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RESEARCH ARTICLE

# Binaural localization of musical pitch using interaural time differences in congenital amusia

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# Abstract

Naturally occurring sounds are routinely periodic. The ability to phase-lock to such periodicity facilitates pitch perception and interaural time differences (ITDs) determination in binaural localization. We examined whether deficient pitch processing in individuals with congenital amusia (tone deafness) is accompanied by impaired ability to lateralize musical pitch at auditory periphery and memorize the location of pitch at the working memory level. If common mechanisms subserve processing of temporal-fine-structure based pitch and ITDs, then deficient processing of one feature should impair performance on the other. Thus, we measured ITD discrimination thresholds using an adaptive-tracking procedure for lateralizing musical tone pairs separated by different semitone intervals. Amusic individuals exhibited normal ITD thresholds comparable to those of matched controls, which were not affected by concurrent pitch changes. For working memory tasks, the amusic group performed significantly worse than matched controls in probed pitch recall, irrespective of the complexity level of concurrent variations along the ITD dimension of the melodic sequence. Interestingly, despite normal peripheral ITD thresholds, amusic individuals performed worse than controls in recalling probed locations of tones within a sequence of musical notes originating from different ITDsimulated locations. Findings suggest that individuals with congenital amusia are unimpaired in temporal fine-structure encoding to determine the location of musical pitch based on binaural ITD information at the auditory periphery. However, working memory for a sequence of sounds' ITD-dependent spatial location is here shown to be impaired and dissociated from the pitch feature of sounds at the working memory level.

# Introduction

Most naturally occurring sounds, including musical pitch, occur at a restricted location in space, so encoding the sound object may implicate both pitch and location information. One important cue for the listener in extracting these sound features relies on the ability to detect the periodic structure of the acoustic waveform. Encoding the sound's spectro-temporal oscillation pattern serves important functions in both binaural sound localization and pitch processing. The binaural cycle-to-cycle disparities present in the temporal fine-structures of

acoustic stimuli provides interaural time difference (ITD) information, the primary cue used for localizing sounds in space [1–4]. Phase-locking pattern to the temporal-fine-structure of acoustical signals is also used by the auditory system in determining a sound object's pitch at the peripheral level, at least for low-frequency tones (i.e., < 5 kHz). Previous research have suggested that efficiency in encoding the temporal-fine-structure of sound waveforms should determine both pitch perception and ITD lateralization performance based on common underlying neural temporal mechanism [5–8].

Here we considered the special case of a population affected by severe impairment in processing pitch. Commonly referred to as tone-deafness, congenital amusia is a neurodevelopmental auditory disorder characterized by deficits in pitch perception and production that cannot be attributed to hearing loss or neurophysiological causes [9]. This lifelong condition has been estimated to affect 1.5%-4% of the general population with slightly higher rates in females [9–11], has been shown to be hereditary [12, 13], and does not appear to co-occur with other cognitive disorders [11]. Besides having pitch discrimination difficulties [14–16], individuals with congenital amusia are impaired in pitch contour identification [17, 18], melodic sequence recognition [19], singing in tune [20], as well as in memorizing pitch-based materials [14, 21–23]. However, amusics show normal processing on some other music related attributes such as musical emotion based on temporal or timbral cues [24], but not when emotion was elicited by the tonality of musical excerpts [25]. Recent theories have suggested that amusic individuals' pronounced difficulties in pitch processing may stem from an inability to use the fine spectro-temporal cues in the resolved harmonics in complex tones without peripheral basis [26]. Consistent with this view, one recent meta analysis has shown that pitch change is an effective moderator of the effect size of performance gap between amusic and control across studies, supporting the hypothesis that amusia stems from a broad disorder of acoustic pitch processing [27].

While much has been discovered about perceptual and memory impairment in amusics, the ability to lateralize musical pitch spatially has been less explored. Previous studies on the relationship between musical pitch and spatial processing in amusics have been investigated using primarily visuo-spatial materials, such as imagined transformations of hand-drawn figures, mapping pitch onto vertical spatial configuration, or three-dimensional mental rotation tasks presented visually [28-30]. These studies have reported inconsistent results regarding whether pitch impairments transfer to affect spatial processing ability in amusic individuals [29, 30]. The contribution of ITD, the most prominent binaural cue, in lateralizing sounds in space could be more susceptible to the influence of an impaired pitch processing system (than visual-spatial processing). As encoding ITDs has been hypothesized to rely on the same specialized mechanism as encoding periodicity and pitch [6-8], an inability to use fine spectrotemporal information could affect spatial hearing ability [8, 26]. However, only one recent study has directly examined spatial processing in amusics by measuring the difference limens in tracking which interval of consecutive bursts of low-pass noise contained the moving sound sensation induced by ITD or ILD cue [26]. One potential explanation that equivalent sensitivity to ITD information contained in low-pass filtered noise was reported between the amusic and control group in this study could be because low-pass noise can be considered as a "reduced pitch" or non-pitch situation. We expect that lateralization of musical pitch based on ITD cue could be more susceptible to the interference due to the coding "noise" associated with musical pitch processing in amusic individuals.

The idea that dysfunction at low-level sensory processing affects perceptual discrimination and short-term memorization of sounds in congenital amusics has been indicated in several recent studies. Specifically, several studies have reported that amusic individuals showed impaired performance on pitch retention tasks which decreased as a function of the physical pitch distance, suggesting that the level of difficulty associated with pitch discrimination affects pitch memory [31–34]. Also, one study reported that decreasing the amount of time given to encode tones impaired pitch discrimination and memory performance in congenital amusia compared to controls [31]. Similar effects have been observed in typical listeners and related neurodevelopmental auditory disorders, suggesting an interdependent relationship between discrimination and working memory performance, both of which are affected by abnormalities in early-steps of auditory processing [32, 34–36]. We hypothesized that an impaired spectro-temporal processing system in amusics could not only affect discrimination of ITDs in musical pitch at the perceptual level, but also when memorizing the ITDs of musical note sequences.

In this work, we examine whether an impaired use of fine spectro-temporal information in encoding sounds in congenital amusics affects lateralizing musical pitch at the discrimination and working memory level using ITD cues. To our knowledge, no prior studies have investigated memory of musical pitch's locations based on binaural ITD information in amusic individuals. We measured psychophysical thresholds in lateralizing fixed-or varying-frequency musical tone pairs in amusics and matched control participants. In the second part of the study, we examined working memory for musical pitch sequence emanating from different ITD-simulated spatial locations. The aim is to determine whether working memory of the melodic sequence's ITD-location feature is affected by concurrent variations along the pitch dimension of the sound sequence. If deficient pitch encoding impairs spatial ITD lateralization based on the hypothesized common underlying mechanism, we predict 1) higher thresholds in lateralizing the ITD in musical tone pairs in amusic individuals when pitches were varied and, 2) less recall of the sound sequence's ITD information when concurrent pitch changes when involved than in fixed-pitch sequence in amusics. We report on an unimpaired temporal-fine-structure processing ability in individuals with congenital amusia in using ITD cues to lateralize musical pitch at the periphery. However, their ability to memorize the location and musical pitch of a sound sequence appears to be impaired and dissociated at the working memory level.

#### Materials and methods

#### **Participants**

Ten amusic individuals (six females, mean age = 26.3 years, SD = 2.2) and ten non-musically trained matched control participants (six females, mean age = 24.8 years, SD = 1.3) participated in this research. All participants had normal hearing and reported no history of psychiatric or neurological disorders. All participants were right-handed speakers of Mandarin Chinese. The two groups were comparable in age, level of education, and musical background or training (see Table 1). We used the Montreal Battery for the Evaluation of Amusia (MBEA; [10]) to screen participants for amusia. Participants who scored 2SD below the mean of the general population mean were classified as amusic [10, 37-40]. Table 2 showed the mean score and standard deviation on the scale, contour, interval, rhythm, metric, and memory subtests of the MBEA for the amusic and control groups as well as the global score. For individual MBEA subtest score, see supporting information (S1 File). A cutoff score of 23.1 on the global score (mean of the six subtests) was used as the criterion for diagnosis of congenital amusia. We selected to use the traditional accuracy cutoff rather than *d*-prime cutoff due to the more liberal criterion suggested for identification of amusic participants [37]. Participants signed written informed-consent forms and were paid for their participation. Note that the same amusic participants took part in all the experiments reported here. The experiment protocol was approved and conducted according to the guidelines of the Research Ethics Committee of National Taiwan University-Taiwan. Note

#### Table 1. Amusic and control group characteristics.

Characteristics	<b>Amusics (N = 10)</b>	Controls (N = 10)	p-value of t-test						
Demographic characteristics									
Age in years	26.3 ± 2.2	24.8 ± 1.3	n.s.						
Gender	6 female	6 female	N/A						
Musical education	$0.5 \pm 0.4$	0.7 ± 0.3	n.s.						
MBEA									
Total score	21.7 ± 2.0	27.9 ± 1.2	<i>p</i> < 0.05						
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Values displayed represents mean ± 1 standard deviation.

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that not all the research institutes here in Taiwan have an IRB affiliated with it, including National Central University (NCU). Therefore, all the research conducted here at NCU have to be submitted to the Research Ethics Committee at National Taiwan University (or other research institutes that have an affiliated IRB) for approval.

#### Task 1: ITD discrimination thresholds for tone pairs

**Stimuli.** Stimuli were generated using MATLAB software (MathWorks, Inc., Version 2009b) on an ASUS computer, and presented at a sampling rate of 44.1 kHz through 16-bit digital-to-analog converters (Creative Sound Blaster X-Fi Titanium). The experiments took place in a double-walled steel acoustically-isolated chamber (interior dimensions 2.0 m (L)  $\times$  2.0 m (W)  $\times$  2.5 m (H); Industrial Acoustics Company). All stimuli were presented through Sennheiser headphones (HD 380 Pro) at 70 dB SPL.

A pair of pure tones with frequency fixed at 261 Hz served as stimuli for the fixed-frequency tone pair condition (equivalent to C4 in Western music scale). There were five stimulus durations for a single tone in the fixed-frequency tone pair condition: 20, 50, 150, 250, and 500 ms. Each fixed-frequency tone pair was separated by a 500 ms within-pair silent interstimulus interval (ISI). For the varying-frequency tone pairs condition, pitch interval size was set at 0, 1, 5, and 10 semitones, which corresponds to tone-pair frequencies at 261/261, 261/277, 261/349, and 261/466 Hz, respectively. Two of the pitch interval sizes were larger than 2 semitones (i.e., above amusic individuals' typical pitch discrimination threshold; [14, 33]). The duration of stimulus was fixed at 150 ms for all the varying-frequency pairs of tones based on results from fixed-frequency part of the study. All stimuli were ramped with a 10-ms linear rise-decay. A low-pass filtered noise with cutoff frequency at 1200 Hz was included to allow comparison with previous results covering ITD detection in amusics [26].

The spatial locations of the sounds were established by setting the ITDs between the left and right stereo channels of each tone. To generate the dichotic waveforms, the ITDs were set

ð 1									
	Scale	Contour	Interval	Rhythm	Metric	Memory	Global		
Amusic									
Mean (SD)	21.5 (4.1)	23.0 (1.7)	20.5 (2.5)	23.0 (2.9)	17.8 (1.5)	24.4 (3.2)	21.7 (2.0)		
Control									
Mean (SD)	26.9 (1.7)	27.5 (1.8)	26.8 (1.7)	27.8 (2.1)	26.0 (4.4)	28.4 (1.1)	27.9 (1.2)		

Table 2. Mean score for each individual subtest of the MBEA and the global score for the amusic and control group.

The total score on each subtest is 30 points. Values displayed represents mean  $\pm 1$  standard deviation. The cutoff score of 23.1 on the global score (mean of the 6 subtests) was used as the criterion for diagnosis of congenital amusia.

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to zero in one randomly-chosen channel and to the desired interaural delay in the other channel using the following Eq (1). A positive ITD in this equation represents a waveform leading in time.

$$X_1(t) = \sin(2\pi f t)$$

$$X_2(t) = \sin(2\pi f (t + ITD))$$
(1)

where  $X_1$  and  $X_2$  represents the two channels of the dichotic pure tone, *t* represents stimulus time, *f* represents stimulus frequency, and *ITD* represents interaural delay in microseconds.

**Procedure.** Difference limens were measured for lateralizing the ITDs in fixed-frequency and varying-frequency pairs of musical-tones using a 2-interval forced-choice (2IFC), 2-down 1-up adaptive design which tracked the participant's 70.7% correct-response threshold [41, 42]. For the fixed-frequency tone-pair blocks, the order of tone durations (20, 50, 150, 250, and 500 ms) was randomly presented. Each participant completed 4 runs of 50 trials each per stimulus duration condition in a random-block design. For the varying-frequency tone-pair blocks, intervals of four different sizes (0, 1, 5, 10 semitones) were randomized across blocks. Each participant completed 5 runs of 50 trials each per stimulus condition in a random-block design.

On the first interval of each trial, the dichotic pure tone led to one randomly selected ear by a specific ITD, and in the second interval, it led to the other ear by the same magnitude of ITD. The participant's task was to determine the location order of presentation of the tones (i.e., left leading, then right, or right leading, then left). Perceptually, this is equivalent to determining whether the two sounds in the two intervals of the trial were heard on the left, then the right, or the right, and then on the left. The participants then pressed either a left or a right key to respond (a left key response meant that they perceived the sound location as right to left). Participants received visual feedback after each trial, in the form of a plot of the staircase response (ITD as a function of trial number) shown on the monitor with a trial-by-trial update (Fig 1).





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The initial value of the total ITD on each run was 400  $\mu$ s (i.e., 200  $\mu$ s in each interval). Two successive correct responses led to a reduction of the ITD by a step size of 0.1 log units [43]. An incorrect response led to an increase in ITD by the same step size. The threshold on each run was estimated as the average of the stimulus values at the reversal points. The first three or four reversals from each run were discarded, and the threshold was estimated as the average of the remaining even number of reversals. On average, six reversals went into the calculation of each threshold.

#### Task 2: Memory for pitch and location within tone sequences

**Stimuli.** Each musical-note sequence contained five 250 ms notes randomly sampled from C4, E4, and G4 on the western music scale (equivalent to 262, 330, and 392 Hz) each separated by a 650 ms inter-tone interval (ITI). A 10 ms linear rise and decay ramp was applied to each stimulus. Each note within the sequence was created dichotically using the same equation as in Task 1 to simulate a randomly sampled ITD value at -650, 0, or 650  $\mu$ s corresponding to left, central, and right positions relevant to the vertical midline of the participant's head.

**Procedure.** For each trial, participants heard a five-tone sequence each originating from a different ITD-simulated locations presented via headphones. After 500 ms of silence, a number (from 1 to 5) probe appeared visually at the center of the screen to indicate the number-cued tone in the 5-note sequence to be compared. The probe sound was presented after 1000 ms interval following the termination of the last sound in the five-tone sequence. Participants compared the probe sound to the tone in the number-cued position in the sound sequence to see whether the relevant feature (pitch or location) matched with the probe sound. A schematic diagram of the experiment procedure is shown in Fig 2.

There were three different types of blocks (pitch, spatial, and intermixed) according to the to-be-encoded sound feature of the musical-note sequence. For spatial (i.e., ITD-location) blocks, participants were informed before each block of trials that they would be required to compare the spatial location (i.e., ITD-location, left, center, or right) to the probe tone with the number-cued position of the tone in the 5-tone sequence. Similarly, for the pitch blocks, participants were instructed before each block of trials to encode the pitch of the probed musical-note of the sound sequence. For the intermixed-blocks, participants were not informed before the block whether the feature to-be-compared would be the ITD or the pitch of the musical-note sequence. Instead, the task cue (pitch or spatial) appeared on the screen simultaneously with the number cue for the intermixed block condition. Participants had to compare the probe sound to number-cued sound in the preceding 5-tone sequence by the cued task condition (pitch or location). Participants pressed "D" key on the keyboard to indicate that the relevant task feature (spatial or pitch) of the probe was the same as the number-cued tone in the sequence, or pressed the "L" key to indicate that the relevant feature of the probe differed from the probe sound in the sequence.

Each block consisted of 160 trials total. In each block, there were four conditions of different difficulty levels with respect to encoding along either pitch or ITD dimensions, resulting in these condition combinations: constant pitch and constant location, constant pitch and varying location, varying pitch and constant location, and varying pitch and varying location. Each condition contained 40 trials × 4 combinations = 160 trials/block. Fig 3 displays an example of the four types of pitch/ITD combination conditions. Each participant completed a total of 4 blocks per each type of block (i.e., pitch, spatial, and intermixed). Block order was counterbalanced across participants. Before the actual experiment, each participant went through a 10-min practice session that contained 30 trials randomly sampled from all the different conditions. The total experiment took approximately 2 hrs to complete.





**Fig 2. Schematic diagram of pitch and location probed recall working memory task.** The sequence consisted of five 250ms musical tones with 650ms ITI. Cued position indicates the number-cued item in the sequence to be compared with the probe tone. Participants indicate whether the cued tone was the same or different with the probe with respect to the indicated feature (i.e., pitch, spatial).

#### Results

#### Duration effects on ITD discrimination thresholds for tone pairs

Fig 4 shows the mean ITD thresholds as a function of tone duration for amusics and control participants (S1 File). We carried out a 2 × 5 two-way mixed ANOVA with group (controls, amusics) as the between-subject factor and duration as the within-subject factor (20, 50, 150, 250, 500 ms). There was a significant main effect of tone duration, F(4, 72) = 2.71, p = 0.037. Linear trend analysis on tone duration was significant, F(1, 18) = 8.34, p = 0.01, indicating lateralization threshold decreased as tone duration increased. Post hoc pair-wise t-tests on tone duration revealed significance on 20 ms and 250 ms-tone only, t(19) = 2.672, p = 0.015. Importantly, however, ITD thresholds in lateralizing fixed-frequency musical pitch did not differ between amusic and matched-control groups, F(1, 18) = 1.90, p = 0.19. There was no significant interaction between tone duration and group, F(4, 72) = 0.864, p = 0.49.

#### Pitch interval effects on ITD discrimination thresholds for tone pairs

Fig 5 shows the mean ITD thresholds for lateralizing musical tone pairs differing in pitchinterval size compared to low-pass noise condition for amusics and matched-controls (S1 File). We analyzed the threshold data in a two-way ( $2 \times 6$ ) mixed ANOVA with group (controls, amusics) as the between-subject factor and pitch interval as the within-subject factor

Serial position	1	2	3	4	5
Frequency	F1	F2	F1	F3	F2
Location	С	R	L.	R	L.
Frequency	F1	F1	F1	F1	F1
Location	С	L	R	С	R
Frequency	F1	F2	F1	F3	F2
Location	С	С	С	С	С
Frequency	F3	F3	F3	F3	F3
Location	L	L	L.	L.	L

**Fig 3.** Schematic representation of the pitch/location stimulus sequence combination for working memory tasks. Frequency symbols F1, F2, F3 represent three different frequencies; location symbols C, R, L indicate sound lateralized to positions central, right, and left of participant's head. Stimulus sequences from the top to bottom illustrate the four combinations of pitch and location constant or varied conditions.

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(noise, 0, 1, 5, 10, varied). There was a significant main effect of pitch interval, F(3.41, 61.46) = 10.72, p < 0.001. Larger pitch intervals produced higher ITD thresholds. ITD thresholds in lateralizing musical tone-pairs separated by different semitones did not differ significantly between amusic and matched-control groups, F < 1.00. The interaction between pitch interval and group was not significant, F < 1.00. Post hoc comparison on ITD thresholds for lateralizing tone pairs with varied interval size compared to same-pitch pair (i.e., zero-interval) produced no significant difference, t(9) = 1.204, p = 0.26. ITD detection thresholds obtained in the low-pass noise condition compared to tone-pair conditions averaged across all tone-interval sizes revealed a significant difference, t(1) = -7.71, p < 0.001.

#### Memory for pitch and location within tone sequences (informed condition)

To understand how working memory for the ITDs of musical-note sequence is affected by concurrent pitch feature of the tone sequence, the accuracy and response time in encoding ITDs when the pitch of the tone sequence remains constant or varied were analyzed. Fig 6 shows accuracy and response time (RT) for encoding pitch and ITD-location tasks for amusic and control groups (S2 File). The main effect for task revealed that recall accuracy for the location task was better than the pitch task across both groups, F(1, 18) = 11.205, p < 0.001. The amusic group exhibited impaired performance on working memory recall compared to controls irrespective of encoding the tone sequence's pitch or location feature, F(1, 18) = 15.61, p = 0.001. There was no significant interaction between task and group. None of the planned comparisons testing the variation effect along either ITD or musical pitch dimension on accuracy in recalling the other dimension of the tone sequence reached significance, t(9) < 0.674, p > 0.34. The response time in recalling pitch or ITD did not differ when the to be encoded



**Fig 4.** Mean **ITD** thresholds as a function of pitch durations for amusic and control participants. ITD thresholds for lateralizing fixed-frequency tone pairs were not significantly different for amusic and control groups. Error bars represent  $\pm 1$  standard deviation.

task information was pitch or location, F(1, 18) = 1.384, p = 0.25. We did not observe any difference between amusic and matched-control groups in the time it takes to recall pitch and ITD-location of tone sequences, F(1, 18) = 0.308, p = 0.59. The interaction between task and group was also nonsignificant, F(1, 18) = 0.885, p = 0.35.

# Memory for pitch and location within tone sequences (uninformed condition)

To see whether recall accuracy would be affected when participants were uninformed of the to be remembered feature of the tone sequence, Fig 7 shows the accuracy and response time for encoding the pitch and ITD-location feature of tone sequence for amusic and control groups (S2 File). This plot revealed that control group had higher mean recall accuracy than the amusic group in encoding both pitch and ITD dimension of the tone sequence, F(1, 18) = 21.28, p < 0.001. Accuracy in recalling a probed ITD was significantly higher than recalling a probed pitch within the tone sequence for both groups, F(1, 18) = 13.62, p = 0.001. None of the planned comparisons showed significant effect of the other dimension information of the sequence on recall accuracy either for the pitch task, t(9) < 0.01, p > 0.99, nor for the location task, t(9) = 1.94, p = 0.08.

Analyses of response time (Fig 7 right) showed that it took participants longer time in recalling pitch than ITD feature of the sound sequence, F(1, 18) = 8.84, p = 0.008 Amusic participants took significantly more time to recall features of sounds than control participants, F(1, 18) = 8.43, p < 0.01. Planned comparisons showed that for control participants, RT mean differences between encoding location-varied and location-constant sequences in the pitch task reached significance, t(9) = -3.25, p = 0.009, but RTs for recalling ITD, whether pitch



**Fig 5.** Mean ITD thresholds for lateralizing musical tone pairs with different pitch-interval size. The noise control condition used low-pass noise with cut-off frequency at 1200 Hz. In the varied condition, tone pairs were randomly selected from 0, 1, 5, 10 semitones. Size of pitch-interval had no effect on lateralizing musical tone pairs in control and amusic groups. Error bars represent  $\pm 1$  standard deviation.

dimension was varied or not, did not differ significantly, t(9) = -1.30, p = 0.22. For the amusic group, variations along the other sound dimension did not significantly affect response time either in recalling pitch, t(9) = -0.96, p = 0.26, or recalling ITD information, t(9) = -0.46, p = 0.65.

#### Discussion

Our results shed new light on how amusic individuals use the spectro-temporal fine structure of sounds to process the spatial location (ITDs) of musical tones at discrimination and working memory level. For discrimination tasks, amusic individuals showed similar ITD lateralization thresholds as typical listeners, even when lateralizing the position of varying musicalpitch intervals based on ITD cues. For working memory tasks, amusic individuals exhibited impaired performance relative to the control group in recalling both the pitch and spatial ITDlocation of the musical tone sequences. Interestingly, variations along the pitch dimension of sound sequence did not affect memory performance in terms of accuracy in encoding the ITD-location of tone sequence for amusic and control groups. This may suggest an independence in processing the pitch and ITD features of sound sequence at working memory level.

Our findings demonstrate intact ITD discrimination ability in congenital amusics even when lateralizing the ITDs contained in varying musical pitch intervals. Amusic individuals showed compatible ITD detection thresholds as normal listeners [44–46] and exhibited improvements in ITD lateralization performance when tone duration was longer, consistent with ITD detection pattern reported for normal listeners [47, 48]. We did not observe pitch variations to have any effect on lateralizing the ITD-dependent location of musical tones, at





**Fig 6.** Mean accuracy and response time (**R**T) for working memory tasks (informed condition). Top panels: Mean proportion correct responses (left panel) and response times (right panel) when the probed recall feature was pitch as a function of location feature remains constant or varied. Bottom panels: Mean proportion correct responses (left panel) and response times (right panel) for the location task. Error bars represent ± 1 standard deviation.

least at the auditory peripheral level. Even when the pitch interval size were increased to more than 5 semitones (i.e., above amusic's pitch discrimination threshold), there was no impairment in ITD detection threshold for the amusic group. It is valid to question why the putative effect of pitch interval size on lateralization not observed for matched controls should be observable in amusic individuals. The reasoning is as follows. Several previous studies have shown that amusic individuals exhibited worse performance than controls when a pitch distance larger than four semitones was employed in pitch change retention tasks [31-34]. One potential explanation was that when the stimuli with the same pitch interval (e.g., 4 semitones) were used for both groups, the stimuli would sound perceptually more similar for amusic individuals compared to controls, resulting in more difficult discrimination for the amusic group [34]. Therefore, even under identical pitch interval condition (e.g., 5 semitones), the perceptual (not physical) difficulty induced by pitch distance could account for the differences found between amusics and controls on pitch memory performance. Although in the current study we failed to observe a similar putative effect of pitch interval size on ITD lateralization, one reason could be due to the difference in the effect of perceptual pitch distance on memory and lateralization tasks. Another reason for this lack of effect could be that ITD processing is less susceptible to an influence of noisy pitch system as pitch interference effect have been reported in rhythm discrimination and temporal judgments among amusic individuals [21, 49].





**Fig 7. Mean accuracy and response time for working memory task (uninformed condition).** Top panels: Mean proportion correct responses (left panel) and response times (right panel) when the probed recall feature was pitch as a function of location feature remains constant or varied. Bottom panels: Mean proportion correct responses (left panel) and response times (right panel) for the location task. Error bars represent ± 1 standard deviation.

Interestingly, studies have shown that amusic individuals exhibited normal metre discrimination when the beat stimuli did not involve variations in musical pitch [50]. This is consistent with the present findings of normal ITD detection thresholds for lateralizing fixed-frequency tone pairs and low-pass noise as the noise condition can be viewed as an "unpitched" situation. Similarly findings have also been reported in the emotional perception domain where amusics were able to recognize musical emotions based on temporal or consonance information of the musical excerpts [24].

The present findings on unimpaired use of temporal-fine structure of sound to code musical pitch's ITD extends previous finding on fine ITD processing in noise for amusic individuals by showing that the ability to process the ITDs contained in musical tones were unaffected in amusic individuals. In addition, our results of fine auditory peripheral processing of spectrotemporal information are consistent with previous reports on normal pitch tracking mechanism up to the level of auditory cortex in amusics, but weak cortical neural representation of pitch to support reliable discrimination and memory [51]. In fact, abnormal neural transmission between the auditory cortex and right inferior frontal cortex of amusic individuals have been reported in several studies [51–56].

Findings on working memory of the pitch sequence's ITD dimension showed that amusics' impaired pitch perception did not affect memory for the location of sound objects based on

ITD information. Manipulating the complexity along the ITD-location dimension did not influence accuracy in recalling the musical pitch of the sound object for amusic as well as for normal listeners. In other words, memory for the ITD-dependent locations of tone sequence was not affected by simultaneously encoding the tone's pitch dimension, irrespective of whether one was informed of the to-be-recalled feature. Similar results have been reported in the visual domain, in which increasing the complexity of the visual-spatial pattern (on screen) had no effect on recall of the letters [57]. Our results extends previous findings by showing that in the auditory domain, ITD-dependent location and pitch seem to store separately at the working memory level even though both ITD and pitch rely on temporal phase locking mechanism at initial stage of auditory processing [5]. Such dissociation of working memory storage and retrieval for pitch and binaural ITDs is in line with the notion that musical pitch is stored separately from other perceptual features [58].

Regarding overall feature processing, our results showed that sound object's ITD location was more easily recalled than pitch feature for both amusic and control groups. One possibility for the difference in recall accuracy could be due to different rehearsal mechanisms for pitch and location features. Whereas location information might be readily rehearsed verbally as right, left or center positions, the musical pitch dimension (i.e., pure tones) does not lend itself easily to assignment of verbal labels as in consonants or pictures (except for people with absolute pitch). An alternative explanation could be the specificity of reference point used to rehearse location and musical pitch features for recall. Several studies have shown that most people are quite accurate when required to sing the first few notes of a familiar melody, suggesting that almost all humans have some degree of "absolute" pitch memory to classify pitch as high or low [59, 60]. Thus one may conceive that musical pitch feature may be rehearsed verbally as higher or lower just as location information can be rehearsed as left and right. The difference in recall accuracy between the localization and pitch task can thus be contributed to the specificity of reference point. While most people probably use the body midline as a consistent reference point in the spatial localization task to classify left and right, the reference point for musical pitch may be more susceptible to individual variability or between-trial adjustments. In addition, the use of a relative label for pitch or spatial location becomes more difficult if the number of items to be memorize increases or the proximity between pitch or location items decreases. For both ITD and pitch memory tasks, normal listeners showed better memory performance than amusic individuals. This finding is in line with several psychophysical reports showing an impaired and easily distracted memory for musical pitch in individuals with amusia [33-35]. Interestingly, amusic individuals exhibited impaired memory for the sound object's ITD simulated spatial-location memory even though the amusics' ITD discrimination thresholds at the perceptual level was compatible to that of normal listeners.

The results of working memory tasks suggest that musical pitch and spatial location of the auditory objects are retained and processed in two separate streams in auditory working memory. Impaired pitch system observed in individuals affected with congenital amusia did not interfere with memory of the spatial locations of musical pitch sequence. Manipulating the complexity level of the musical pitch dimension had no effect on recall performance of the spatial location of the pitch sequence, supporting a dissociation of processing between pitch and ITD features of auditory objects at working memory level. Our finding is consistent with recent EEG and MEG evidence showing a topographical difference between sound frequency and spatial location processing in auditory working memory [61]. In addition, the independent processing of pitch and ITD features observed here is consistent with the putative model of auditory dorsal and ventral streams for processing spatial and non-spatial properties of sounds, respectively [62, 63]. Since we observed a lack of interference between pitch and ITD features of sound here, one could infer that perhaps no binding or no robust binding exist

between these two sound features. However, this did not completely rule out the possibility that a weak binding exists between pitch and ITD features of sound in working memory among amusic individuals. Future studies that manipulate the difficulty levels of the pitch or ITD dimension of tone sequences, or tailor the perceptual difficulty of pitch interval stimuli based on an individual's pitch discrimination threshold could further shed light on the issue of feature binding in auditory working memory.

# Conclusions

The present study showed that individuals affected by congenital amusia are unimpaired in extracting the temporal fine-structure of sounds to lateralize the location of musical pitches using ITD information in the auditory periphery and at working memory level. Concurrent variations along the pitch feature of the sound object did not interfere with peripheral ITD discrimination. At the working memory level, amusic individuals showed impaired recall of both the musical pitch and ITD-dependent location features of the sound object. Increasing the complexity level along either sound feature had no effect on processing of the other feature, suggesting independent processing of pitch and ITD features of sound in working memory. Consistent with the dorsal and ventral account of segregated processing streams, the present findings showed no evidence of feature binding between musical pitch and ITD-dependent location in auditory working memory. Our findings demonstrate fine peripheral signal encoding and provide further evidence of a dissociative, but impaired, pitch and ITD encoding process at the auditory working memory level in amusic individuals.

# **Supporting information**

**S1 File. MBEA score and Expt. 1 data.** Used for Figs <u>4</u> & <u>5</u>. (XLSX)

**S2 File. Expt. 2 data.** Used for Figs <u>6 & 7</u>. (XLSX)

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