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## Tinnitus and musical hallucinosis: The same but more

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#### ABSTRACT

While tinnitus can be interpreted as a simple or elementary form of auditory phantom perception, musical hallucinosis is a more complex auditory phantom phenomenon not only limited to sound perception, but also containing semantic and musical content. It most often occurs in association with hearing loss. To elucidate the relation between simple and complex auditory phantom percepts a source localized electroencephalography (EEG) study is performed. The analyses showed in both simple and complex auditory phantoms an increase in theta-gamma activity and coupling within the auditory cortex that could be associated with the thalamocortical dysrhythmia model. Furthermore increased beta activity within the dorsal anterior cingulate cortex and anterior insula is demonstrated, that might be related to auditory awareness, salience and its attribution to an external sound source. The difference between simple and complex auditory phantoms relies on differential alpha band activity within the auditory cortex and on beta activity in the dorsal anterior cingulate cortex and (para) hippocampal area. This could be related to memory based load dependency, while suppression within the primary visual cortex might be due the presence of a continuous auditory cortex activation inducing an inhibitory signal to the visual system. Complex auditory phantoms further activate the right inferior frontal area (right sided Broca homolog) and right superior temporal pole that might be associated with the musical content. In summary, this study showed for the first time that simple and complex auditory phantoms might share a common neural substrate but differ as complex auditory phantoms are associated with activation in brain areas related to music and language processing.

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#### Introduction

Many people perceive an auditory percept in the absence of any objective physical sound source (Jastreboff, 1990). This has been attributed as a mechanism that resolves sensory uncertainty, possibly explaining its high prevalence (De Ridder et al., in press). This phantom sound can be a tone, hissing, or buzzing sound and in some cases the auditory phantom can present as music or voices. The hearing of a simple tone or noise has been referred to as tinnitus, from the Latin word *tinnire* for "to ring", while hearing voices and music are named respectively verbal and musical hallucinations. While tinnitus can be interpreted as a simple or elementary form of auditory phantom perception, musical and verbal hallucinations are more complex auditory phantom phenomena not only limited to sound perception, but also containing semantic

content. Whereas verbal hallucinations are a typical feature of a psychiatric condition (i.e. psychosis or schizophrenia), musical hallucinations often result from severe auditory deprivation or deafness due to deafferentation or a lesion situated anywhere along the auditory pathway beside other sometimes unknown factors (Braun et al., 2003; Griffiths, 2000). Musical hallucinations have been reported as arising from lesions of early stages of sound processing (brainstem, pons, thalamus and auditory radiation), and of higher-level auditory association cortices such as the temporal lobe (Cope and Baguley, 2009) and insula (Isolan et al., 2010). The cause of the lesion also appears unimportant, with musical hallucinosis being caused by intracranial aneurysms, ischemic infarction, hemorrhage and tumors (Cope and Baguley, 2009). The commonly used term musical hallucinosis refers to a state characterized by the presence of music perception in the absence of an external sound source, and without impairment of consciousness. In most cases people with musical hallucinosis are initially unaware that these sounds are subjectively generated, but readily become aware that they are internally generated as nobody else hears the music. This is analogous to some forms of tinnitus. This however is in contrast to verbal hallucinations in the setting of psychosis. Musical hallucinosis is also different from vivid auditory imagery as the auditory percepts in musical hallucinosis are







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involuntary. It is thus very similar to tinnitus, which most commonly is also constantly present, in contrast to the intermittent character of verbal hallucinations.

Although many studies investigate the neural correlates of tinnitus (De Ridder et al., 2011a) and verbal hallucinations (Diederen et al., 2010; Sommer et al., 2010), few studies address musical hallucinosis (Griffiths, 2000; Kasai et al., 1999) and none have compared simple versus complex auditory phantom percepts. As both tinnitus and musical hallucinosis are often related to sound deprivation, in contrast to psychotic verbal auditory phantoms, tinnitus and musical hallucinosis as auditory phantom perceptions might share a common neural substrate differing only in its complexity, with musical hallucinosis encompassing areas processing higher-level semantic and melodic sound patterns (Griffiths, 2000).

Thalamocortical dysrhythmia has been proposed to explain the positive and negative symptoms in neurological disorders like movement disorders, epilepsy, neuropathic pain, depression and tinnitus (Llinás et al., 1999). This pathophysiological model is based on deafferentation and might explain both tinnitus and musical hallucinosis, as both clinical entities are related to auditory deafferentation. According to this model tinnitus is caused by an abnormal, spontaneous and constant gamma band activity associated with low frequency theta or delta activity generated as a consequence of hyperpolarization of specific thalamic nuclei; in this case, the medial geniculate body. In normal circumstances auditory stimuli increase thalamocortical alpha oscillations to gamma band activity (Crone et al., 2001; Joliot et al., 1994). In the deafferented tinnitus state however, oscillatory alpha activity decreases (Lorenz et al., 2009) and theta band activity increases (Llinas et al., 1999; Steriade, 2006). As a result, lateral inhibition is reduced inducing a surrounding gamma band activity known as the "edge effect" (Llinás et al., 1999, 2005).

The difference between tinnitus and musical hallucinosis might be related to the right homolog of Broca's area and the right superior temporal pole. Previous research already showed that activation in the right homolog of Broca's area and right superior temporal gyrus is important in verbal hallucinations (Copolov et al., 2003; Sommer et al., 2008; Woodruff et al., 1995). The main difference between cerebral activity during auditory phantoms and activity during normal inner speech appears to be the lateralization in the right inferior frontal gyrus (Sommer et al., 2008). Records of magnetoencephalography (MEG) and single photon emission computed tomography (SPECT) in the presence and absence of musical hallucinosis in a case report showed increase of blood flow in the right superior temporal gyrus and right inferior frontal gyrus during musical hallucination (Kasai et al., 1999). Both areas have not been associated to tinnitus.

To elucidate the relation between simple and complex auditory phantom percepts a source localized electroencephalography (EEG) study is performed comparing resting state EEG recordings between healthy subjects, patients with a simple (i.e. tinnitus) and complex auditory phantoms (i.e. musical hallucinosis). Resting state EEG recordings were performed during a period of auditory phantom perception. In this study we assume that phantom sounds are related to activity within a complex neural network of different brain areas. Based on the thalamocortical dysrhythmia model we hypothesize that simple and complex auditory phantoms might share a common neural substrate characterized by a decrease in oscillatory alpha activity (Lorenz et al., 2009) associated with an increase in theta and gamma band activity, typical for thalamocortical dysrhythmia. Except for these spectral differences, we also hypothesize that simple and complex auditory phantoms differ in extend of involved brain areas as musical hallucinosis should involve music and language processing areas in contrast to tinnitus. In order to define a neural signature of "phantom percept" (simple and complex), the resting state electrical brain activity of both patient groups will be compared to healthy subjects. To delineate the shared network and specify the differences between simple and complex auditory phantom percepts subsequently both pathologies will also be compared electrophysiologically in a source localized way.

#### Methods

#### Participants

Ten patients (M = 65.75 years; Sd = 15.92; 10 females) with continuous chronic musical hallucinosis (i.e. complex auditory phantom percept) were recruited from the TRI multidisciplinary Tinnitus Clinic at the University Hospital Antwerp, Belgium. Ten tinnitus patients, 10 patients with musical hallucinosis and 10 healthy control subjects were selected from a large database in the TRI multidisciplinary Tinnitus Clinic at the University Hospital Antwerp. The patients and controls had the same age and gender. For the healthy subjects, none of these subjects was known to suffer from tinnitus or pain. Exclusion criteria for the healthy subject database were known psychiatric or neurological illness, psychiatric history or drug/alcohol abuse, history of head injury (with loss of consciousness) or seizures, headache, or physical disability and report of having severe hearing loss. The tinnitus patients and musical hallucinosis patients were further selected so that laterality (both tinnitus and musical hallucinosis were bilaterally perceived) loudness (both phantoms are perceived equally loud), distress level and hearing loss were not significantly different. See Table 1 for a demographic comparison among the three different groups.

Simple or complex auditory phantom percepts were considered chronic if its onset dated back one year or more. Simple or complex auditory phantoms were selected with comparable hearing loss: all patients were screened for the extent of hearing loss using a pure tone audiometry using the British Society of Audiology procedures at .125 kHz, .25 kHz, .5 kHz, 1 kHz, 2 kHz, 3 kHz, 4 kHz, 6 kHz and 8 kHz (Audiology, B.S.o, 2008; Meeus et al., 2010, 2011) (see Fig. 1).

A numeric rating scale (NRS) for loudness ("How loud is your tinnitus/ musical hallucinosis?": 0 = no tinnitus/musical hallucinosis and <math>10 =as loud as imaginable) as well as a validated Dutch translation of the Tinnitus Questionnaire (TQ) (Meeus et al., 2007) was assessed. The TQ is comprised of 52 items and is a well-established measure for the assessment of a broad spectrum of tinnitus-related psychological complaints. The TQ measures emotional and cognitive distress, intrusiveness, auditory perceptual difficulties, sleep disturbances, and somatic complaints. The global TO score can be computed to measure the general level of psychological and psychosomatic distress. In several studies, this measure has been shown to be a reliable and valid instrument in different countries (Hiller and Goebel, 1992; McCombe et al., 2001). Also for NRS loudness (M = 6.58, Sd = 1.57 for simple auditory phantoms; M = 6.28, Sd =1.91 for complex auditory phantom) and TQ (M = 54.31, Sd = 14.54for simple auditory phantoms; M = 53.51, Sd = 15.09 for complex auditory phantom) the tinnitus patients and patients with musical hallucinosis had a comparable loudness and distress. Patients who had a musical hallucinosis described their hallucinosis as hearing one or different songs that could change in character.

Table	1
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Demographics.
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	Healthy subjects	Auditory phantom percept		Statistical
		Simplex	Complex	comparisons
Gender	10 females	10 females	10 females	n.s. <sup>a</sup>
Age (years)	M = 67.25	66.88	M = 65.75	n.s. <sup>b</sup>
Sd	Sd = 15.92	Sd = 10.77	Sd = 15.92	
NRS loudness	-	M = 6.58	M = 6.28	n.s. <sup>b</sup>
		Sd = 1.57	Sd = 1.91	
TQ	-	M = 54.31	M = 53.51	n.s. <sup>b</sup>
		Sd = 14.54	Sd = 15.09	
Lateralization	-	Bilateral	Bilateral	n.s. <sup>a</sup>
Sound	-	Narrow band noise	Music	-

n.s. no significant effect.

<sup>a</sup> Comparison between groups using a  $\chi^2$ -test.

<sup>b</sup> Comparison between groups using one-way ANOVA.

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