Autonomic Neuroscience: Basic and Clinical 165 (2011) 191–194

Contents lists available at ScienceDirect

Autonomic Neuroscience: Basic and Clinical

journal homepage: www.elsevier.com/locate/autneu

Insular lateralization in tinnitus distress

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ARTICLE INFO

Article history:
Received 31 August 2010
Received in revised form 28 June 2011
Accepted 29 June 2011

Keywords:
Tinnitus
Insula
eLORETA
HRV
Autonomic Nervous System

ABSTRACT

Tinnitus affects 15% of the population. Of these 1–2% are severely disabled by it. The role of the autonomic system in tinnitus is hardly being investigated. The aim of this study is to investigate the relationship between tinnitus distress and lateralization of the anterior insula, known to be involved in interoceptive awareness and (para)sympathetic changes. For this, Tinnitus Questionnaire scores are correlated to Heart Rate Variability markers, and related to neural activity in left and right anterior insula. Our results show that tinnitus distress is related to sympathetic activation, in part mediated via the right anterior insula.

1. Introduction

Tinnitus is a symptom that affects 15% of the population (Axelsson and Ringdahl, 1989). Most people who have tinnitus can effectively cope with it, however a small percentage of tinnitus sufferers demonstrate maladaptive coping (Scott et al., 1990; Budd and Pugh, 1996; Tyler et al., 2006): 1–2% of tinnitus sufferers are severely disabled by their tinnitus (Axelsson and Ringdahl, 1989). This maladaptive coping group suffers significantly more from associated somatic complaints such as headaches, neck and shoulder pain, low back pain, muscle tension, sleep and concentration problems (Hiller et al., 1997; Scott and Lindberg, 2000) and demonstrates cognitive inefficiency (Hallam et al., 2004), poor stress coping (Scott and Lindberg, 2000) and depression (Harrop-Griffiths et al., 1987; Sullivan et al., 1988; Scott and Lindberg, 2000; Dobie, 2003; Folmer and Shi, 2004).

The amount of distress people experience related to tinnitus can be evaluated by the use of validated tinnitus questionnaires. Tinnitus distress is associated to a higher orthosympathetic (OS) tone (Datzov et al., 1999) and tinnitus suppression induces an increased parasympathetic (PS) tone (Matsushima et al., 1996). Previous functional imaging studies show that specific frontal cortical areas closely relate to emotion perception and interoception. The right anterior insula seems to be specifically involved in the representation of subjective feelings (Craig, 2003; Critchley et al., 2004). Based on human lesion and electrical stimulation studies it has also been suggested that the right insula controls cardiac OS activity whereas the left insula is predominantly associated to PS activity (Oppenheimer et al., 1992; Oppenheimer, 1993, 2006; Oppenheimer et al., 1996). Functional Magnetic Resonance Imaging (fMRI) studies of sympathetic skin conductance response seem to confirm this lateralization by revealing right insula activation (Critchley et al., 2000). Furthermore, when correlating dichotic visual stimuli with Heart Rate Variability (HRV) the same lateralization effect is found (Wittling et al., 1998a; Wittling et al., 1998b).

Heart Rate Variability (HRV) is a simple and non-invasive quantitative marker of autonomic function. As a result of continuous variations of the balance between OS and PS neural activity influencing heart rate, intervals between consecutive heartbeats (RR intervals) show spontaneously occurring oscillations. For HRV spectral analysis three main underlying frequencies have been used in literature: the very-low-frequency range (VLF $\leq$ 0.04 Hz), the low-frequency range (LF: 0.04–0.15 Hz) and the high frequency range (HF: 0.15–0.4 Hz). The high frequency component of HRV is believed to be influenced by vagal activity and is also related to the frequency of respiration (Yasuma and Hayano, 2004). Low-frequency (LF) power is modulated by baroreceptor activities and fluctuations in heart rate in the LF range reflect OS as well as PS influences. Low-frequency power, therefore, cannot be considered to reflect pure OS activity. However if normalized units of LF and HF are considered, the OS and PS influences respectively are emphasized (Electrophysiology, 1996). In HRV frequency domain, normalized units (n.u.) of LF and HF components therefore reflect OS and PS influences respectively.

The aim of this study is to investigate the relation between tinnitus distress and lateralisation of the anterior insula, known to be involved in interoceptive awareness and OS as well as PS changes. For this, tinnitus questionnaire (TQ) scores (Goebel and Hiller, 1994) are

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doi:10.1016/j.autneu.2011.06.007

correlated to HRV markers, and related to neural activity in left and right anterior insula.

2. Methods

Ten patients with strictly right-sided unilateral tinnitus are analyzed. EEG and ECG signals are recorded simultaneously over 5 min in supine position using a 32 channel digital EEG (Neuroscan, Compumedics, Houston, TX) in a dimly illuminated and soundproof room (sampling rate = 500 Hz, band passed 0.15–100 Hz). Electrodes are referenced near the vertex and impedances checked to remain below 5 kΩ. To minimize respiratory influences on HRV, respiration is controlled at 12 bpm using auditory cues. All patients complete a validated Dutch version of the TQ (Meeus et al., 2007), which reflects the amount of tinnitus related distress perceived by the patient (Goebel and Hiller, 1994).

2.1. ECG analyses

ECG signals are processed by time and frequency domain methods as recommended by the Task force (Electrophysiology, 1996): QRS complexes are recognized from the short-term artifact-free ECG recordings from which peaks (R-waves) are detected and from which intervals between two consecutive peaks (RR intervals) are calculated. Once HRV time series are extracted they are analyzed in the time and frequency domain using HRV Analysis Software 1.1 for windows developed by The Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Finland. Pearson correlations between OS (LF n.u.) and PS (HF n.u.) markers of HRV and TQ-scores are performed.

2.2. EEG analyses

EEG segments contaminated by artifacts are rejected offline by visual inspection. The remaining data are analyzed in the frequency domain by means of Fast Fourier Transform (FFT) analysis. Two regions of interest (ROI) corresponding to the right and left anterior insula are selected in the MNI atlas (Fig. 1). A spatial filter approach known as beamforming (Congedo, 2006) targeting these two ROIs is applied in order to obtain current density estimations within these ROIs by the eLORETA method (Pascual-Marqui, 2007). The log-current density is correlated with the TQ-scores, in all 1 Hz spaced discrete Fourier frequencies in the range 1 Hz–60 Hz. Significant trends are formulated with a $p<0.05$.

3. Results

TQ-scores ($M = 40.2$; $SD = 13.7$) correlate positively with the OS marker, the Low Frequency normalized units (r = 0.58), and negatively with the PS marker, the High Frequency normalized units (r = −0.58).

In addition, current density analyses show that increased cortical activity in the left anterior insula at 11 Hz (r = 0.56; alpha band) and decreased activity at 4 Hz (r = −0.63; theta band) and in the high gamma band frequencies (54 Hz, r = −0.58; 59 Hz, r = −0.74) relate to increased TQ-scores. In the right anterior insula increasing TQ-scores were found with increased activity in delta band frequencies (2 Hz, r = 0.67) and gamma band frequencies (32 Hz, r = 0.74; 39 Hz, r = 0.56). No significant decreases are noted in this area.

4. Discussion

Our results show a positive relation between OS load and tinnitus distress as measured by the TQ (Goebel and Hiller, 1994). In addition the right anterior insula, an area related to OS influence, shows

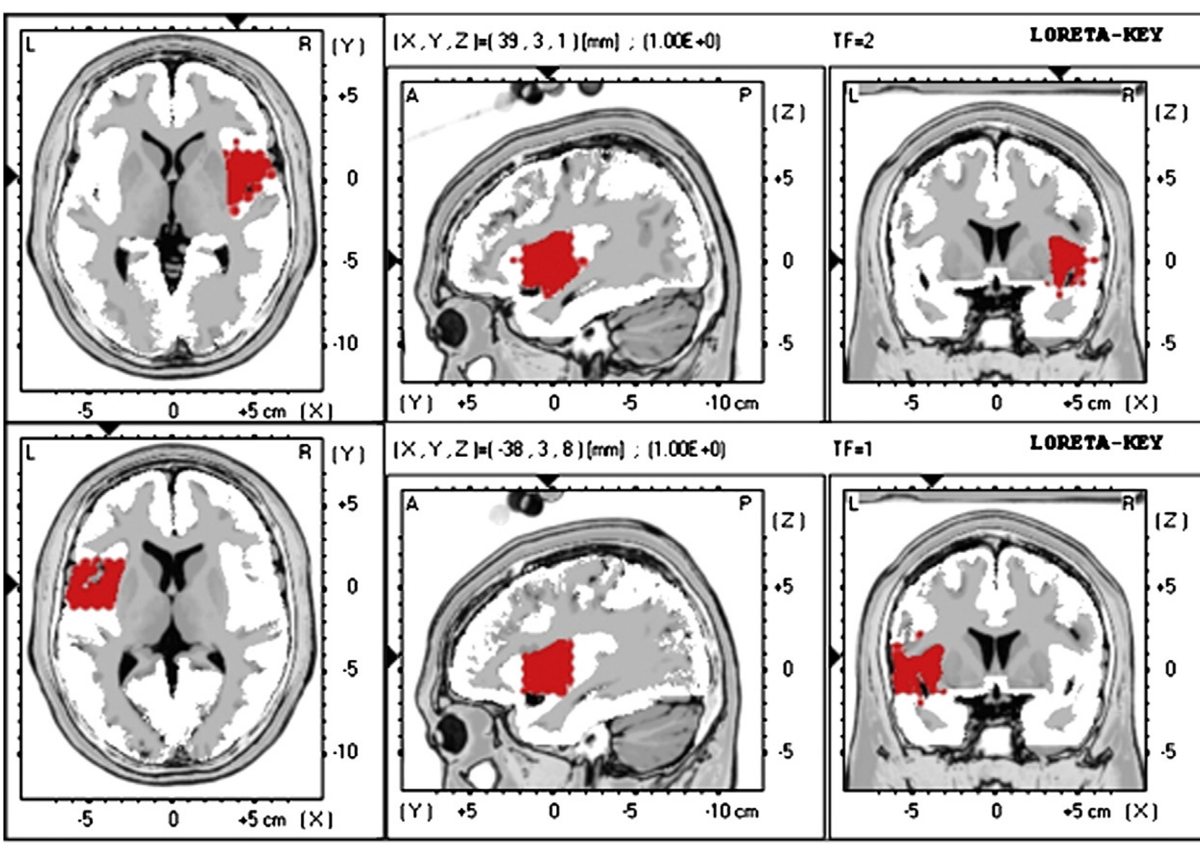

Fig. 1. Regions of interest: Right anterior insula (upper panel) and left anterior insula (lower panel). Displayed sections are the axial (left), sagittal (middle), and coronal (right) sections.