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Research Report

Alterations of the emotional processing system may underlie preserved rapid reaction time in tinnitus

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ARTICLE INFO

Article history:
Accepted 13 April 2014
Available online 23 April 2014

Keywords:
Tinnitus
fMRI
Emotion
IADS

ABSTRACT

Although alterations of the limbic system have been linked to tinnitus persistence, the neural networks underlying such alteration are unclear. The present study investigated the effect of tinnitus on emotional processing in middle-aged adults using functional magnetic resonance imaging and stimuli from the International Affective Digital Sounds database. There were three groups of participants: bilateral hearing loss with tinnitus (TIN), age- and gender-matched controls with bilateral hearing loss without tinnitus (HL) and matched normal hearing controls without tinnitus (NH). In the scanner, subjects rated sounds as pleasant, unpleasant, or neutral. The TIN and NH groups, but not the HL group, responded faster to affective sounds compared to neutral sounds. The TIN group had elevated response in bilateral parahippocampus and right insula compared to the NH group, and left parahippocampus compared to HL controls for pleasant relative to neutral sounds. A region-of-interest analysis detected increased activation for NH controls in the right amygdala when responding to affective stimuli, but failed to find a similar heightened response in the TIN and HL groups. All three groups showed increased response in auditory cortices for the affective relative to neutral sounds comparisons. Our results suggest that the emotional processing network is altered in tinnitus to rely on the parahippocampus and insula, rather than the amygdala, and this alteration may maintain a select advantage for the rapid processing of affective stimuli despite the hearing loss. The complex interaction of tinnitus and the limbic system should be accounted for in development of new tinnitus management strategies.

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http://dx.doi.org/10.1016/j.brainres.2014.04.024
0006-8993/

1. Introduction

Subjective tinnitus, often described as ringing in the ears, is a common auditory disorder and is frequently associated with hearing loss (Adams et al., 1999; Lockwood et al., 1998). Tinnitus has been noted in patients with severed auditory nerves, which suggests that the internal noise need not originate in the periphery but may have correlates in the central nervous system (House and Brackmann, 1981; Lockwood et al., 2002). Behavioral studies were among the first to show an association between tinnitus and emotional processing exemplified in impaired sleeping habits, increased stress level, frustration, depression, irritability, and anxiety (Andersson and Vretblad, 2000; Andersson, 2002; Bartels et al., 2010; Hallam et al., 1988; Rutter and Stein, 1999; Sindhusake et al., 2004; Tyler and Baker, 1983). In recent years, studies have utilized neural imaging techniques to advance our knowledge of the neural correlates of tinnitus (Burton et al., 2012; Golm et al., 2013; Haller et al., 2010; Leaver et al., 2011; Mirz et al., 2000b). However, few studies have explicitly investigated the limbic-auditory link using functional brain imaging tools. A reason tinnitus remains difficult to treat is because mechanisms for its persistence are not fully understood. Therefore, the goal of the present study was to investigate the neural alterations associated with tinnitus, related to changes in the limbic system reflected in emotional processing of unpleasant and pleasant sounds.

Alterations of the limbic system associated with bothersome tinnitus is one of the most studied mechanisms in tinnitus persistence (Henry et al., 2002; Jastreboff, 1990; Jastreboff and Jastreboff, 2000; Mirz et al., 2000a; Muhlau et al., 2006; Shargorodsky et al., 2010). Jastreboff (1990) advanced the idea that the amygdala, a key region of the limbic system, plays a central role in the development of bothersome tinnitus. He suggested that the tinnitus signal is similar to an alarm bell, which can have a range of emotional associations. The negative emotional significance given to the signal from the limbic system enhances its detection and results in the tinnitus percept becoming chronic. Jastreboff's theory is supported by recent findings of Kumar et al. (2012). Kumar and his colleagues collected fMRI data from normal hearing adults and employed effective connectivity analysis to evaluate connections between the auditory cortex and the amygdala. They observed that the backward connections from the amygdala to the auditory cortex are associated with the evaluation of emotional content of sounds and the forward connections are associated with the evaluation of acoustic information (Kumar et al., 2012). The feedback connections from the amygdala to the auditory cortex may explain the emotional significance attributed to the tinnitus precept. Therefore one hypothesis, tested in the present study, was that individuals with tinnitus would show a heightened response in the amygdala to affective sounds, in particular to the unpleasant sounds.

In addition to the amygdala, other limbic regions associated with tinnitus are parahippocampus and insula. De Ridder et al. (2011) conducted a resting state EEG study on individuals with mild to severe tinnitus and found that tinnitus-related distress is correlated with abnormal activity in a network consisting of frontal and limbic structures, including the parahippocampus and insula. An fMRI study, which involved reading unpleasant and neutral sentences, noted increased activity in the insula and frontal regions in individuals with tinnitus compared to non-tinnitus controls while viewing unpleasant sentences (Golm et al., 2013). The authors proposed that the increased activity in the insula may be correlated with tinnitus distress. Note that the Golm et al. (2013) group used unpleasant stimuli and they did not find significant differences in parahippocampal response between groups. Based on these studies, we expected that individuals with tinnitus would show a heightened response in the parahippocampus and the insula to affective sounds, and this would be most notable for the unpleasant sounds.

Previous studies have also implicated the ventral medial prefrontal cortex (vmPFC) and nucleus accumbens (NAc) as regions associated with tinnitus. Structural imaging studies have provided evidence that the vmPFC and NAc may typically work toward the cessation and decreased intrusiveness of tinnitus by stimulating the thalamic reticular nucleus intercepting of the tinnitus signal and preventing its conscious perception (Muhlau et al., 2006; Rauschecker et al., 2010). Therefore decreased functioning of the vmPFC and NAc may be associated with tinnitus persistence.

In addition to limbic regions, elevated response patterns have also been observed in central auditory areas in tinnitus. Major regions shown to exhibit hyperactivity in tinnitus are the inferior colliculus and auditory cortex (Jastreboff and Sasaki, 1986; Leaver et al., 2011; Melcher et al., 2009; Zhang et al., 2011). Elevated response from the inferior colliculus in subjects with tinnitus has been shown in human studies using fMRI and broadband band sound presented to tinnitus and non-tinnitus controls (Melcher et al., 2009). Additionally, in a study using fMRI and sounds matched to the subject's tinnitus, hyperactivity in the auditory cortex was observed in tinnitus (Leaver et al., 2011). Therefore, we anticipated the tinnitus group would exhibit increased response in auditory regions. Based the aforementioned impact of tinnitus on auditory regions and the auditory nature of the disorder, we used sounds instead of non-auditory stimuli because of a greater expectation of the impact of tinnitus on the auditory modality.

The international affective digital sounds (Bradley and Lang, 2007), used in the present study, were previously rated by young, healthy participants to be pleasant, unpleasant, and neutral. The few studies that have investigated tinnitus using functional imaging and affective stimuli have primarily used unpleasant or neutral stimuli (Golm et al., 2013; Mirz et al., 2000b; Schlee et al., 2008). For instance, the Golm et al. (2013) group displayed unpleasant and neutral sentences to the volunteers. Additionally, a recent functional connectivity study used unpleasant tones matched to an individual's tinnitus and neutral tones different than the individual's tinnitus to evoke a response from the tinnitus network (Schlee et al., 2008). Confirming their prediction, they found the unpleasant tones stimulated the tinnitus network to a greater extent than the control sounds (Schlee et al., 2008). The Mirz et al. (2000a) research team used an unpleasant tinnitus-like tone to investigate how tinnitus may alter brain function in healthy adults. As expected, they found increased