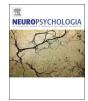
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## Neural bases of congenital amusia in tonal language speakers

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#### ABSTRACT

Congenital amusia is a lifelong neurodevelopmental disorder of fine-grained pitch processing. In this fMRI study, we examined the neural bases of congenial amusia in speakers of a tonal language - Cantonese. Previous studies on non-tonal language speakers suggest that the neural deficits of congenital amusia lie in the musicselective neural circuitry in the right inferior frontal gyrus (IFG). However, it is unclear whether this finding can generalize to congenital amusics in tonal languages. Tonal language experience has been reported to shape the neural processing of pitch, which raises the question of how tonal language experience affects the neural bases of congenital amusia. To investigate this question, we examined the neural circuitries sub-serving the processing of relative pitch interval in pitch-matched Cantonese level tone and musical stimuli in 11 Cantonese-speaking amusics and 11 musically intact controls. Cantonese-speaking amusics exhibited abnormal brain activities in a widely distributed neural network during the processing of lexical tone and musical stimuli. Whereas the controls exhibited significant activation in the right superior temporal gyrus (STG) in the lexical tone condition and in the cerebellum regardless of the lexical tone and music conditions, no activation was found in the amusics in those regions, which likely reflects a dysfunctional neural mechanism of relative pitch processing in the amusics. Furthermore, the amusics showed abnormally strong activation of the right middle frontal gyrus and precuneus when the pitch stimuli were repeated, which presumably reflect deficits of attending to repeated pitch stimuli or encoding them into working memory. No significant group difference was found in the right IFG in either the whole-brain analysis or region-of-interest analysis. These findings imply that the neural deficits in tonal language speakers might differ from those in non-tonal language speakers, and overlap partly with the neural circuitries of lexical tone processing (e.g. right STG).

#### 1. Introduction

Congenital amusia is a lifelong neurodevelopmental disorder that influences musical pitch processing (Ayotte et al., 2002; Peretz et al., 2002; Hyde and Peretz, 2003, 2004; Foxton et al., 2004). It is estimated to affect about 3–4% of the population (Peretz et al., 2008). Earlier studies suggest that this disorder is music-specific, leaving pitch processing in language intact (Ayotte et al., 2002; Peretz and Hyde, 2003). However, recent studies with more refined design found that amusia does affect pitch processing in language (Patel et al., 2005; Nguyen et al., 2009; Liu et al., 2010; Tillmann et al., 2011a, 2011b). Among non-tonal language speakers, the amusics were found to be impaired in intonation processing when pitch differences in speech stimuli were controlled and reduced (Liu et al., 2010). The amusics also had difficulty with accurate discrimination of non-native lexical tones (Nguyen et al., 2009; Tillmann et al., 2011a). Among tonal language speakers, those with congenital amusia exhibited inferior performance in the perception of native tones as well as nonnative tones (Nan et al., 2010; Jiang et al., 2012b; Wang and Peng, 2014; Liu et al., 2013, 2015; Huang et al., 2015a, 2015b). For instance, Nan et al. (2010) found that Mandarin-speaking amusics performed worse than musically intact controls in the identification and discrimination of Mandarin tones, though there was individual variation in the severity of lexical tone impairment. Furthermore, there is some evidence that the deficiency in tonal language speakers is not confined to auditory pitch processing, but prevails to higher-level phonological processing, impeding the categorical perception of lexical tone (Jiang et al. 2012b; Huang et al., 2015a). All these findings suggest that the musical pitch deficit prevails to pitch processing in language.

In spite of the ample behavioral evidence of pitch impairment in music and speech, however, the neural bases of congenital amusia remain unclear, especially in different language populations. Understanding the neural bases of congenital amusia is important, not only for shedding light on the nature of congenital amusia, but also

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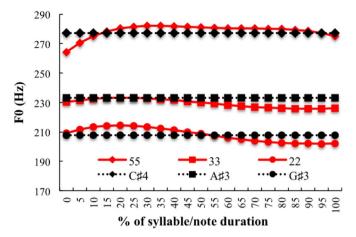
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Received 6 July 2016; Received in revised form 20 January 2017; Accepted 30 January 2017 Available online 31 January 2017 0028-3932/ © 2017 Elsevier Ltd. All rights reserved. for guiding the intervention. In non-tonal languages, although one study has found deficient pitch processing in the auditory cortices in congenital amusia (Albouy et al., 2013), the majority of neuroimaging studies have found that the auditory cortices of the amusics respond normally to pitch, especially in implicit pitch processing tasks (Omigie et al., 2013; Peretz et al., 2005, 2009; Hyde et al., 2011; Moreau et al., 2013; Norman-Haignere et al., 2016). For instance, in a functional MRI (fMRI) study, Hyde et al. (2011) found that the auditory cortices of the amusics responded normally to unattended pitch changes in a sequence of pitch stimuli. Instead, the functional deficits are localized in the music-selective neural circuitry in the right inferior frontal gyrus (IFG), which is believed to support musical pitch encoding and pitch memory (Zatorre et al., 1994; Holcomb et al., 1998; Griffiths et al., 1999). Furthermore, the right IFG showed anatomical abnormality in terms of the white and grey matter concentration in the amusic brain (Hyde et al., 2006, 2007; Albouy et al., 2013). Functional and structural connectivity between the right IFG and right auditory cortex is also disrupted (Hyde et al., 2011; Loui et al., 2009; Albouy et al., 2013).

The aforementioned studies have provided important data regarding the neural bases of congenital amusia in non-tonal language speakers. However, it remains unclear whether these findings can generalize to congenital amusia in different language populations, or might be under the influence of (non-tonal) language experience to some extent. In particular, it is worth examining the neural bases of congenital amusia in tonal language speakers. Long-term experience of a tonal language has been widely demonstrated to shape the neural processing of pitch (Bidelman et al., 2011, 2013; Tong et al., 2005; Luo et al., 2006; Gandour et al., 2002, 2004; Gu et al., 2013). In tonal languages, pitch is systematically used to convey information, like in music. Probably because of the overlap in pitch usage, cross-domain transfer between music and tonal language experience in pitch processing has been widely report at both behavioral and neural levels (Bidelman et al., 2011, 2013; Pfordresher and Brown, 2009; Deutsch et al., 2006; Peng et al., 2013; Wong et al., 2012; Alexander et al., 2005; Delogu et al., 2006, 2010; Lee and Hung, 2008; Lee et al., 2014; Smayda et al., 2015). Furthermore, as mentioned before, tonal language speakers with congenital amusia have been found to exhibit degraded performance in lexical tone perception (Nan et al., 2010; Jiang et al., 2012b; Wang and Peng, 2014; Liu et al., 2013, 2015; Huang et al., 2015a, 2015b), which also suggests that musical processing is intimately linked with lexical tone processing. Such crossdomain transfer hints at possibly shared neural pathways of musical and lexical tone processing in tonal language speakers with congenital amusia. However, this hypothesis has not been systematically examined at the neurobiological level before. As the majority of previous neuroimaging studies focused on non-tonal language speakers, little is known about the neural bases of amusia in tonal language speakers.

To fill in the gap, in the current fMRI study, we examined the effect of tonal language experience on the neural circuitries of pitch processing in lexical tone and musical stimuli in Cantonese speakers with congenital amusia. We hypothesize that the neural circuitries subserving pitch processing in lexical tone and music are commonly impaired in Cantonese-speaking congenital amusics. In particular, we aim to examine whether the neural deficits in tonal language speakers lie in music-selective neural circuitry in the right IFG as in non-tonal language speakers, or overlap with the neural circuitries of lexical tone processing (cf. Tong et al., 2005; Luo et al., 2006; Gandour et al., 2002, 2004; Wong et al., 2004; Li et al., 2010; Gu et al., 2013; Zhang et al., 2016). We chose Cantonese in this study because it has three level tones that contrast a relatively flat pitch contour at various pitch height, which can be matched with musical notes in pitch (see Fig. 1).

We adopted a *group* (amusic and normal)  $\times$  *domain* (speech and music)  $\times$  *pitch interval* (repetition, fixed pitch interval, and varied pitch interval) design to examine the neural bases of relative pitch perception, a fundamental human perceptual ability in both lexical



tone and musical perception (Saffran and Griepentrog, 2001; Itoh et al., 2005). It has been found that the absolute pitch height of a tone varies dramatically in the productions of speakers with different pitch ranges, and thus cannot be a reliable index of the tone category perceptually (Peng et al., 2012; Zhang et al., 2012, 2013). On the other hand, the pitch location of a tone within a speaker's pitch range is relatively constant across speakers (e.g. Wong and Diehl, 2003). For example, a high tone tends to be located close to the upper bound of a speaker's pitch range, while a low tone tends to be located close to the lower bound of a speaker's pitch range, no matter whether this speaker speaks with a high or low pitch range (Peng et al., 2012). It has been found that tonal language speakers rely on the relative pitch height of a tone with reference to a speaker's pitch range in lexical tone perception (Zhang et al., 2012, 2013; Zhang and Chen, 2016). Similarly, relative pitch relationship is critical for musical perception. A musical melody can be perceived as the same melody when presented at different keys, presumably because the relative pitch intervals between notes are constant across keys. Recognizing the same melody presented at different keys is to some extent analogous to recognizing the same tone produced by speakers with different pitch ranges, both of which rely on the constancy of the relative pitch relationship between notes/ tones

We used an adaptation paradigm (e.g. Celsis et al., 1999; Chandrasekaran et al., 2011; Joanisse et al., 2007; Zhang et al., 2016) to examine the neural activities underlying relative pitch processing in lexical tone and musical stimuli, via a comparison of three conditions - repetition, fixed interval, and varied interval. The repetition condition, where a pair of tone/music sounds was simply repeated eight times in a block, served as the control condition. The fixed interval condition included eight pairs of tone/music sounds with repeated pitch interval at various pitch height in a block. The pitch interval was identical between the fixed interval and repetition condition, but the pitch height was different. The varied interval condition included eight pairs of tone/music sounds with varied pitch intervals at various pitch height in a block. Repetition of the pitch interval in the repetition and fixed interval conditions is expected to habituate the Blood Oxygenation Level Dependent (BOLD) signal in brain regions sensitive to relative pitch processing. The varied interval condition would result in a release from habituation, increasing the BOLD signal in those same regions. It has been found that implicit lexical tonal changes presented in an adaptation paradigm activated the superior temporal gyrus (STG) bilaterally in Cantonese speakers, among other

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