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Review Article

Incorporating Auditory Cortex Potentials and Gap Pre-pulse Inhibition of Acoustic Startle: A Probable Way to Objectively Assess Tinnitus

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ABSTRACT

Background and Objectives: Tinnitus is a complex condition that varies in loudness, quality, location, and distress. Different definitions, heterogeneity, and lack of objective measuring have challenged the understanding the mechanisms involved and definitive cure. The integrative model correlates each of these characteristics to separate parallel and overlapping subnetworks that process tinnitus's perception and emotional reaction. Many of these networks are common with the gap pre-pulse inhibition of acoustic startle (GPIAS) neural circuity. GPIAS, which measures tinnitus in animals, has recently been used for humans with various recording methods. The present study aimed to review the evidence achieved with gap stimuli in patients with tinnitus to support the potential of cortical responses recorded with the GPIAS stimulus and to objectively detect tinnitus in humans.

Methods: Studies were identified by searching electronic databases with relevant keywords.

Results: The role of the auditory cortex in processing short gaps, the possibility of evaluating the gap detection ability with GPIAS, and the advantage of cortical responses in reflecting both stimulus properties and different aspects of tinnitus emphasize the importance of this issue. The results of most studies have proven the gap detection deficiency in tinnitus. However, the validity of the auditory startle reflex still needs to be verified due to the inherent variability and different methods.

Conclusion: Further human studies are recommended because the perception of tinnitus can be controlled. An appealing research line in this area is multi-channel cortical evoked potentials. Defects of GPIAS with cortical recording can indicate tinnitus.

Keywords: Pre-pulse inhibition, Gap pre-pulse inhibition of acoustic startle (GPIAS), Cortical auditory evoked potentials, Tinnitus, Objective tinnitus assessment

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What is "already known" in this topic:

Tinnitus is a complex condition that has not definitive cure. The gap pre-pulse inhibition of acoustic startle (GPIAS) that measuring tinnitus in animal, has recently been used for humans with various recording methods. Cortical auditory evoked potentials (CAEP) with GPIAS stimulus potentially can be employed as a non-invasive objective tool in tinnitus measurement which can examine gap processing and temporal acuity by the auditory cortex. There are common neural areas in the GPIAS and tinnitus network in which the auditory cortex seems to be one of the essential areas for both of GPIAS and tinnitus.

What this article adds:

The present study aims to investigate in the literature whether CAEP with the GPIAS paradigm can be utilized as an objective tool to identify or classify tinnitus in humans, according to the same acoustic sensory input pathway of CAEP and GPIAS. The results of most studies have proven the gap detection deficiency in tinnitus, but the validity of this method still needs to be proved in future human studies.

Introduction

Tinnitus, perceiving sound in the brain or ear without an external sound source, has affected the quality of life for millions of people worldwide. The prevalence of this phantom feeling is estimated at 10%-15% [1], although up to 30% has been reported [2]. Although the prevalence of tinnitus increases with age, chronic tinnitus can occur at any age [3], even in children [4]. Among people with tinnitus, 1%-3% suffer from emotional distress, cognitive dysfunction, and or autonomic arousal caused by tinnitus [5], and the term "tinnitus disorder" has recently been introduced to describe this type of tinnitus [6].

No valid treatment for chronic tinnitus can eliminate the symptoms [7, 8]. Differences in the definition of tinnitus, heterogeneity, and problems measuring tinnitus challenge the tinnitus studies [9]. Consequently, the exact pathophysiological pathways are still not fully understood [10]. Various networks seem to be responsible for diverse aspects of tinnitus. Based on the integrative or global workspace model, the degree of involvement of loudness, memory, awareness, salience, and distress subnetworks causes tinnitus subtypes and variability in different people [11].

The comprehensive, objective assessment methods facilitate the investigation of neurophysiological hypotheses that lead to efficacious therapeutic solutions. Correspondingly, it became possible to subphenotype tinnitus, which is the basis for standardizing tinnitus assessment methods.

Objective tinnitus testing overcomes the limitations of subjective assessment, such as individual and intra-individual variability, non-usability in certain populations, and pediatric and forensic medicine [12]. It is also likely to help detect tinnitus in an earlier phase. In chronic tinnitus with symptoms lasting more than 3 months, tinnitus-related networks may become progressively centralized and resistant to treatment [13, 14].

To date, the clinical diagnosis of tinnitus in humans has only been based on subjective methods, such as self-assessment questionnaires, visual rating scales, and psychoacoustic assessments. Various objective methods have been employed to investigate tinnitus in humans, such as electroencephalography (EEG), magnetoencephalography, auditory brainstem responses (ABR), cortical auditory evoked potentials (CAEP), auditory evoked magnetic field, functional magnetic resonance imaging, positron emission tomography, single photon emission computed tomography, molecular genetics and blood-based biochemical markers [15]. CAEP can potentially be employed as a non-invasive objective tool in tinnitus measurement. CAEP offers a good temporal and reasonable spatial resolution, such as high-density auditory evoked potentials (AEPs). Tinnitus has distinct components, including perceptual characteristics (such as pitch, loudness, timbre, and location) and its effects on behavior and emotion. Each current tool (psychoacoustic assessments and questionnaires) measures only one aspect of perception or impact, and it seems reasonable and necessary to estimate the different aspects of tinnitus in light of the workspace model. The source localization of multi-channel CAEPs provides a comprehensive assessment and holistic comprehension of tinnitus by spa-

tial examination of different auditory and non-auditory neural hubs and networks. Another advantage of CAEPs over other objective methods is using specific stimulus protocols to investigate the probable central mechanisms of tinnitus. For instance, comparing CAEP parameters at frequencies with and without hearing loss can be used to study discordant frequency-dependent map reorganization in the auditory cortex in line with edge theory [16, 17]. Another special stimulus paradigm considered in this study is the gap pre-pulse inhibition of acoustic startle (GPIAS). This protocol can examine gap processing and temporal acuity by the auditory cortex.

GPIAS is one of the modifications of acoustic startle reflex (ASR), the most widely used method to detect tinnitus in animals, and is currently being studied in humans. The startle reflex involves the contraction of the facial and skeletal muscles and autonomic physiological response that reacts to strong and sudden stimuli in various modalities (visual, auditory, tactile) [18]. It can be recorded in different species and holds several crucial types of plasticity that are good candidates for research on brain mechanisms. These startle reflex modulations include pre-pulse inhibition (PPI), gap pre-pulse inhibition (GPI), habituation, sensitization, and fear potentiation.

The results of animal studies implicate that the cortico-striatal-pallido-thalamic circuit generates PPI. The neural circuitry of PPI in rodents reflects automated processing in the pre-attention phase. Still, it can be modulated by cognitive processing due to the descending axons it receives from the forebrain [19]. Although GPIAS is a kind of PPI, they are probably different regarding temporal features and neural circuits involved in gap detection. The auditory cortex seems to be one of the essential areas for GPIAS but it is not for PPI [20, 21]. Although the PPI circuit is well established in animals and many similarities exist between the measurements of the PPI between rodents and humans [22], the neural pathways of the PPI in humans are poorly understood and are still hypothesized. Human behavioral, physiological, and pharmacological studies suggest a complex neural network from the brainstem to higher-level cortical regions and the connections between the thalamus and striatum with the temporal, prefrontal, frontal, and parietal cortices [23-25]. Common neural areas exist in the PPI/GPIAS and tinnitus network. The extensive anatomical overlap between the PPI/GPIAS regulatory regions and the tinnitus networks supports that tinnitus, as a deficit of sensory-gating disorder, can affect the GPIAS and that cortical recordings can trace these effects. Thus, the present study aims to investigate in the literature whether CAEP with the GPIAS paradigm can be utilized as an objective tool to identify or classify tinnitus in humans according to the same acoustic sensory input pathway of CAEP and GPIAS.

Materials and Methods

Studies were identified by searching electronic databases and trial registers of PubMed, EMBASE, Medline, ClinicalTrials.gov, Google Scholar, and Web of Science. Keywords and equivalent terms applied alone or in combination were tinnitus, ear ringing, or phantom auditory sensation; acoustic startle reflex, pre-pulse inhibition, gap pre-pulse inhibition acoustic startle, ASR, PPI, or GPIAS; objective tinnitus assessment, objective tinnitus evaluation, objective tinnitus measurement, tinnitus detection with stimuli included gap, gap-induced auditory evoked potentials, tinnitus-related neural activity, gap detection, temporal resolution or temporal acuity; EEG, auditory evoked potentials (AEP), CAEP, auditory late latency response (ALLR), auditory middle latency response (AMLR), ABR, auditory cortex or A1. Our search was limited to available peer-reviewed and full-text journal articles written in English from 2006 onwards that directly addressed the gap-elicited assessments in humans with tinnitus.

Results

By searching for the keywords mentioned above, 93 related articles were obtained, of which 73 studies were conducted on animals and 20 on humans. The GPIAS method was performed in animal studies on different species (mice, guinea pigs, hamsters, gerbils, and rats) after inducting tinnitus by pharmacological methods (salicylate and quinine) or exposure to loud noises [26]. Turner first introduced the GPIAS method for rapid tinnitus screening in animal models. Subsequently, GPIAS was used in several studies to measure tinnitus in animal models. The stimuli used for GPIAS in animal studies included broadband noise (BBN) or narrowband noise (NNB) with a central frequency ranging from 500 Hz to 36 kHz and a presentation intensity of 55 to 120 dB sound pressure level (SPL). The gap in the stimulus differed in durations from 2 to 100 ms. Most studies have considered a statistically significant decrease in GPIAS compared to the control group as a measure of tinnitus presence. Some studies devoted a statistical comparison of the startle amplitude in the trials with and without gaps to confirm the existence of tinnitus. If the amplitude was not significant in these two conditions, it indicated the presence of tinnitus in the animal. Another method was to consider a fixed threshold so the tinnitus group would be regarded as if the GPIAS ratio were above that

threshold. The control group would be considered if this ratio was below the threshold.

In 20 human studies of search, three silent gap-based stimulus patterns were used, including the gap in noise (GIN), multi-deviant mismatch negativity (MMN), and GPIAS paradigms. Nine out of 20 studies examined these stimulus patterns in normal individuals without tinnitus, which were not considered in this study. Table 1 summarizes the characteristics of the other 11 studies performed in the tinnitus group.

Several ways were found to examine the GPIAS paradigm and discover the gap in human studies. Some studies employed direct behavioral measurements of gap detection and psychometric functions. In this regard, two psy-

Table 1. A Summary of 11 human studies performed in the tinnitus group with gap-embedded stimuli

Author (y)	Samples	Stimulus Paradigm	Recording Tool	Stimulus Characteristics	Gap Duration	Results
Fournier & Hébert, 2013 [28]	Tinnitus with normal hearing (n=15)+control (n=17)	PPI and GPIAS	Eye-blink EMG	Startle: 50 ms broadband noise bursts (20 Hz-20 kHz) at 105 dB (A) SPL Background: Low-frequency centered at 500 Hz (200-1200 Hz) or high-frequency at 4 kHz (3.5-4.5 kHz) continuous noise set at 65 dB (A) SPL	50 ms	Normal PPI and deficient GPI (in both low and high-frequency background noise) in tinnitus.
Campolo et al. 2013 [27]	Tinnitus with hearing loss (n=13)+control (n=13)	GIN	A psycho-acoustic GO/NO-GO gap detection task	One-third octave wide NBN of 90 s duration located above, below, or at the subject's tinnitus pitch at a level 15 dB above the NBN threshold	50 ms	The tinnitus group had no defects in gap detection compared to the control.
Mahmoudian et al. 2013 [63]	Tinnitus (n=28)+control (n=33)	Deviant	MMN	500, 1000, and 1500 Hz pure tones of 75 ms at 65 dB SPL as standard stimuli with silent gap, intensity, frequency, location, and duration as deviant	7 ms	MMN amplitude for the gap duration deviant was significantly smaller in the tinnitus group compared to controls, suggesting a cortical deficit in processing short gaps
Mehdizade-Gilani et al. 2013 [64]	Tinnitus with normal hearing (n=20)+control (n=20)	GIN	Psycho-acoustic gap detection in background noise	Estimation of gap threshold by Identification of 4.6 of shortest gap embedded in series of 6-s background white noise at 50 dB SL	2-6, 8, 10, 12, 15, 20 ms	Threshold Value of gap detection statistically significant increases in the tinnitus group.
Mahmoudian et al. 2015 [65]	Tinnitus people (n=28) were allocated randomly into two groups AES and PES. Following AES, participants were categorized into two groups: RI and NRI	Deviant	MMN	500, 1000, and 1500 Hz pure tones of 75 ms at 65 dB SPL as standard stimuli with silent gap duration, intensity, frequency, location, and duration as deviant	7 ms	MMN amplitude increase after intervention for all deviant except silent gap duration.
Shadwick & Sun, 2014 [29]	Tinnitus with normal hearing (n=7)+control (n=9)	GPIAS	Eye-blink EMG	Startle: 50 ms broadband noise at 100 dB SPL Background: narrowband noise with a 100 Hz bandwidth presented at 38-40 dB SPL centered at a frequency of patient's tinnitus	100 ms	Reduced GPIAS in the tinnitus group, but it was not significantly different.

Author (y)	Samples	Stimulus Paradigm	Recording Tool	Stimulus Characteristics	Gap Duration	Results
Boyen, 2015 [12]	Bilateral tinnitus (n=22)+age-matched and hearing loss–matched subjects without tinnitus (n=20)+control (n=10)	GIN	Adaptive psycho-acoustic test	Four different band-passed (BP) stimuli of Gaussian noise with different bandwidths (4000–8000, 4000–5000, 5000–6300, and 6300–8000 Hz) at three different sound levels (5, 10 and and 25 dB SL) and 300 ms duration.	30 ms gaps at the start of the test (then the gap size decreased or increased according to subjects' answers)	The tinnitus group did not display elevated gap thresholds in the four stimuli.
Ku et al. 2017 [52]	Tinnitus (n=16)+control (n=18)	GPIAS	CAEP	Background noise: 600 Hz and 8 KHz frequencies at 20 dB SL Startle: 1-kHz tone the burst of 20-ms duration at 65 dB SL	20, 50, and 100 ms gaps	The effect of tinnitus on the N1-P2 complex is observed only in the 20 ms gap duration and 8 KHz background noise. In other stimulus conditions, inhibition defects occur in both tinnitus and control.
Mohebbi et al. 2019 [66]	Compensated tinnitus with normal hearing (n=20), decompensated tinnitus (n=20), and control (n=20)	Deviant	MMN	500, 1000, and 1500 Hz pure tones of 75 ms at 65 dB SPL as standard stimuli with silent gap duration, intensity, frequency, location, and duration as deviant	7 ms	Reduced MMN amplitude for the gap duration deviant in decompensated Tinnitus group compared with Controls and compensated Tinnitus
Morse & Werff, 2019 [51]	Tinnitus (n=13)+control (n=13)	GIN	CAEP	White noise stimuli at 50 dB SL with a duration of 3 s in which a gap is embedded	2 ms, individual threshold+2 ms, 20 ms	No significant differences in gap-evoked CAEPs between tinnitus and control groups. P1 latency decreased for threshold and 20 ms gap in BBN for tinnitus.
Wilson et al. 2019 [30]	Tinnitus (n= 12)+control (n=18)	GPIAS	PAMR	Background noise: BBN, NBN centered at 1 kHz (1 octave wide) or a one-octave wide noise centered on a tinnitus pitch frequency at 70 dB SPL Startle: 20-ms broadband noise burst at 105 dB SPL	20 ms	No significant effect of the background conditions and reduced GPIAS were observed in the tinnitus group.

Abbreviations: PPI: Pre-pulse inhibition; GPIAS: Gap pre-pulse inhibition of acoustic startle; EMG: Electromyography; GPI: Gap pre-pulse inhibition; GIN: Gap in noise; NBN: Narrow band noise; MMN: Mismatch negativity; AES: Auditory electrical stimulation; PES: Placebo electrical stimulation; RI: Residual inhibition; NRI: Non-residual inhibition; CAEP: Cortical auditory evoked potentials; PAMR: Postauricular muscle reflex; BBN: Broadband noise.

choacoustic studies analyzed the conscious detection of silent gaps [12, 27]. Because the acoustic startle response involves many muscles, including limbs and head muscles, components of the startle reflex, including eye-blink and post-auricular muscle response, were recorded in some human studies of GPIAS using electromyography or motion-tracking system [28-30]. Recording EEG is another way to study gap detection ability and GPIAS in human studies. In this regard, three studies have recorded the mismatched negativity (MMN) using the gap deviation paradigm in tinnitus. In the other two human studies, CAEP has been used, one via the GIN stimulus pattern and the other by GPIAS.

Discussion

Continuous advances in the study of GPIAS in experimental tinnitus animal models have led to the emergence of different methods of GPIAS recording as objective research and diagnostic tool in tinnitus. Among the various methods, multi-channel CAEP recording is a new and compelling option as a biomarker of healthy brain circuitry. Cortical responses with the GPIAS paradigm investigate tinnitus' cognitive, attentional, and temporal processing defects. The method of detecting tinnitus with GPIAS is based on the "filling the gap" theory. It hypotheses that when the gap embedded in the background noise holds the same frequency as the tinnitus, gap inhibition does not occur in the startle response because tinnitus "fills in" the silent gaps in the background noise. However, some studies have proven against it. When the background noise frequency opposes the tinnitus frequency, a startle inhibition defect is sometimes induced [29, 30]. However, these studies do not rule out that the GPIAS indicates tinnitus. To further test the "filling the gap" hypothesis, human studies are preferable to animal studies because the perception of tinnitus can be addressed.

Many neurophysiological tinnitus models agree on maladaptive cortical and subcortical plasticity due to reduced auditory input (deafferentation) as a neural basis of tinnitus [31-33]. According to the edge theory, hyperactivity occurs in the adjacent regions with hearing loss [34]. Numerous studies have demonstrated correlations between the predominant pitch of tinnitus and the edge frequency [35, 36]. However, some inconsistent evidence exists [37, 38]. Since the auditory cortex is one of the hubs involved in tinnitus networks (due to an increase in neuronal excitability or an increase in synchrony in the auditory cortex) [39], changes in the dynamic properties of auditory cortex responses (spatial distribution, amplitude, and latency of CAEP components) can be utilized as objective diagnostic tools in tinnitus. Although some studies have found differences between the tinnitus and control groups in the early response of N1 and the late response of P300 [40, 41], there is still no agreement on which component may be a biomarker of tinnitus [42-45]. The existent objective methods rely on differentiating tinnitus from non-tinnitus based on the morphology of subcortical/cortical responses [46] and the pattern of EEG activity [47]. The EEG and AEP methods with the machine learning algorithms, source analysis, and multiscale entropy measures have provided a new possibility to more accurately differentiate tinnitus neural activity from non-tinnitus and compare different subtypes of tinnitus [48]. Source localization of CAEP is preferable rather than more complex machine learning methods to optimize the interpretability of the results [49].

The auditory cortex is essential in temporal acuity. Gap detection is one way to measure temporal processing, both in humans and animals. Recording CAEPs with gap-embedded stimulus patterns is a new perspective to assess tinnitus. Although the brainstem circuit regulates the startle reflex, the auditory cortex contributes to the discovery gap detection in the GPIAS stimulus pattern [19] due to the corticofugal radiations from the auditory cortex's layer 5 and 6 neurons to the superior colliculus, inferior colliculus, olivary complex, cholinergic pedunculopontine tegmental area and the cochlear nucleus [50]. According to the reviewing related articles, only two human studies recorded CAEP with gap stimuli. The GIN stimulus paradigm in Morse et al.'s study showed no significant differences in gap-evoked CAEPs between the tinnitus and control groups [51]. However, Ku et al. recorded CAEPs with the GPIAS paradigm and observed the effect of tinnitus on the N1-P2 complex only in a 20-ms gap duration and 8 kHz background noise. The inhibition deficit was not marked in both groups, with a 50-ms gap duration and tinnitus pitch unmatched by the background noise frequency (600 Hz) [52]. The results of this study do not support the concept of tinnitus filling in the gap and propose additional studies on the effects of background frequencies and gap duration on gap processing. The results of cortical inactivation studies in animals have shown that the auditory cortex is necessary to detect short gaps (<50 ms) but not for longer gaps (75-100 ms). Weible et al. study showed that cortical interneurons that constantly compare spike activity before and after the gap are involved in detecting gaps shorter than 25 ms [53]. Cortex gap termination response neurons are neural manifestations of detecting short gaps [54].

In a comprehensive review, the effectiveness of the GPIAS method was studied for the objective detection of tinnitus, but all human and animal studies with various response recording methods were studied. Consequently, the difference in stimulation parameters and data interpretation between laboratories was mentioned. Also, it was emphasized and recommended the preference for using human samples (due to the possibility of controlling the perception of tinnitus) and recording the evoked potentials with gap stimuli [55]. In a 2020 review paper, studies on EEG evoked by gap-embedded stimuli to detect tinnitus were collected and reviewed [56]. In that study, all brain responses with short, medium, and long latencies and all stimuli with gaps were reviewed. Still, the current review focuses on CAEP studies record-

ed with GPIAS stimuli in humans only. The difference between the current literature review and other previous review studies is the focus on the cortical evoked potential recording method (not other reflex-based methods or other evoked potentials), GPIAS stimuli (not other gap-embedded stimuli), and human samples suffering from tinnitus (not tinnitus induced animals). Although few studies were conducted to analyze these criteria, the possibility of applying cortical responses with GPIAS stimuli was soon optimistic, and it was recommended to conduct more extensive studies.

The results of the previous reviews indicate that it is difficult to interpret the effect of tinnitus on gap processing due to the small number of studies and different study methodologies. One of the reasons for these contradictions is the inherent variability of the acoustic startle reflex, which subsequently affects the efficacy of GPIAS in assessing tinnitus. Factors influencing this variability have been investigated in various studies on animal models, including startle stimulus and background noise properties (type, intensity, frequency), the distance between startle stimulus and gap (-stimulus interval), the distance between trials (inter-trial interval), gender differences, circadian rhythm, sample age (due to the effect of development and maturity), habituation, facilitation due to the gap, salience or importance of pre-pulse stimulus and attention to the pre-pulse stimulus (in humans) [57, 58]. Determining the most effective parameters differentiating tinnitus from normal conditions in the GPIAS method leads to its validation and standardization for tinnitus diagnosis. Among the factors mentioned above, the factors of gap position, gap duration, gap distance from the startle, and background noise frequency are the most influential. Although longer gaps provide more inhibition in the startle response [59, 60], only short gaps with distance from the startle (gap-embedded situation) process in the auditory cortex can be well evaluated with the CAEP tool [54]. In most PPI studies, intervals of 30 to 240 are usually used between the gap and startle; however, the results of studies have shown that the maximum inhibition occurs at a distance of 100-120 ms [22, 61]. The background noise frequency mainly affects the gap processing, and therefore in some studies, even normal people have shown less inhibition in low-frequency background noise [52, 62]. Hence, it is recommended to accurately match high-frequency background noise with tinnitus frequency and use a frequency higher than 1 kHz as low-frequency background noise to reduce the inherent effect of frequency on gap processing [52]. Further studies on this method are needed to determine if the defects of GPIAS are due to tinnitus or other abnormalities in the auditory or nervous system.

Conclusion

Although objective markers, such as imaging techniques or electrophysiological responses, have been studied to prove the presence or effects of tinnitus, no objective tool has been yet introduced to detect tinnitus in humans. There is no consensus among studies on the GPIAS method to assess tinnitus in humans. However, the possibility that the defects of GPIAS can be interpreted as an indicator of tinnitus has not been ruled out. To determine the efficacy of GPIAS in the proper and objective evaluation of tinnitus, human studies are the most logical because the perception of tinnitus can be controlled. An appealing research line in this area is EEG-based cortical evoked potentials. By manipulating acoustic stimulus parameters during CAEP recording, it is possible to determine the most influential parameter for the diagnosis of tinnitus and possibly explain the difference between the results of the studies.

Ethical Considerations

Compliance with ethical guidelines

The authors attest that all ethical considerations have been considered in compiling and referencing the content.

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Authors' contributions

Conceptualization and supervision: Akram Pourbakht; Methodology: Seyyed Jalal Sameni and Malihe Mazaheryazdi; Investigation and writing–review & editing: All authors; Writing–original draft: Soheila Shayanmehr; Funding acquisition and resources: Nariman Rahbar.

Conflict of interest

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مقاله مروری

ترکیب پتانسیل‌های برانگیخته قشر شنوایی و مهار رفلکس استارتل آکوستیکی با گپ پیش تحریکی: روشی برای ارزیابی عینی وزوز گوش

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چکیده

مقدمه وزوز گوش یک شرایط پزشکی پیچیده است که از نظر بلندی، کیفیت صدا، مکان و اضطراب ناشی از وزوز بین افراد متغیر است. تفاوت در تعریف وزوز، ناهمگونی انواع آن و فقدان روش‌های عینی ارزیابی وزوز، شناخت دقیق مکانیسم های تولید کننده آن و ارائه راهکارهای درمانی را محدود کرده است. بر اساس مدل جامع درک وزوز، شبکه های عصبی جداگانه و هم‌پوشانی کننده ای برای درک وزوز و واکنش های هیجانی نسبت به وزوز وجود دارند. بسیاری از این شبکه‌ها با مدارهای عصبی مولد مهار رفلکس استارتل آکوستیکی با گپ پیش تحریکی (GPIAS) مشترک هستند. GPIAS روشی رایج برای ارزیابی وزوز در حیوانات است واخیرا با روش های ثبتی مختلف در انسان ها نیز استفاده می شود. هدف مطالعه کنونی مروری بر شواهد حاصل از محرکات دارای گپ در مبتلایان وزوز است و از کاربرد احتمالی ثبت پاسخ های قشری با محرکات GPIAS به عنوان ابزار عینی ارزیابی وزوز حمایت می کند.

مواد و روش‌ها با جست‌وجو در پایگاه داده‌های الکترونیک، مطالعات انجام شده در این رابطه گردآوری و مورد بررسی قرار گرفتند.

یافته‌ها نقش قشر شنوایی در پردازش گپ‌های کوتاه، امکان ارزیابی توانایی کشف گپ با GPIAS و مزیت پاسخ های قشری در بررسی هر دو ویژگی‌های محرک و جنبه‌های مختلف وزوز، بر اهمیت این روش برای ارزیابی وزوز تأکید می کنند. نتایج اغلب مطالعات بر اختلال کشف گپ در مبتلایان وزوز دلالت داشتند. گرچه اعتبار این روش به دلیل تغییر پذیری ذاتی و روش های مختلف ثبت پاسخ هنوز نیاز به تأیید دارد.

نتیجه‌گیری انجام مطالعات انسانی در آینده با این روش توصیه می‌شود زیرا کنترل درک وزوز در انسان راحت تر است. ثبت پتانسیل‌های برانگیخته قشری بصورت چند کاناله یک زمینه تحقیقاتی جدید در این حوزه فراهم می‌کند. نقایص GPIAS در پاسخ‌های قشری می‌تواند نشان دهنده وجود وزوز باشد.

کلیدواژه‌ها:
مهار پیش تحریکی، مهار رفلکس استارتل با گپ پیش تحریکی، پتانسیل‌های برانگیخته قشر شنوایی، وزوز گوش، ارزیابی عینی وزوز

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