetes. *BMC Neurosci.* **13**: 151.
68. Nitsche, M.A. & W. Paulus. 2001. Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. *Neurology* **57**: 1899–1901.
69. Elmer, S., M. Burkard, B. Renz, *et al.* 2009. Direct current induced short-term modulation of the left dorsolateral prefrontal cortex while learning auditory presented nouns. *Behav. Brain Funct.* **5**: 29.
70. Beeli, G., S. Koeneke, K. Gasser, *et al.* 2008. Brain stimulation modulates driving behavior. *Behav. Brain Funct.* **4**: 34.
71. Fregni, F., P.S. Boggio, M. Nitsche, *et al.* 2005. Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Exp. Brain Res.* **166**: 23–30.
72. Marshall, L., M. Mölle, M. Hallschmid, *et al.* 2004. Transcranial direct current stimulation during sleep improves declarative memory. *J. Neurosci.* **24**: 9985–9992.
73. Marshall, L., M. Mölle, H.R. Siebner, *et al.* 2005. Bifrontal transcranial direct current stimulation slows reaction time in a working memory task. *BMC Neurosci.* **6**: 23.
74. Cerruti, C. & G. Schlaug. 2009. Anodal transcranial direct current stimulation of the prefrontal cortex enhances complex verbal associative thought. *J. Cogn. Neurosci.* **21**: 1980–1987.
75. Herwig, U., P. Satrapi & C. Schönfeldt-Lecuona. 2003. Using the international 10–20 EEG system for positioning of transcranial magnetic stimulation. *Brain Topogr.* **16**: 95–99.
76. Sharma, V.V., M. Thaut, F. Russo, *et al.* 2019. Absolute pitch and musical expertise modulate neuro-electric and behavioral responses in an auditory Stroop paradigm. *Front. Hum. Neurosci.* **13**: 932.
77. Levitin, D.J. 1994. Absolute memory for musical pitch: evidence from the production of learned melodies. *Percept. Psychophys.* **56**: 414–423.
78. Athos, E.A., B. Levinson, A. Kistler, *et al.* 2007. Dichotomy and perceptual distortions in absolute pitch ability. *Proc. Natl. Acad. Sci. USA* **104**: 14795–14800.
79. Vernon, P.E. 1977. Absolute pitch: a case study. *Br. J. Psychol.* **68**: 485–489.
80. Rogenmoser, L., H.C. Li, L. Jäncke, *et al.* 2021. Auditory aversion in absolute pitch possessors. *Cortex* **135**: 285–297.
81. Ohnishi, T., H. Matsuda, T. Asada, *et al.* 2001. Functional anatomy of musical perception in musicians. *Cereb. Cortex* **11**: 754–760.
82. Oechslin, M.S., A. Imfeld, T. Loenneker, *et al.* 2010. The plasticity of the superior longitudinal fasciculus as a function of musical expertise: a diffusion tensor imaging study. *Front. Hum. Neurosci.* **3**: 76.
83. Zatorre, R.J. 1989. Intact absolute pitch ability after left temporal lobectomy. *Cortex* **25**: 567–580.
84. Suriadi, M.M., K. Usui, T. Tottori, *et al.* 2015. Preservation of absolute pitch after right amygdalohippocampotomy for a pianist with TLE. *Epilepsy Behav.* **42**: 14–17.
85. Schulz, R., S. Horstmann, H. Jokeit, *et al.* 2005. Epilepsy surgery in professional musicians: subjective and objective reports of three cases. *Epilepsy Behav.* **7**: 552–558.
86. Usui, K., J. Shinozaki, N. Usui, *et al.* 2020. Retained absolute pitch after selective amygdalohippocampotomy. *Epilepsy Behav. Rep.* **14**: 100378.

87. Johannes, S., M.E. Jöbges, R. Dengler, *et al.* 1998. Cortical auditory disorders: a case of non-verbal disturbances assessed with event-related brain potentials. *Behav. Neurol.* **11**: 55–73.
88. Wertheim, N. & M.I. Botez. 1961. Receptive amusia: a clinical analysis. *Brain* **84**: 19–30.
89. Hickok, G. & D. Poeppel. 2007. The cortical organization of speech processing. *Nat. Rev. Neurosci.* **8**: 393–402.
90. Rauschecker, J.P. & S.K. Scott. 2009. Maps and streams in the auditory cortex: nonhuman primates illuminate human speech processing. *Nat. Neurosci.* **12**: 718–724.
91. Rauschecker, J.P. 2018. Where, when, and how: are they all sensorimotor? Towards a unified view of the dorsal pathway in vision and audition. *Cortex* **98**: 262–268.
92. Kim, S.G. & T.R. Knösche. 2016. Intracortical myelination in musicians with absolute pitch: quantitative morphometry using 7-T MRI. *Hum. Brain Mapp.* **37**: 3486–3501.
93. Kim, S.G. & T.R. Knösche. 2017. Resting state functional connectivity of the ventral auditory pathway in musicians with absolute pitch. *Hum. Brain Mapp.* **38**: 3899–3916.
94. Bernstein, I.H. & B.A. Edelman. 1971. Effects of some variations in auditory input upon visual choice reaction time. *J. Exp. Psychol.* **87**: 241–247.
95. Ariga, A. & S. Saito. 2019. Spatial–musical association of response codes without sound. *Q. J. Exp. Psychol.* **72**: 2288–2301.
96. Jiang, Q. & A. Ariga. 2020. The sound-free SMARC effect: the spatial-musical association of response codes using only sound imagery. *Psychon. Bull. Rev.* **27**: 974–980.
97. Pratt, C.C. 1930. The spatial character of high and low tones. *J. Exp. Psychol.* **13**: 278–285.
98. Dolscheid, S., S. Hunnius, D. Casasanto, *et al.* 2014. Prelinguistic infants are sensitive to space–pitch associations found across cultures. *Psychol. Sci.* **25**: 1256–1261.
99. Akiva-Kabiri, L., O. Linkovski, L. Gertner, *et al.* 2014. Musical space synesthesia: automatic, explicit and conceptual connections between musical stimuli and space. *Conscious. Cogn.* **28**: 17–29.
100. Linkovski, O., L. Akiva-Kabiri, L. Gertner, *et al.* 2012. Is it for real? Evaluating authenticity of musical pitch-space synesthesia. *Cogn. Process.* **13**: 247–251.
101. Hutchins, S., S. Hutka & S. Moreno. 2015. Symbolic and motor contributions to vocal imitation in absolute pitch. *Music Percept.* **32**: 254–265.
102. Behroozmand, R., N. Ibrahim, O. Korzyukov, *et al.* 2014. Left-hemisphere activation is associated with enhanced vocal pitch error detection in musicians with absolute pitch. *Brain Cogn.* **84**: 97–108.