



Research paper

Tinnitus-related abnormalities in visual and salience networks during a one-back task with distractors

Ana A. Amaral ^{a, b, *, 1}, Dave R.M. Langers ^{b, c, 2}^a Champalimaud Neuroscience Programme, Champalimaud Centre for the Unknown, Avenida Brasília, 1400-038 Lisbon, Portugal^b Department of Otorhinolaryngology/Head and Neck Surgery, University Medical Center Groningen, University of Groningen, P.O. Box 30.001, 9700 RB Groningen, The Netherlands^c National Institute for Health Research (NIHR) Nottingham Hearing Biomedical Research Unit, University of Nottingham, Nottingham NG1 5DU, United Kingdom

ARTICLE INFO

Article history:

Received 8 September 2014

Received in revised form

23 February 2015

Accepted 16 March 2015

Available online 2 April 2015

ABSTRACT

Tinnitus is highly prevalent in the general population. Tinnitus sufferers often report having difficulties focusing on a task at hand and ignoring the tinnitus percept. Behavioral studies have shown evidence for impairments in attention, interference inhibition, and various other executive functions in tinnitus. However, few neuroimaging studies have directly addressed this issue. In the present functional Magnetic Resonance Imaging (fMRI) study we employed a 1-back task, requiring subjects to monitor relevant auditory and visual information. Additionally, interfering stimuli were presented to investigate selection of relevant information and inhibition of irrelevant information. Significant behavioral group differences were not found, although performance worsened for increasing tinnitus severity. Significant group differences in evoked neural activation neither occurred in the central auditory system, nor in the attentional fronto-parietal network. However, the anterior insula and the vermis of the cerebellum showed significantly stronger task-related activation in the tinnitus group when compared to the controls. Furthermore, deactivation in the primary visual cortex that occurred in the control group for various combinations of modalities and distractors was significantly less in the tinnitus group. These results are consistent with previous studies that showed the involvement of various networks in tinnitus, particularly the salience and visual networks, which are also implicated in attention. Although we did not demonstrate cognitive impairment in tinnitus, significantly different evoked responses were found in various brain regions that we attribute to an abnormal involvement of attention control mechanisms in tinnitus.

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1. Introduction

Subjective tinnitus can be defined as an auditory percept that has no objectifiable external source, and no cause that can be

attributed to any physical sound source resulting from inside the body. Tinnitus is highly prevalent in the general population. It has been reported that prolonged tinnitus requiring medical evaluation affects 10–15% of adults (Heller, 2003; Henry et al., 2005).

Abbreviations: A, target stream in the auditory modality; ADHD, attention deficit hyperactivity disorder; alns, anterior insula; ANCOVA, analysis of covariance; ANOVA, analysis of variance; BA6, Brodmann area 6/premotor and supplementary motor areas; BOLD, blood oxygen level-dependent; DMN, default mode network; EEG, electroencephalography; FA, flip angle; FDR, False Discovery Rate; fMRI, functional magnetic resonance imaging; FOV, field of view; FWE, family-wise error; HADS, Hospital Anxiety and Depression Scale; HQ, Hyperacusis Questionnaire; L, target stream in the left ear; LAC, left auditory cortex; lPutamen, left putamen; PVC, primary visual cortex; R, target stream in the right ear; RAC, right auditory cortex; ROI, region of interest; RT, reaction time; SPM, statistical parametric map; SVC, secondary visual cortex; TA, acquisition time; TE, echo time; THI, Tinnitus Handicap Inventory; TR, repetition time; V, target stream in the visual modality

* Corresponding author. Champalimaud Neuroscience Programme, Champalimaud Centre for the Unknown, Avenida Brasília, 1400-038 Lisbon, Portugal.

E-mail address: ana.amaral@neuro.fchampalimaud.org (A.A. Amaral).

¹ Present address: Champalimaud Neuroscience Programme, Champalimaud Centre for the Unknown, Avenida Brasília 1400-038 Lisbon, Portugal.

² Present address: Department of Otorhinolaryngology/Head and Neck Surgery, University Medical Center Groningen, University of Groningen, BB20, P.O. Box 30.001, 9700 RB Groningen, The Netherlands.

Depression and emotional difficulties in personal relationships constitute important comorbid factors influencing the quality of life of tinnitus sufferers. Additionally, tinnitus sufferers often report impaired cognitive processing and concentration difficulties (Hallam et al., 1988; Erlandsson and Hallberg, 2000).

It has been hypothesized that attention plays a role in the establishment of an increased chronic awareness of tinnitus through a negative reinforcement of the subjects' emotional response, which prevents habituation and adaptation (Jastreboff, 1990; Andersson, 2002; Jastreboff and Jastreboff, 2006). Rauschecker et al. (2010) proposed that a failure of the limbic system to block the auditory signal acts as an emotion-related "sensory gating" mechanism that leads to the chronic perception of tinnitus. Attentional processes may be involved in the modulation of the sensory and limbic systems (Zikopoulos and Barbas, 2006; Wolf et al., 2014). Others proposed that the tinnitus percept emerges as a result of various distributed brain networks, which have common nodes (De Ridder et al., 2011, 2013). While asserting that there must be a minimal core network, this model proposes that individual differences in tinnitus perception are determined by other core-connected networks involved in the generation of the tinnitus percept (De Ridder et al., 2013). Because these latter models essentially focus on physiology, they do not directly elucidate the role of attention as a main player in the generation of the tinnitus percept. In a recent review, Roberts et al. (2013) stressed the need for further research to better understand the role of attention in tinnitus. The present study aims to investigate attentional engagement in tinnitus by studying its interactions with auditory and non-auditory stimuli presented during task-performance.

Behavioral studies have addressed the role of attention and cognition in tinnitus using various tasks. It has been reported that tinnitus subjects are slower in a dual task condition (Hallam et al., 2004), which might be related to switching of attention and multitasking functions. Rossiter et al. (2006) employed working memory and visual divided-attention tasks and reported impaired performance for tinnitus subjects, although only in their most demanding dual task. Stevens et al. (2007) used visual tasks involving selective and divided attention, and showed increased reaction times for their severe tinnitus group on both tasks, and both in easy and hard conditions. Recently, Heeren et al. (2014) showed that tinnitus subjects have a specific deficit related to the control of attention, which is required for the efficient allocation of resources to relevant input. This study did not find evidence for general cognitive impairment attributable to tinnitus. Most of these studies have additionally addressed the effect of anxiety and depression, but found that this could not account for the behavioral differences (Rossiter et al., 2006; Stevens et al., 2007). Overall, these studies suggest that cognitive problems in tinnitus subjects are likely related to attention. Furthermore, because some studies use visual tasks this suggests that non-auditory attention and tinnitus processing interact. Moreover, tinnitus interference likely depends on task demand.

The processing of a tinnitus percept might be comparable to that of a task-irrelevant sound present in the environment (Hallam et al., 2004; Stevens et al., 2007), which can cause interference and consequently impair performance (Hesser et al., 2009). Andersson et al. (2000) used a color-word Stroop task and reported that their tinnitus group was slower to name the colors than the control group without tinnitus, suggesting that inhibition of interference is impaired. When performing a task with stimuli presented to one ear, while ignoring task-irrelevant stimuli presented to the other ear, unilateral tinnitus subjects show less interference from the irrelevant stimuli when these are presented to the non-tinnitus ear (Cuny et al., 2004). This experiment suggests

that attention is being permanently drawn to the tinnitus ear. Although habituation usually takes place to repeated irrelevant stimulus presentations (Thompson and Spencer, 1966), tinnitus seems to behave differently. This suggests that tinnitus is a consequence of a habituation deficit to the tinnitus percept, resulting in a constant reorientation of attention, causing increased awareness.

There are a number of tinnitus studies addressing brain function in tinnitus in relation to attention. Electroencephalography (EEG) and magnetoencephalography (MEG) studies showed that selective attention plays a role in tinnitus (Jacobson et al., 1996; Paul et al., 2014; but see also Diesch et al., 2012). Positron emission tomography (PET) studies showed altered tinnitus-related activity in frontotemporal and parietotemporal regions (Mirz et al., 1999, 2000a, 2000b), which have been implicated in auditory attention (Zatorre et al., 1999). In another study, Andersson et al. (2006) showed that tinnitus loudness and annoyance were decreased during task performance compared to baseline. At the same time, cerebral blood flow decreased in attentional regions as well as auditory cortex, suggesting that attention can modulate responses in the tinnitus brain and influence the concurrent perceptual tinnitus severity. Using functional Magnetic Resonance Imaging (fMRI), Husain et al. (2011) addressed effects of sensory and cognitive processes in chronic tinnitus in the presence of hearing loss, and found no behavioral differences with controls. Normal hearing controls showed stronger responses in the left middle and inferior frontal gyri than tinnitus subjects with hearing loss, during passive listening. Additionally, tinnitus group responses were shown to be stronger in the temporal gyri and the right superior frontal gyrus than normal hearing controls' responses. These studies indicate that task-performance interferes with the tinnitus percept, possibly by distracting subjects from it. Tinnitus-related behavioral effects have not been consistently shown, suggesting a relation with task-difficulty. Nevertheless, tinnitus-related neural responses have been found in regions known to be part of the attention and short-term memory networks; however, in some studies interactions with hearing loss cannot be completely discarded.

In the present fMRI study we employed a 1-back task, requiring normal hearing subjects to monitor relevant sensory information and perform successive stimulus comparisons. Additionally, interfering stimuli were presented requiring inhibition of irrelevant input. Auditory and visual stimuli were employed to understand attentional processes operating on interference in the same and in different sensory modalities as the tinnitus. Various interfering conditions were employed to modulate task difficulty and attentional demands. Based on previous findings we hypothesize that tinnitus subjects will show impaired behavioral outcomes when compared to the control group, especially in difficult conditions. Additionally, it is expected that the tinnitus group differently engages the sensory and attentional systems in the brain, and particularly the auditory, visual and fronto-parietal regions.

2. Methods

2.1. Subjects

Twenty-one healthy controls and thirteen subjective tinnitus subjects were included, matched regarding age, handedness and hearing loss. All subjects participated in the present fMRI study on two separate days, each comprising a 1-h neuroimaging session that was preceded by an approximately ½-h training session. A subset of results from the unimodal session involving only the control subjects has been previously published (Amaral and Langers, 2013). We presently focus on comparisons between the control and tinnitus groups.

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