Journal Club

Editor's Note: These short, critical reviews of recent papers in the *Journal*, written exclusively by graduate students or postdoctoral fellows, are intended to summarize the important findings of the paper and provide additional insight and commentary. For more information on the format and purpose of the Journal Club, please see http://www.jneurosci.org/misc/ifa_features.shtml.

The Neural Causes of Congenital Amusia

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Review of Norman-Haignere et al.

Congenital amusia is a lifelong disorder in pitch processing and music perception that affects ~4% of the population (Peretz et al., 2002; Peretz and Hyde, 2003). Despite having normal hearing and speech recognition, as well as no prior brain lesions or cognitive deficits, individuals with congenital amusia have difficulty recognizing melodies and detecting pitch changes (Peretz et al., 2002; Tillmann et al., 2009; Liu et al., 2010). Their "musical deafness" is thought to reflect underlying impairments in pitch perception and memory. However, the underlying neural causes of congenital amusia are still actively debated.

Previous studies have suggested three possible neural causes for congenital amusia. One is that congenital amusia is associated with reduced frontotemporal connectivity, which makes it difficult for people with the disorder to consciously access pitch information encoded in their auditory cortex (Loui et al., 2009; Hyde et al., 2011; Albouy et al., 2013, 2015; but see Chen et al., 2015). Alternatively, the pitch-related deficits may be caused by dysfunctions in the frontal cortex (Hyde et al., 2006, 2011; Albouy et al., 2013). For example, Albouy et al. (2013) revealed that low gamma oscillations (30–40 Hz range) in the right dorsolateral prefrontal cortex (DLPFC) were lower in amusics than in healthy controls. A third possibility, however, is that individuals with congenital amusia have abnormal pitch responsive region(s) in their auditory cortex, despite the fact that the auditory cortex seems to have normal responses to pitch changes (Hyde et al., 2011; Moreauet al., 2013; but see Albouy et al., 2013; Zendel et al., 2015). Norman-Haignere et al. (2016) examined the third possibility by investigating pitch-specific activation in the auditory cortex. Amusic subjects and age- and education-matched controls passively listened to harmonic tones and frequency-matched noise during an fMRI scan. Results revealed that: (1) amusics and controls both exhibited stronger activation in pitch-responsive voxels to harmonic tones than to noise in a similar anatomical location. (2) No difference was found in pitch-responsive voxels activation between amusics and controls. (3) The selectivity of pitch-responsive voxels in the auditory cortex showed no difference between amusics and controls.

In sum, Norman-Haignere et al. (2016) demonstrated that pitch-responsive regions in amusics' auditory cortex are comparable in extent, selectivity, and anatomical location to those of controls. These results therefore suggest that the congenital amusia is unlikely caused by deficits in these regions, and combined with other studies (Hyde et al., 2011; Moreau et al., 2013; Zendel et al., 2015), they suggest that amusics' pitch-processing deficits are due to impairments in regions outside of the pitch-responsive areas. Considering amusics can exhibit a normal priming effect of note expectancy (faster response to expected notes) based on the musical pitch context (Omigie et al., 2012) and that some amusics have deficits in music perception but not pitch discrimination (Tillmann et al., 2009; Liu et al., 2010), it is plausible that congenital amusia results from deficits in frontotemporal connectivity or dysfunctions in the frontal cortex.

Recent neurological findings support this argument. Studies on individuals with congenital amusia have revealed reduced white matter density in the right inferior frontal gyrus (Hyde et al., 2006), cortical malformations in the right inferior frontal gyrus and right auditory cortex (Hyde et al., 2007), and abnormal deactivation in the right inferior frontal gyrus (Hyde et al., 2011). A more recent magnetoencephalography study has also reported decreased low-gamma oscillations in the right DLPFC during pitch memory task (Albouy et al., 2013). These studies, however, are unable to distinguish whether congenital amusia is the result of weak connectivity or if it is due to the deficits in the prefrontal cortex.

A recent study by Schaal et al. (2015) supports the possibility that the neural causes of congenital amusia are located in the frontal cortex. Based on previous findings (Albouy et al., 2013), Schaal et al. (2015) demonstrated that modulating the right DLPFC with transracial alternating current stimulation (tACS) at 35 Hz selectively improved pitch memory, but not visual memory, in amusics. Participants received either 35 or 90 Hz tACS during a

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pitch short-term memory span task and visual short-term span task. Results showed that 35 Hz tACS significantly improved the behavioral performance in pitch memory task in amusics to the extent that there was no significant performance difference between amusics and controls. Such results suggest a causal relationship between congenital amusia and dysfunctions in the prefrontal cortex, especially the right DLPFC.

Given that individuals with congenital amusia have normal pitch-responsive regions in the auditory cortex and an increase of activity in the DLPFC can lead to performance facilitation in a pitch memory task (Schaal et al., 2015; Norman-Haignere et al., 2016), we might conclude that the impairments in right DLPFC are the main causes of congenital amusia. It is also possible, however, that the applied stimulation of 35 Hz tACS has modulated the connectivity between the right DLPFC and the auditory cortex rather than the right DLPFC itself. Further study is needed to rule out this possibility.

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