

## Tinnitus specifically alters the top-down executive control sub-component of attention: Evidence from the Attention Network Task



<sup>c</sup> Department of Oto-Rhino-Laryngology & Head and Neck Surgery, Université Catholique de Louvain, Belgium

## ARTICLE INFO

Tinnitus  
Attention Networks Task  
Executive control  
Phantom perception  
DLPFC

## ABSTRACT

© 2014 Elsevier B.V. All rights reserved.

Tinnitus, which can be defined as the perception of noxious disabling internal sounds in the absence of corresponding external stimulation, has a lifetime prevalence of 16–21% [1]. While about 75–80% of the patients show some habituation to these internal sounds [2], tinnitus is associated with significant daily life impairment when such habituation fails, often leading to anxious and depressive states [3–6]. Understanding the origin and underlying

0166-4328/© 2014 Elsevier B.V. All rights reserved.

mechanisms of chronic tinnitus thus constitutes a crucial challenge for current basic research, in view of the huge psychological consequences of this pathology.

Although uncertainty still abounds regarding the neurobiological mechanisms underlying tinnitus, there is now convincing evidence from functional neuroimaging [7–9] and neurophysiology [10] that this condition is related to abnormal functioning of the central auditory system. Moreover, during the last decades, several authors have argued that impairment in attentional processes may also be involved in tinnitus, particularly by hampering the habituation mechanism [11–13]. This involvement of non-auditory deficit is reinforced by the fact that tinnitus is not only related to abnormal activity in auditory, but also in non-auditory brain regions [8,14]. Centrally, alterations have been found in the prefrontal cortex [15–17], a region playing a crucial role in attentional processes [18,19]. As pointed out by several authors [17,20–24], these alterations might be specifically related to the prevention of tinnitus habituation as well as to its psychological consequences in the daily life.

These findings suggest that attention processes may play an important role in the maintenance, and perhaps the development, of the disorder. Although uncertainty still abounds regarding whether the former is a causal factor or a by-product of the disorder, it has been shown that patients with tinnitus exhibit attention deficits. However, while some studies showed that tinnitus leads to altered performance in selective [24], divided [25,26] and sustained [27] attention, other suggested that these alterations might rely on reduced top-down executive control (i.e. the ability to resolve conflicts among responses and voluntarily regulate the allocation of attention resources) rather than on attentional processes per se [26,28]. It has also been suggested that the attentional deficits in tinnitus may merely be part of a general impairment in speed processing [29]. As a consequence, it is still unclear whether these deficits are the consequence of a general alteration in the executive control of attention, the consequence of genuine alterations in a specific attentional ability, or merely the results of a general slowdown effect in cognitive processing.

A possible explanation for these discrepancies among earlier results is the use of very diverse tasks, simultaneously exploring several attentional abilities. These earlier studies were in fact not based on a firm theoretical model of attention and were thus not able to precisely compare the impairments across different sub-components of the attentional system. A more systematic and reliable exploration of the attentional system, based on a unified task relying on a cognitive model and offering a specific evaluation of each attentional sub-component, is clearly needed. The Attention Network Test (ANT) [30], based on a strongly validated model of attention [31,32], constitutes an adapted tool for this purpose. This task, based on a combination of the Posner's cueing task [33] and the Flanker task [34], efficiently evaluates the three independent attentional networks identified in the model, namely (1) The *alerting network*, allowing to achieve and maintain a state of alertness, i.e. high sensitivity or readiness to react to incoming stimulation; (2) The *orienting network*, allowing to select information from sensory input by engaging or disengaging attention to one stimulus among others and/or shifting the attentional resources from one stimulation to another; (3) The *executive control network*, allowing to resolve conflicts among responses and involving the top-down control of attention.

Typically, the different components of attention have been examined using different paradigms. Thus, three different tasks may be used to examine these attention components within the same individuals. In that case, it is not possible to examine how these components simultaneously interact. The ANT, however, allows the examination of these components all at once and to examine how they interact. It is noteworthy that neuroimaging

studies provided demonstration of distinct brain activation patterns related to each attentional network, i.e. superior temporal and thalamic activation for alerting, superior parietal lobule and temporal fusiform gyrus activation for orienting, thalamic and superior–inferior frontal activation for executive control [35].

Hence, the ANT has been recently used to differentiate the attention deficits associated with diverse neurological conditions. For instance, it has been reported that individuals with mild cognitive impairment exhibited a specific alteration of the orienting network [36], while multiple sclerosis led to a specific impairment of the alerting network [37]. Similarly, this task has been also used across a wide range of psychiatric conditions. For instance, while autism spectrum disorders are associated with a global impairment of the three attentional networks [38], a specific impairment in the executive control network was found in schizophrenia [39], addiction [40], and anxiety disorders [41].

Although the ANT could bring insights on the hypothesized impact of tinnitus on attentional processes, this task has surprisingly not yet been used among individuals with tinnitus. The aim of the present study was to offer the first insights into the integrity or deficit of the three attentional networks in tinnitus. In order to better understand the attentional impairments in this pathology, we wished to explore the hypothesis of a differential deficit between these networks. Since previous data suggested that tinnitus depletes top-down executive resources that are recruited during an attentional task [25,26,29] and since this condition is related to less activation in frontal brain areas [15–17], we hypothesized that patients with tinnitus would present a specific deficit for the executive control network, as this network mostly relies on frontal areas.

## 2. Materials and methods

### 2.1. Ethics Statement

Participants were provided with full details regarding the aims of the study and the procedure. All participants gave their written informed consent. The study was approved by the Ethical Committee of the Psychological Science Research Institute of the Université Catholique de Louvain and carried out according to the Declaration of Helsinki.

### 2.2. Participants

The participants were recruited through an advertisement sent to the Belgian Association of Patients suffering from Tinnitus. The inclusion/exclusion criteria were similar to previous studies in the field [29,42]. Eligible participants (a) were between the age 20 and 80 years old, (b) had experienced constant unilateral or bilateral tinnitus within the past 6 months, (c) undertook a medical check-up by a physician specialized in hearing disorders, (d) had sufficient hearing abilities to follow the instructions. Participants were excluded if (a) there was an active diagnosis of any acute or chronic brain neurological condition; (b) they used a tinnitus masking apparatus, or (c) they presented major general cognitive impairment. This last aspect was evaluated using the Mini Mental State Exam (MMSE) [43], a semi-structured neuropsychiatric interview. All the participants reported a MMSE score above 27/30, which depicted the absence of any major cognitive impairment (i.e., scores below 24/30 are considered a problematic) [43]. Tinnitus characteristics and impact on daily life were assessed using the Tinnitus Psychological Impact Questionnaire (QIPA; see below) [44].

The clinical group of Tinnitus subjects (TS) consisted of 20 participants (10 men, 10 women) aged between 20 and 72 years old ( $M = 46.85$ ,  $SD = 15.79$ ). Patients were matched for age, gender, and

**Table 1**  
Participants characteristics as a function of training allocation (SD in parentheses).

	Tinnitus group (N = 20)	Control group (N = 20)
<b>Demographic measures</b>		
Age <sup>NS</sup>	46.85 (15.85)	45.65 (14.93)
Gender ratio (female/male) <sup>NS</sup>	10/10	10/10
Educational level (in years) <sup>NS</sup>	21.30 (3.88)	22.65 (1.53)
<b>Clinical scores</b>		
Beck Depression Inventory (BDI) <sup>NS</sup>	6.35 (9.38)	7.80 (8.85)
State and Trait Anxiety Inventory A (STAI-A) <sup>NS</sup>	23.95 (9.42)	23.65 (9.39)
Mini Mental State Exam (STAI-B) <sup>NS</sup>	29.00 (.92)	29.50 (.76)
<b>Tinnitus characteristics (QIPA)<sup>a</sup></b>		
Tinnitus duration (in years) <sup>**</sup>	10.90 (13.78)	
Presence on a day <sup>**</sup>	6.40/7 (1.85)	
Extent to which it triggered negative emotions <sup>**</sup>	25.80/80 (16.87)	
Ruminations triggered by tinnitus <sup>**</sup>	7.20/21 (4.86)	
Difficulties in everyday life <sup>**</sup>	29.10/70 (17.57)	
Coping strategies to alleviate tinnitus distress		
(a) Intensity <sup>**</sup>	32.10/77 (9.08)	
(b) Efficacy <sup>**</sup>	6.65/14 (3.50)	

Notes. <sup>NS</sup> = Non-significant; <sup>\*\*</sup> $p < .001$ ; <sup>a</sup> = for tinnitus descriptions, one-sample  $t$ -tests were conducted in order to test whether patients significantly differed from the minimum score on that variable.

education level (i.e., same level of graduation) with 20 control subjects (CS) who were free of any history of tinnitus, psychiatric, and neurological disorder. CS were recruited through the volunteer pool of the Université Catholique de Louvain and in the community by word of mouth. Each participant had a normal-to-corrected vision. Education level was assessed according to the number of years of education completed since starting primary school. Participants were paid 5 euros for their participation. Their demographic characteristics appear in Table 1. It should be noted that, as shown in Table 1, for each dimension of the QIPA scale, all the tinnitus patients reported a score significantly higher than the one obtained in the absence of symptoms or impairment on that dimension (all  $t$  values  $> 3.66$ , all  $ps < .001$ ).

### 2.3. Measures

#### 2.3.1. Questionnaires

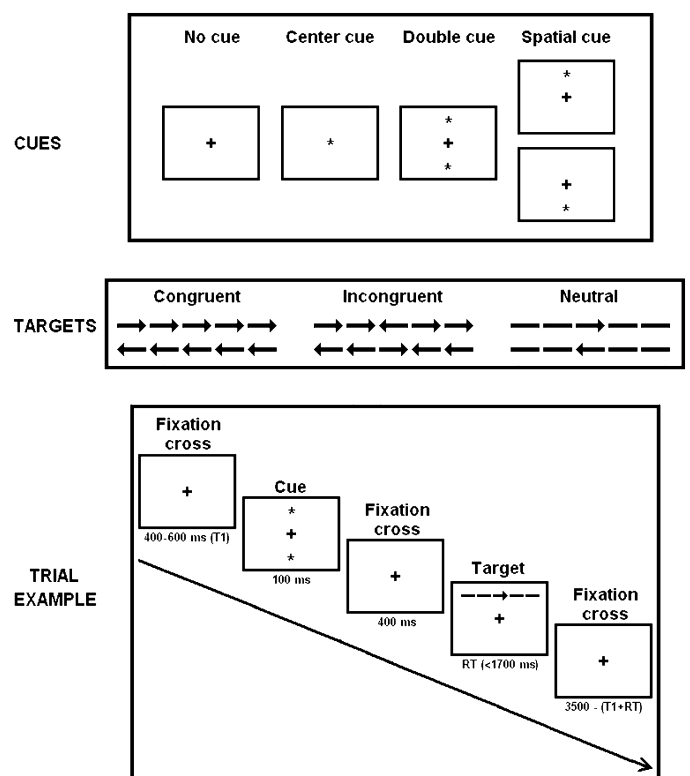
TS were first instructed to fill-in the QIPA. The QIPA is a 42-item self-report questionnaire that explores different facets of the tinnitus' characteristics and of its impact on daily life functioning [44]. This scale exhibits good psychometric properties, including both internal and external validity [45]. Specifically, the QIPA assesses the tinnitus duration (in years) as well as six dimensions of tinnitus experience during the past week. The first dimension measures the amount of time the tinnitus was present on a single day (in one item). The second dimension assesses through 12 items the extent to which the tinnitus triggered negative emotions. A third dimension, including three items, targets the negative rumination triggered by the tinnitus and a fourth dimension, including 10 items, measures the difficulties in everyday life resulting from the tinnitus. Finally, the fifth dimension evaluates the coping strategies initiated to alleviate tinnitus distress and the sixth one assesses the feeling of self-efficacy for these coping strategies.

In tinnitus and control subjects, we also assessed several usual psychological scores. Validated self-completion questionnaires were used to assess depression (Beck Depression Inventory) [45] and anxiety proneness (trait version of the State and Trait Anxiety Inventory) [46].

#### 2.3.2. Experimental measures

The Attention Network Test (ANT) was administered in order to determine the efficiency of three independent attentional networks: alerting, orienting and executive control [30]. Participants had to determine as fast and accurately as possible the

direction of a central arrow (the target) located in the middle of a horizontal line projected either at the top or at the bottom of the screen. They provided their answer by pressing the corresponding button (left or right) on the keyboard. Each target was preceded by a cue condition, with four possible cue types (Fig. 1, upper part): no cue, center cue (an asterisk replacing the fixation cross), double cue (two asterisks respectively appearing above and below the fixation cross) or spatial cue (an asterisk appearing above or below the fixation cross and indicating the location of the upcoming target). Moreover, flankers were located in the horizontal line on each



**Fig. 1.** Description of the Attention Network Test. Notes. This figure illustrates the four possible cues (upper part), the six possible targets (middle part) and an example of the trials used in the task (lower part, i.e. neutral trial preceded by a double cue, the correct response being "right").

Source: Adapted from Fan et al. [30].

side of the target, with three possible flanker types (Fig. 1, middle part): either two arrows in the same direction as the target (congruent condition), two arrows in the opposite direction (incongruent condition), or two dashes (neutral condition). As shown in Fig. 1 (lower part), each trial had the following structure: (1) a central fixation cross (random duration between 400 and 1600 ms); (2) a cue (100 ms); (3) a central fixation cross (400 ms); (4) a target and its flankers, appearing above or below the fixation cross (the target remained on the screen until the participant responded or for 1700 ms if no answer was given); (5) a central fixation cross [lasting for 3500 ms minus the sum of the first fixation period's duration and the reaction time (RT)]. Reaction time (RT, in milliseconds) and accuracy (percentage of correct responses) were recorded for each trial.

The experiment comprised 288 trials, divided in three blocks of 96 trials each (with a short break between blocks). There were 48 possible trials, based on the combination between four cues (no cue, center cue, double cue, spatial cue), three flankers (congruent, incongruent, neutral), two directions of the target arrow (left, right) and two localizations (upper or lower part of the screen). Trials were presented in a random order and each possible trial was presented twice within a block. The task was programmed and presented using E-Prime 2 Professional® (Psychology Software Tools, Pittsburgh, PA, USA). The distance between participant's eyes and the screen was around 50 centimeters, and the target stimuli subtended a visual angle of about 4° in the horizontal field. The task was administrated individually in a dimly lit and quiet room during a single session of 35 min.

## 2.4. Procedure

The participant first signed the informed consent and filled in the questionnaires. Then, they read the instructions on the computer screen. These instructions were emphasized by the experimenter and a training session started, consisting in 24 randomly selected trials. Finally, the experimenter recalled the instructions and answered the remaining questions before starting the experimental task. After the experimental task, participants were fully debriefed.

## 3. Results

### 3.1. Power analysis

An a priori power analysis was conducted to determine the appropriate total sample size for testing our hypotheses (G\*Power 3.1.3) [47]. The power analysis indicated that a sample of 14 participants by group would yield adequate power (i.e. 80%) to detect a medium effect size of  $f = .25$  at  $p < .05$  using a 2 (groups)  $\times$  4 (cues)  $\times$  3 (flankers) repeated-measures design (which is the more powerful statistical test used in the present study, see below). These results thus confirmed that the present study has enough statistical power to test our hypothesis.

### 3.2. Data reduction and data analytic plan

Data reduction was first performed following the recommendations of Ratcliff [48] for dealing with outliers and errors in RT tasks: (1) trials with incorrect responses were excluded from the RT analyses (.72% of trials); (2) RTs shorter than 200 ms or longer than 2000 ms were removed from analyses (less than .001% of trials with correct responses); (3) RTs more than 1.96 standard deviations below or above each participant's mean for each experimental condition were discarded as outliers (.02% of the remaining trials). A preliminary analysis showed no difference in RT or accuracy according to the direction (left or right) and localization (upper or

lower) of the arrow, and these trials were thus merged, leading to 24 trials for each of the 12 experimental conditions (four cues  $\times$  three flankers).

A first general 2  $\times$  4  $\times$  3 repeated-measures analysis of variance (ANOVA) was then performed separately for RT and accuracy with Group (TS, CS) as between-subjects factor, and Cue (no cue, center cue, double cue, spatial cue) and Flanker (congruent, incongruent, neutral) as within-subjects factors.

In a subsequent analysis, a subtraction method [30] was used to isolate the effect of the three attentional networks: (1) The alerting effect was calculated by subtracting the mean result (i.e. RT or accuracy score) for double cue trials from the mean result for no cue trials (No cue – Double cue); (2) The orienting effect was calculated by subtracting the mean result for spatial cue trials from the mean result for center cue trials (Center cue – Spatial cue); (3) The executive control effect was calculated by subtracting the mean result for congruent trials (summed across cue types) from the mean result for incongruent trials (Incongruent – Congruent). For both alerting and orienting effects, higher subtraction scores for RT (and lower for accuracy) indicated greater efficiency. On the contrary, higher subtraction scores for RT (and lower for accuracy) indicated less efficiency in the executive control of attention, as conflicts in the incongruent conditions increased the RT as compared to congruent ones [36]. On the basis of these subtraction effects, a second general 2  $\times$  3 repeated-measures ANOVA was performed separately for RT and accuracy with Group (TS, CS) as between-subjects factor and Attention Network (Alerting, Orienting, Executive Control) as within-subjects factor.

Since two separate ANOVAs were performed for RT and accuracy, the significance threshold of these ANOVAs has been adjusted for multiple comparisons using Bonferroni corrections to consider chance capitalization. For each ANOVA, significant main effects and interactions were then followed by corrected post hoc independent samples *t*-tests. Independent samples *t*-tests were also computed to explore group differences in scores of clinical scales. Analyses of covariance (ANCOVA) were performed to test the influence of potential biasing variables (i.e., gender, age, medication, depression, anxiety, and MMSE score) on RTs and accuracy scores in ANT. Finally, two-tailed Pearson correlations were used to explore the links between the experimental data and the QIPA score. As our main interest concerns the exploration of a potential deficit in TS as compared to CS, the results section will focus on group comparison.

### 3.3. Statistical analyses

#### 3.3.1. Clinical scores

As shown in Table 1, TS and CS did not significantly differ in terms of age [ $t(38) = .25$ ,  $p = .81$ ], gender, education [ $t(58) = 1.45$ ,  $p = .16$ ], depression [ $t(38) = .50$ ,  $p = .62$ ], and trait anxiety [ $t(58) = .10$ ,  $p = .93$ ], nor in the MMSE score [ $t(38) = 1.47$ ,  $p = .15$ ].

#### 3.3.2. Experimental measures

**3.3.2.1. General analysis.** A 2 (groups)  $\times$  4 (cues)  $\times$  3 (flankers) repeated-measures ANOVA was performed separately for RT and accuracy. The results for each group in each experimental condition are presented in Table 2.

- Accuracy: No main effect of group was found [ $F(1,38) = .55$ ,  $p = .46$ ,  $\eta_p^2 = .01$ ] nor any interaction with Cue [ $F(3,114) = .37$ ,  $p = .77$ ,  $\eta_p^2 = .01$ ], Flanker [ $F(2,76) = .97$ ,  $p = .39$ ,  $\eta_p^2 = .03$ ], or Group  $\times$  Cue  $\times$  Flanker interaction [ $F(6,228) = .75$ ,  $p = .61$ ,  $\eta_p^2 = .02$ ].
- RT: A significant main effect of group was found [ $F(1,38) = 6.53$ ,  $p < .02$ ,  $\eta_p^2 = .15$ ]: TS presented longer RT than CS. An interaction between Group and Flanker was also found [ $F(2,76) = 6.04$ ,



**Table 2**

Mean latencies for correct responses and accuracy for subjects with tinnitus and control subjects in each experimental condition of the Attention Network Test (ANT) (SD in parentheses).

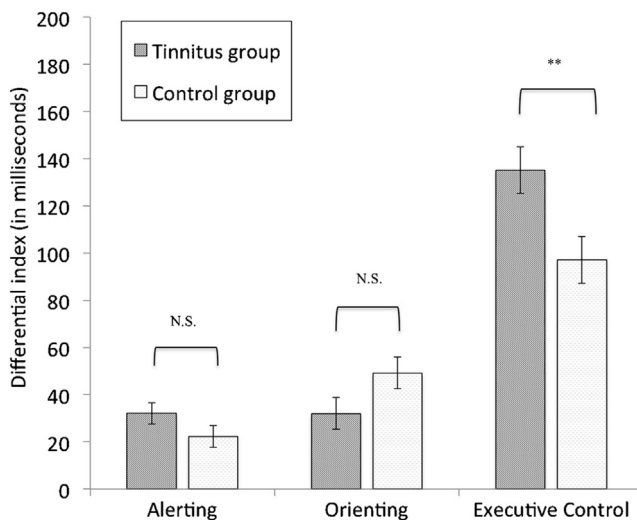
	Group	No cue	Center cue	Double cue	Spatial cue
<b>Congruent</b>					
Reaction Times (ms)	TS	628 (152)	641 (125)	618 (116)	628 (152)
	CS	533 (78)	565 (74)	594 (85)	533 (78)
Accuracy (% Correct)	TS	99.20 (2.78)	99.40 (1.47)	98.15 (5.79)	98.75 (3.91)
	CS	99.80 (.89)	99.80 (.89)	100.00 (.00)	99.80 (.89)
<b>Incongruent</b>					
Reaction Times (ms)	TS	790 (160)	790 (159)	781 (184)	740 (177)
	CS	680 (92)	681 (91)	668 (100)	609 (101)
Accuracy (% Correct)	TS	97.15 (4.61)	96.75 (7.39)	97.30 (5.84)	97.55 (5.11)
	CS	98.50 (2.97)	98.45 (5.42)	98.45 (4.93)	98.95 (2.19)
<b>Neutral</b>					
Reaction Times (ms)	TS	655 (126)	630 (144)	622 (129)	596 (112)
	CS	571 (77)	553 (73)	552 (73)	510 (73)
Accuracy (% Correct)	TS	99.00 (2.87)	99.00 (3.15)	99.20 (2.09)	98.60 (3.25)
	CS	99.80 (.89)	98.75 (2.67)	99.60 (1.79)	99.60 (1.79)

Note. TS = subjects with tinnitus; CS = control subjects.

$p = .004$ ,  $\eta_p^2 = .14$ ]. There were no Group  $\times$  Cue interaction [ $F(3,114) = 2.92$ ,  $p = .10$ ,  $\eta_p^2 = .07$ ], nor Group  $\times$  Cue  $\times$  Flanker interaction [ $F(6,228) = .564$ ,  $p = .76$ ,  $\eta_p^2 = .02$ ].

Between-group post hoc comparison ( $t$ -tests) revealed that TS presented longer RT than CS for Congruent [ $t(38) = 2.38$ ,  $p < .05$ ], Incongruent [ $t(38) = 2.69$ ,  $p < .01$ ] and Neutral [ $t(38) = 2.48$ ,  $p < .05$ ] flankers. The difference was, using paired  $t$ -test on TS performance, significantly higher for Incongruent than for both Congruent [ $t(19) = 10.71$ ,  $p < .001$ ] and Neutral [ $t(19) = 10.66$ ,  $p < .001$ ] flankers.

**3.3.2.2. Analysis of attentional networks (subtraction method).** A 2 (groups)  $\times$  3 (attentional networks) repeated-measures ANOVA was performed separately for RT and accuracy. The results related to the RT indexes of these three attentional networks are illustrated in Fig. 2.



**Fig. 2.** Differential reaction times (RT) indexes (in milliseconds) among patients with tinnitus and matched control participants for the three attentional networks, namely Alerting ( $RT_{No\ Cue} - RT_{Double\ Cue}$ ), Orienting ( $RT_{Center\ Cue} - RT_{Spatial\ Cue}$ ) and Executive Control ( $RT_{Incongruent} - RT_{Congruent}$ ). Notes. The presence of tinnitus is associated with a specific alteration for executive control ( $*p < .001$ ), with preserved alerting and orienting abilities. Error bars represent standard errors of the mean.

- Accuracy: No main effect of Group was found [ $F(1,38) = .61$ ,  $p = .44$ ,  $\eta_p^2 = .02$ ] nor interaction between Group and Attentional Network [ $F(2,76) = .53$ ,  $p = .59$ ,  $\eta_p^2 = .01$ ].
- RT: A main effect of Group [ $F(1,38) = 5.53$ ,  $p = .02$ ,  $\eta_p^2 = .13$ ] was found, the Attentional Network indexes being higher among TS than CS. Centrally, an interaction between Group and Attentional Network was found [ $F(2,76) = 5.67$ ,  $p < .005$ ,  $\eta_p^2 = .13$ ]: As compared to CS, TS were impaired for the Executive Control index [ $t(38) = 2.73$ ,  $p < .01$ ], but not for Alerting [ $t(38) = .151$ ,  $p = .14$ ] nor for Orienting [ $t(38) = 1.81$ ,  $p = .09$ ].

### 3.3.2.3. Complementary analyses.

- To test for the links between tinnitus characteristics (mirrored by the QIPA score and the years of tinnitus duration) and ANT performance of Tinnitus subjects, Pearson's correlations were performed. While no significant correlation was found between all the QIPA dimensions including tinnitus duration and alerting [ $r_s < .18$ ,  $p_s > .33$ ] or orienting [ $r_s < .24$ ,  $p_s > .19$ ], the extent of the executive control impairment was significantly correlated with the number of years the participants had suffered from tinnitus [ $r(20) = .55$ ,  $p = .01$ ] as well as with the intensity of the coping strategies they used to reduce the tinnitus as assessed in the QIPA section focusing on coping strategies [ $r(20) = -.54$ ,  $p = .02$ ].
- To test for potential biasing effect of demographic (i.e. gender, age, medication, education) and psychopathological variables (i.e. depression, anxiety), and MMSE scores were included as covariates in our ANOVA as well as our correlational analyses (using partial correlations). No significant influence of these variables on any experimental result was observed ( $p > .05$  for every test).

## 4. Discussion

This study was the first to directly investigate the integrity of attentional networks in Tinnitus subjects (TS) by means of the ANT, a reliable and theoretically-grounded task. The central result is that TS do not present a general attentional deficit but rather a specific deficit for the attentional network related to the top-down executive control of attention.

This observation refines earlier observations suggesting that TS present globally longer RT than CS [29]. TS would thus suffer from impairments in executive control ability, which is necessary to focus attentional resources on task-relevant information (i.e. the central arrow in ANT) and to inhibit the processing of confusing and task-irrelevant stimuli (i.e. incongruent flankers). In other words,

the present findings suggest that the attentional deficits in TS are mainly due to a reduced ability to detect and resolve the conflict between task-relevant stimulus and the interference provoked by task-irrelevant stimuli. It should be noted that there are important links between executive attention and prepotent response inhibition (i.e. the capacity to deliberately control or suppress an automatic behavior), and that both the former and the latter mechanisms are involved in top-down resource-demanding control [49]. Our results are therefore consistent with those having demonstrated specific inhibitory control impairment in TS [24,28]. This executive control impairment in TS appears specifically associated with tinnitus, as no influence of depressive or anxious states, medication, gender, level of education, or general cognitive processing was found.

In contrast, the present findings also suggest that alerting and orienting attentional networks are preserved among TS, depicting that they are able to take the cues into account to improve their performance. More specifically, TS have a preserved ability to (1) increase one's phasic alertness and establish a vigilance state to prepare the processing of an upcoming stimulus (as indexed by alerting index); and (2) orient attentional resources toward specific information by successively disengaging attention from earlier focus, moving it toward the new target and engaging attention to it.

The differential deficit in executive control cannot be explained by a higher complexity of this network as compared to alerting and orienting networks, since earlier studies have clearly shown a reverse deficit (preserved executive control network with impaired alerting or orienting ones) in other clinical populations [36,50]. However, it should be noted that alerting, as operationalized in the context of the ANT (i.e., by comparing the performance with and without warning signals) refers more to phasic than tonic alertness. Alertness can be subdivided into phasic and tonic alertness. While the former refers to the ability to sustain attention over a period of time, the latter involves a rapid change in cognitive state after a presentation of a warning signal that prepares the individual to fast reactions [51]. Future studies should thus also explore whether tonic alertness is preserved or impaired among TS. Finally, no group differences were observed for the accuracy levels in any attention network, which clearly proves that TS correctly understood the requirements of the task. It is noteworthy that this observation is in line with earlier studies indicating that tinnitus impaired more the top-down executive control of attention than the cognitive efficiency of attention (i.e. response accuracy) [29].

Although no causal link can be inferred from correlation analyses [52], we observed highly significant correlations between the increased RT for incongruent trials and some tinnitus characteristics (years of tinnitus duration and amount of coping strategies initiated to alleviate tinnitus distress). This is in accordance with previous accounts arguing that impairment in attentional processes may be involved in preventing habituation mechanisms to alleviate the perception of noxious disabling internal sounds [e.g. 3–6]. Moreover, it has also been reported that the inability to adequately initiate strategies to alleviate tinnitus distress is among the strongest predictors of long-term tinnitus chronification [e.g. 53,54]. Since the impairment in executive control of attention specifically correlates with tinnitus duration and intensity of tried coping strategies in the present study, this finding adds to a small but growing empirical literature suggesting that the executive control deficit may be, at least partially, related to tinnitus maintenance. Future studies are thus clearly needed to directly test whether the impairments in executive control of attention predict non-habituation to tinnitus and its chronification.

This hypothesis makes sense in view of the current knowledge about the cerebral correlates of attentional networks and the brain impairments in TS. On the one hand, executive control of attention

is related to the physiological recruitment of prefrontal brain areas whereas alerting and orienting mostly rely on temporal-thalamic and parietal-fusiform structures, respectively [35,55,56]. On the other hand, it has been reported that tinnitus is not only related to abnormal activity in the auditory system, but also to failure of limbic and non-auditory brain regions to block the tinnitus signal [8,14]. In previous studies, the prefrontal cortex has been identified as an important hub [15–17]. It has been also reported an increased functional connectivity between limbic regions and the task-positive network in TS, which is a brain network involved in top-down allocation of attention [57]. More centrally, it has been suggested that alterations in prefrontal cortex activity might especially be related to the prevention of habituation to tinnitus as well as to its psychological consequences [20–23]. Here we showed a specific impairment of executive control, i.e. the attentional network relying on frontal brain areas, which is in accordance with these earlier findings pointing out that alterations of prefrontal brain areas could act as a direct mechanism of tinnitus chronification. However, again, further studies with the use of functional neuroimaging in TS performing the ANT are clearly needed to directly test this hypothesis.

At the therapeutic level, our results provide support to the potential interest of rehabilitation programs focusing on executive control of attention. Several efficient rehabilitation programs have been recently proposed in TS [e.g. 58–60], including a global rehabilitation using multi-determined tasks. In view of the present results, rehabilitation strategies should be adapted to focus on attentional remediation of executive control, whereas rehabilitating the preserved alerting and orienting networks appears of little usefulness. Several procedures have already been developed to specifically rehabilitate each attentional network [61–63], and those focusing on executive control rehabilitation [64,65] could be adapted to TS. Recently it has also been suggested that mindfulness training may have impact on executive control of attention [e.g. 66,67]. Mindfulness training consists in a psychological intervention that trains participants to disengage their attention from task-irrelevant thoughts or sensations by redirecting their focus to a particular arbitrary concrete focus, such as breathing sensations [68]. Randomized controlled trials already provided evidence that mindfulness may help to alleviate the psychological distress resulting from tinnitus [e.g. 42, 69–71]. Future studies should thus further explore the impact of such a program on the executive attention impairment among TS, and explore whether such an improvement may, in turn, reduce the psychological distress resulting from tinnitus.

Finally, inducing virtual lesions in frontal brain areas in TS by means of neuromodulation procedures also constitutes a potential therapeutic tool since earlier studies already indicated the effectiveness of repetitive transcranial magnetic stimulation (rTMS) over auditory temporal cortical areas in TS patients [e.g. 72–74]. A promising alternative for the alleviation of tinnitus is the use of transcranial direct current stimulation (tDCS), a form of non-invasive brain stimulation able to induce transient and likely lasting tinnitus relief [75,76]. In addition, the stimulation of the prefrontal regions, particularly the dorsolateral part, seems to be a potential strategy for enhancing neuromodulation effects to alleviate tinnitus in TS [e.g. 75,77–79]. However, the hypothesis that tinnitus impacts the executive control network through prefrontal regions dysfunction is in need of experiments directly testing the involvement of these brain regions *during* a task directly assessing executive control of attention. To achieve this aim, one interesting way could be to combine neuromodulation of cortical activity by tDCS, functional neuroimaging to assess cortical activity changes and behavioral results using the ANT in tinnitus subjects.

In the present study, we did not measure participants' hearing threshold levels and did not match the experimental and control

groups on this variable. However, the impact of this weakness is limited since all the stimuli were presented visually. Moreover, consistently with previous studies in the field, we used a visual attentional task. However, one cannot exclude that the attentional impairments in tinnitus would be different for auditory than visual stimuli. Future experiments should thus directly examine the impact of the stimuli modality (auditory versus visual) used in the task on the different networks. While our results are clearly significant and based on a sound experimental design, they will also have to be replicated in larger groups of TS. Future studies should indeed examine whether the same pattern of results are observed in patients who exhibit severe tinnitus and who are treatment-resistant. One cannot exclude that these patients may exhibit a different pattern of impairments, including accuracy disturbances or alterations in the two other attentional networks. In the same vein, future studies should also examine whether the present findings differ from individuals who cope well to tinnitus in their daily life to those who do not. Neuroimaging and neuromodulation studies should also be conducted to confirm the implication of frontal brain areas in executive control impairments.

Despite its limitations, we believe that the present study, by offering the first exploration of attentional networks using the ANT and by showing a clear differential deficit between impaired executive control and preserved alerting and orienting, is a valuable first step toward a better understanding of the cognitive processes involved in attentional deficits in tinnitus.

## Funding

Authors are funded by the Belgian Fund for Scientific Research (F.R.S.-FNRS, Belgium), by the IRSIB-INNOVIRIS, by the Bourse d'Excellence Scientifique Wallonie-Bruxelles-International, and by the Belgian Foundation "Vocatio", but these foundations did not exert any editorial direction or censorship on any part of this article.

## Conflicts of interest

All authors report no competing financial interests or potential conflicts of interest, and no financial relationships with commercial interests.

## Acknowledgments

Alexandre Heeren (Post-doctoral Research Fellow), Pierre Maurage (Research Associate), and Anne De Volder (Senior Research Associate) are funded by the Belgian Fund for Scientific Research (F.R.S.-FNRS, Belgium). Laurent Renier (Post-doctoral Research Fellow) is supported by the "Institut d'Encouragement de la Recherche Scientifique et de l'Innovation de Bruxelles" (IRSIB-INNOVIRIS). The writing of this paper also received the support from the Belgian Foundation "Vocatio" and the "Bourse d'Excellence Scientifique Wallonie-Bruxelles-International" (both awarded to Alexandre Heeren).

## References

- [1] Krog NH, Engdahl B, Tambs K. The association between tinnitus and mental health in a general population sample: result from the HUNT Study. *J Psychosom Res* 2010;69:289–98.
- [2] Cuny C, Norena A, El Massioui F, Chery-Croze S. Reduced attention shift in response to auditory change in subjects with tinnitus. *Audiol Neurootol* 2004;9:294–302.
- [3] Andersson G. The role of psychology in managing tinnitus: a cognitive behavioral approach. *Semin Hear* 2001;22:65–76.
- [4] Folmer RL, Griest SE, Martin WH. Chronic tinnitus as phantom auditory pain. *Otolaryngol Head Neck* 2001;124:394–400.
- [5] Jacobson GP, Calder JA, Newman CW, Peterson EL, Wharton JA, Ahmad BK. Electrophysiological indices of selective auditory attention in subjects with and without tinnitus. *Hear Res* 1996;97:66–74.
- [6] Robinson SK, Viirre ES, Stein MB. Antidepressant therapy in tinnitus. *Hear Res* 2007;226:221–31.
- [7] Crippa A, Lanting CP, Van Dijk P, Roerdink JB. A diffusion tensor imaging study on the auditory systems and tinnitus. *Open Neuroimaging J* 2010;4:16–25.
- [8] Lanting CP, De Kleine E, Van Dijk P. Neural activations underlying tinnitus generation: results from PET and fMRI. *Hear Res* 2009;255:1–13.
- [9] Lanting CP, De Kleine E, Eppinga RN, Van Dijk P. Neural correlates of humans somatosensory integration in tinnitus. *Hear Res* 2010;267:78–88.
- [10] Weisz N, Müller S, Schlee W, Dohrmann K, Hartmann T, Elbert T. The neural code of auditory phantom perception. *J Neurosci* 2007;27:1479–84.
- [11] Andersson G. Psychological aspects of tinnitus and the application of cognitive-behavioral therapy. *Clin Psychol Rev* 2002;22:977–90.
- [12] Jastreboff PJ, Jastreboff MM. Tinnitus retraining therapy (TRT) as a method for treatment of tinnitus and hyperacusis patients. *J Am Acad Audiol* 2000;11:162–77.
- [13] Roberts LE, Hussain FT, Eggermont JJ. Role of attention in the generation and modulation of tinnitus. *Neurosci Biobehav Rev* 2013;37:1754–73.
- [14] Leaver AM, Renier L, Chevillet MA, Morgan S, Kim HJ, Rauschecker JP. Dysregulation of limbic and auditory networks in tinnitus. *Neuron* 2011;69:33–43.
- [15] Schlee W, Mueller N, Hartmann T, Keil J, Lorenz I, Weisz N. Mapping cortical hubs in tinnitus. *BMC Biol* 2009;7:80.
- [16] Vanneste S, Plazier M, van Der Loo E, van De Heyning P, Congedo M, De Ridder D. The neural correlates of tinnitus-related distress. *Neuroimage* 2010;52:470–80.
- [17] MacDonald AW, Cohen JD, Stenger AV, Carter CS. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science* 2000;288:1835–8.
- [18] Wang L, Liu X, Guise KG, Knight RT, Ghajar J, Fan J. Effective connectivity of the fronto-parietal network during attention control. *J Cognitive Neurosci* 2010;22:543–53.
- [19] De Ridder D, Elgoyhen AB, Romo R, Langguth B. Phantom percepts: tinnitus and pain as persisting aversive memory networks. *Proc Natl Acad Sci USA* 2011;108:8075–80.
- [20] De Ridder D, Vanneste S, Weisz N, Londero A, Schlee W, Elgoyhen AB, et al. An integrative model of auditory phantom perception: tinnitus as a unified percept of interacting separable subnetworks. *Neurosci Biobehav Rev* 2014 [in press].
- [21] Langguth B, Landgrebe M, Kleinjung T, Sand GP, Hajak G. Tinnitus and depression. *World J Biol Psychiatry* 2011;12:489–500.
- [22] Rauschecker JP, Leaver AM, Mulhau M. Tuning out the noise: limbic-auditory interactions in tinnitus. *Neuron* 2010;66:819–26.
- [23] Seydell-Greenwald A, Leaver AM, Turesky TK, Morgan S, Kim HJ, Rauschecker JP. Functional MRI evidence for a role of ventral prefrontal cortex in tinnitus. *Brain Res* 2012;1485:22–39.
- [24] Stevens C, Walker G, Boyer M, Gallagher M. Severe tinnitus and its effect on selective and divided attention. *Int J Audiol* 2007;46:208–16.
- [25] Hallam RS, McKenna L, Shurlock L. Tinnitus impairs cognitive efficiency. *Int J Audiol* 2004;43:218–26.
- [26] Rossister S, Stevens C, Walker G. Tinnitus and its effect on working memory and attention. *J Speech Lang Hear Res* 2006;49:150–60.
- [27] McKenna LM, Hallam RS, Shurlock L. Cognitive functioning in tinnitus patients. In: Reich G, Vernon J, editors. *Proceedings of the 5th International Tinnitus Seminar*. Portland: American Tinnitus Association; 1996. p. 589–95.
- [28] Andersson G, Erikson J, Lundh LG, Lyttkens L. Tinnitus and cognitive interference: a Stroop paradigm study. *J Speech Lang Hear Res* 2000;43:1168–73.
- [29] Das SK, Wineland A, Kallogjeri D, Piccirillo JF. Cognitive speed as an objective measure of tinnitus. *Laryngoscope* 2012;122:2533–8.
- [30] Fan J, McCandliss BD, Sommer T, Raz A, Posner MI. Testing the efficiency and independence of attentional networks. *J Cogn Neurosci* 2002;14:340–7.
- [31] Petersen SE, Posner MI. The attention system of the human brain: 20 years after. *Annu Rev Neurosci* 2012;35:73–89.
- [32] Posner MI, Rothbart MK. Research on attention networks as a model for the integration of psychological science. *Annu Rev Psychol* 2007;58:1–23.
- [33] Posner MI. Orienting of attention. *Q J Exp Psychol A* 1980;41:19–45.
- [34] Eriksen BA, Eriksen CW. Effects of noise letters upon the identification of a target letter in a nonsearch task. *Percept Psychophys* 1974;16:143–9.
- [35] Fan J, McCandliss BD, Fossella J, Flombaum JL, Posner MI. The activation of attentional networks. *Neuroimage* 2005;26:471–9.
- [36] Fernández PJ, Campoy G, García Santos JM, Antequera MM, García-Sevilla J, Castillo A, et al. Is there a specific pattern of attention deficit in mild cognitive impairment with subcortical vascular features? Evidence from the Attention Network Test. *Dement Geriatr Cogn Disord* 2011;31:268–75.
- [37] Urbanek C, Weinges-Evers N, Bellmann-Strobl J, Bock M, Dörr J, Hahn E, et al. Attention Network Test reveals alerting network dysfunction in multiple sclerosis. *Mult Scler* 2010;16:93–9.
- [38] Keehn B, Müller RA, Townsend J. Atypical attentional networks and the emergence of autism. *Neurosci Biobehav Rev* 2013;37:164–83.
- [39] Orellana G, Slachevsky A, Peña M. Executive attention impairment in first-episode schizophrenia. *BMC Psychiatry* 2012;12:154.
- [40] Maurage P, de Timary P, Billieux J, Collignon M, Heeren A. Attentional alterations in alcohol-dependence are underpinned by specific executive control deficits. *Alcohol Clin Exp Res* 2014 [in press].
- [41] Pacheco-Unguetti AP, Acosta A, Marqués E, Lupiáñez J. Alterations of the attentional networks in patients with anxiety disorders. *J Anxiety Disord* 2011;25:888–95.

- [42] Philippot P, Nef F, Clauw L, de Romrée M, Segal Z. A randomized controlled trial of mindfulness-based cognitive therapy for treating tinnitus. *Clin Psychol Psychother* 2011;19:411–9.
- [43] Crum RM, Anthony JC, Basset SS, Folstein MF. Populations-based norms for the mini-mental state examination by age and educational level. *J Am Med Assoc* 1993;269:2361–91.
- [44] Philippot P, Clauw L, de Romrée M. Validation du questionnaire d'impact psychologique de l'acouphène (QIPA) [submitted for publication].
- [45] Beck AT, Steer RA. Beck depression inventory manual. San Antonio, TX: Psychological Corporation; 1987.
- [46] Spielberger DC, Gorsuch RL, Lushene RL, Vagg PR, Jacobs GA. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1983.
- [47] Faul F, Erdfelder E, Lang A, Buchner A. G\*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 2007;39(175):e191.
- [48] Rothbart MK, Rueda MR. The development of effortful control. In: Mayr U, Awh E, Keele SW, editors. *Developing individuality in the human brain: a tribute to Michael I Posner*. Washington, DC: American Psychological Association; 2005. p. 167–88.
- [49] Radcliff R. Methods for dealing with reaction time outliers. *Psychol Bull* 1993;114:510–32.
- [50] Tales A, Muir JL, Bayer A, Jones R, Snowden RJ. Phasic visual alertness in Alzheimer's disease and ageing. *Neuroreport* 2002;13:2557–60.
- [51] Posner MI. Chronometric explorations of mind. Hillsdale, NJ: Erlbaum; 1978.
- [52] Maurage P, Heeren A, Pesenti M. Does chocolate consumption really boost Nobel award chances? The peril of over-interpreting correlations in nutrition and health studies. *J Nutr* 2013;143:931–3.
- [53] Jakes SC, Hallam RS, Rachman S, Hinchcliffe R. The effects of reassurance relaxation training and distraction on chronic tinnitus sufferers. *Behav Res Ther* 1986;24:497–507.
- [54] Kirsch CA, Blanchard EB, Parnes SM. Psychological characteristics of individuals high and low in their ability to cope with tinnitus. *Psychosom Med* 1989;51:209–17.
- [55] Fan J, Flombaum JI, McCandliss BD, Thomas KM, Posner MI. Cognitive and brain consequences of conflict. *Neuroimage* 2003;18:42–57.
- [56] Matsumoto K, Tanaka K. Conflict and cognitive control. *Science* 2004;303:969–70.
- [57] Schmidt SA, Akrofi K, Carpenter-Thompson JR, Hussain FT. Default mode, dorsal attention and auditory resting state networks exhibit differential functional connectivity in tinnitus and hearing loss. *PLoS ONE* 2013;8:e76488.
- [58] Henry JA, Dennis KC, Schechter MA. General review of tinnitus: prevalence, mechanisms, effects, and management. *J Speech Lang Hear Res* 2005;48:1204–35.
- [59] Londero A, Viaud-Delmon I, Baskind A, Delerue O, Bertet S, Bonfils P, et al. Auditory and virtual 3 D virtual reality therapy for chronic subjective tinnitus: theoretical framework. *Virt Real* 2010;14:143–51.
- [60] Silchencko AN, Adamchic I, Hauptmann C, Tass PA. Impact of acoustic coordinated reset neuromodulation on effective connectivity in a neural network of phantom sound. *Neuroimage* 2013;77:133–47.
- [61] Robertson IH. Cognitive rehabilitation: attention and neglect. *Trends Cogn Sci* 1999;3:385–93.
- [62] Robertson IH, Tegnér R, Tham K, Lo A, Nimmo-Smith I. Sustained attention training for unilateral neglect: theoretical and rehabilitation implications. *J Clin Exp Neuropsychol* 1995;17:416–30.
- [63] Thimm M, Fink GR, Kust J, Karbe H, Sturm W. Impact of alertness training on spatial neglect: a behavioural and fMRI study. *Neuropsychologia* 2006;44:1230–46.
- [64] Serino A, Ciaramelli E, Di Santantonio A, Malagu S, Servadei F, Ladavas E. A pilot study for rehabilitation of central executive deficits after traumatic brain injury. *Brain Inj* 2007;21:11–9.
- [65] Sturm W, Willmes K, Orgass B, Hartje W. Do specific attention deficits need specific training. *Neuropsychol Rehabil* 1997;7:81–103.
- [66] Heeren A, Van Broeck N, Philippot P. The effects of mindfulness training on executive processes and autobiographical memory specificity. *Behav Res Ther* 2009;47:403–9.
- [67] Tang YY, Ma YH, Wang J, Fan YX, Feng SG, Lu QL, et al. Short-term meditation training improves attention and self-regulation. *Proc Natl Acad Sci USA* 2007;104:17152–6.
- [68] Segal ZV, Teasdale JD, Williams JMG. Mindfulness-based cognitive therapy for depression: a new approach to preventing relapse. New York: Guildford Press; 2002.
- [69] Gans JJ, O'Sullivan P, Bircchiff V. Mindfulness-based tinnitus stress reduction pilot study: a perception-shift program. *Mindfulness* 2014 [in press].
- [70] Kreuzer PM, Goetz M, Holl M, Schecklmann M, Landgrebe M, Staudinger S, et al. Mindfulness-and body-psychotherapy-based group treatment of chronic tinnitus: a randomized controlled pilot study. *BMC Complement Altern Med* 2012;12:235.
- [71] Sadlier M, Stephens SDG, Kennedy V. Tinnitus rehabilitation: a mindfulness meditation cognitive behavioural therapy approach. *J Laryngol Otol* 2008;122:31–7.
- [72] Kleinjung T, Eichhammer P, Langguth B, Jacob P, Marienhagen J, Hajak G, et al. Long-term effects of repetitive transcranial magnetic stimulation (rTMS) in patients with chronic tinnitus. *Otolaryngol Head Neck* 2005;132:566–9.
- [73] Plewnia C, Reimold M, Najib A, Reischl G, Plonke SK, Gerloff C. Moderate therapeutic efficacy of positron emission tomography-navigated repetitive transcranial magnetic stimulation for chronic tinnitus: a randomized, controlled pilot study. *J Neurol Neurosurg Psychiatry* 2007;78:152–6.
- [74] Smith JA, Mennemeier M, Bartel T, Chelette KC, Kimbrell T, Triggs W, et al. Repetitive transcranial magnetic stimulation for tinnitus: a pilot study. *Laryngoscope* 2007;117:529–34.
- [75] Fregni F, Marcondes R, Boggio PS, Marcolin MA, Rigonatti SP, Sanchez TG, et al. Transient tinnitus suppression induced by repetitive transcranial magnetic stimulation and transcranial direct current stimulation. *Eur J Neurol* 2006;13:996–1001.
- [76] Garin P, Gilain C, Van Damme JP, de Fays K, Jamart J, Osseman M, et al. Short- and long-lasting tinnitus relief induced by transcranial direct current stimulation. *J Neurol* 2011;258:1940–8.
- [77] Frank E, Schecklmann M, Landgrebe M, Burger J, Kreuzer P, Poepl TB, et al. Treatment of chronic tinnitus with repeated sessions of prefrontal transcranial direct current stimulation: outcomes from an open-label pilot study. *J Neurol* 2012;259:327–33.
- [78] Kreuzer PM, Landgrebe M, Schecklmann M, Poepl TB, Vielsmeier V, Hajak G, et al. Can temporal repetitive transcranial magnetic stimulation be enhanced by targeting affective components of tinnitus with frontal rTMS? A randomized controlled pilot trial. *Front Syst Neurosci* 2011;5:88.
- [79] Vanneste S, Plazier M, Ost J, van Der Loo E, van De Heyning PV, De Ridder D. Bilateral dorsolateral prefrontal cortex modulation for tinnitus by transcranial direct stimulation: a preliminary clinical study. *Exp Brain Res* 2010;202:779–85.