

# Acute exacerbation of chronic subjective tinnitus: a cross-sectional study

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*To the Editor:* Tinnitus is the impression of sounds in the absence of external sounds. Tinnitus affects 10% to 15% of adults, and about 20% of those with tinnitus considered it bothersome.<sup>[1]</sup> The impact of tinnitus is well-recognized in the general population and military veterans. Tinnitus reduces the quality of life by generating anxiety and concentration problems, impairing the ability to do intellectual work, making it difficult to sleep, and causing depression which, in severe cases, leads to suicide. The incidence of tinnitus is increasing as a result of the population aging, the pace of life accelerating, increased noise exposure from construction and entertainment activity, and increases in armed conflicts in some areas. However, there is an absence of studies concerning the exacerbation of tinnitus. The present study reports tinnitus aggravating data that address this gap, to prevent the occurrence of tinnitus-related comorbidities and improve the management of tinnitus.

This study recruited 602 patients with chronic subjective tinnitus who were hospitalized in the Department of Otolaryngology-Head and Neck Surgery at The Third Affiliated Hospital of Sun Yat-Sen University, in Guangdong, China, between January 2018 and March 2020. An acute exacerbation of chronic tinnitus was defined as the Tinnitus Handicap Inventory (THI) score increased by 6 points or more compared to the previous score. The study was approved by the Ethical Committee of The Third Affiliated Hospital of Sun Yat-Sen University (No. [2019] 02-479-01). The purpose of the study was explained to all patients, and written informed consent was obtained from participants in the study.

Patients participating in the study received a detailed physical examination at their first visit. Their medical

history was also obtained, including demographic characteristics, occupation, smoking and drinking behavior, and the duration of tinnitus and accompanying symptoms. Tinnitus severity was assessed with the THI score, and the Self-rating Anxiety Scale (SAS) and Self-rating Depression Scale (SDS) were used to assess anxiety and depression, respectively. Patients were also administered the Pittsburgh Sleep Quality Index (PSQI), and a score >5 was considered to indicate a sleep disorder, and they were administered the Psychosomatic Tension Relaxation Inventory (PSTRI), and a score ≥65 indicated that the patient was relatively stressed. The Fatigue Severity Scale (FSS) was also administered to measure the fatigue severity associated with tinnitus. An average pure-tone threshold loss ≥10 dB was considered to indicate an aggravated hearing loss. If a patient described worsening tinnitus after an abrupt change in barometric pressure, we considered the change in pressure to be the cause. Traveling by air and other behaviors can cause a pressure difference inside and outside the tympanic membrane.

In this study, there were 398 patients in the stable chronic subjective tinnitus group (208 females [52.3%] and 190 males [47.7%]), with an age range of 15 to 85 years. The acute exacerbation of chronic subjective tinnitus group included 204 patients (105 females [51.5%] and 99 males [48.5%]), with an age range of 17 to 84 years. There were no significant differences between the groups in sex distribution, smoking and drinking behavior, and duration of tinnitus (all  $P > 0.05$ ). However, the proportions of young and middle-aged individuals in the acute exacerbation of chronic tinnitus group were greater than those in the stable chronic tinnitus group (both  $P = 0.001$ ).

There were significant differences between the groups in aggravated hearing loss, fatigue, stress, negative emotions

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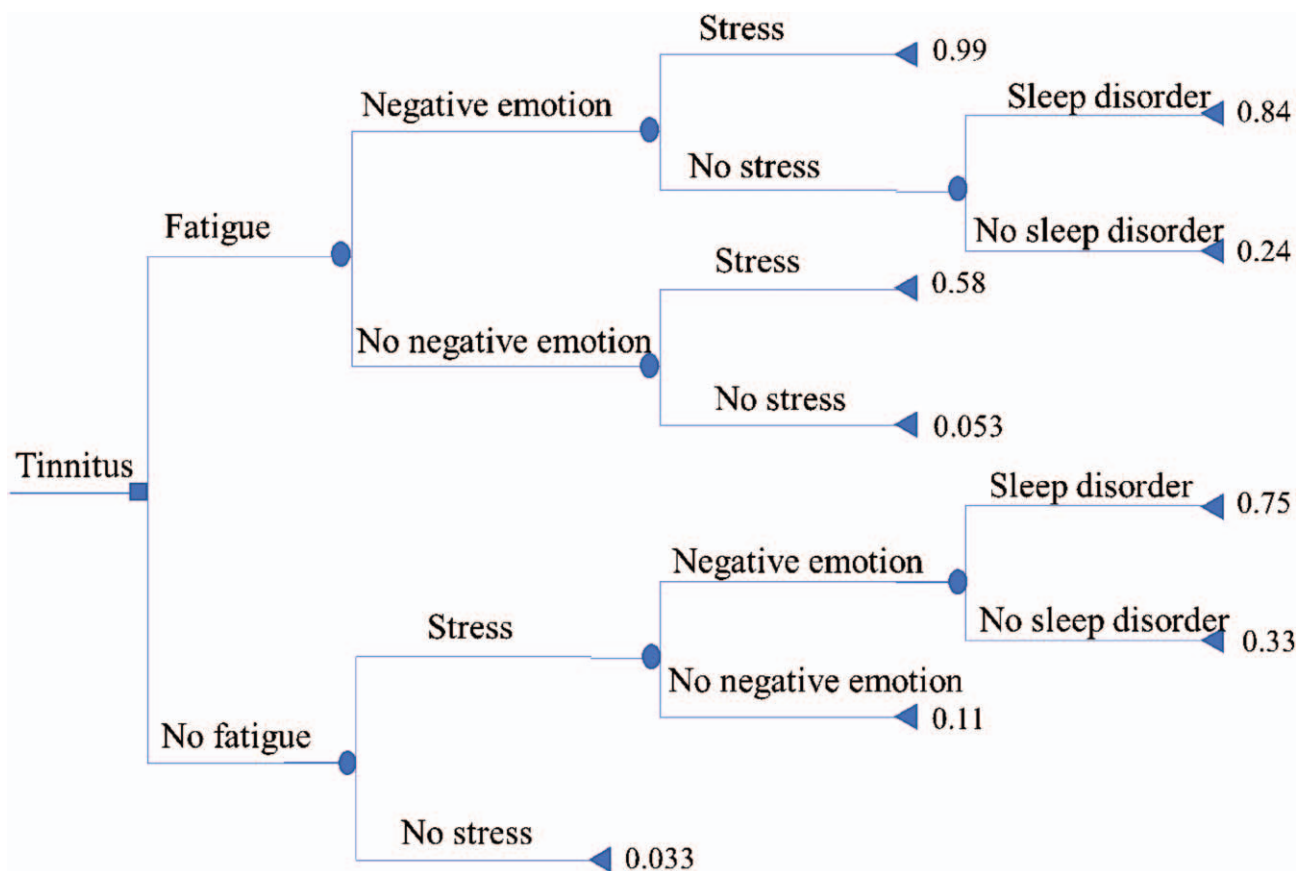
(anxiety and depression), sleep disorders, upper respiratory tract infections, noise exposure, and abrupt changes in barometric pressure (all  $P < 0.001$ ). The frequency of head and neck trauma, use of traditional Chinese medicine, electrical injury, and surgery were not statistically different between the groups ( $P = 0.397, 0.057, 0.616, \text{ and } 0.410$ , respectively).

A decision tree was used to analyze the influence of fatigue, stress, negative emotions, and sleep disorders on the acute exacerbation of tinnitus. As shown in Figure 1, 99% of chronic subjective tinnitus patients with fatigue, stress, and negative emotions had aggravated tinnitus. 84% of chronic subjective tinnitus patients with fatigue, negative emotions, sleep disorders, and no stress had aggravated tinnitus. 58% of chronic subjective tinnitus patients with fatigue, stress, and no negative emotions had aggravated tinnitus. The importance of the four factors was then evaluated using a random forest model. Based on the value of the mean decrease Gini ( $G$ ) which is used to analyze the importance of a certain factor in decision tree, fatigue and stress were found to be the most important factors, followed by negative emotions and sleep disorders ( $G_{\text{fatigue}} = 56.6, G_{\text{stress}} = 58.5, G_{\text{negative emotions}} = 46.2, G_{\text{sleep disorder}} = 17.0$ ).

We identified fatigue and stress to be the two most important manifestations of aggravated chronic tinnitus.

However, patients often complain of insomnia, short sleep time, and waking up easily, which can cause doctors to misjudge the role of sleep disorders in the acute exacerbation of chronic tinnitus. These complaints can also result in doctors ignoring the effects of fatigue and stress, while the objective sleep quality score of a patient shows no serious sleep disorder and the fatigue-stress assessment shows the patient has increased levels of fatigue and stress. Stress events may cause a psychosocial stress response, which may cause functional changes in the immune system, such as alterations in immune defense, immune homeostasis, and immune surveillance, and these changes may be related to the occurrence and aggravation of tinnitus. To put it another way, fatigue and stress might cause a physiological stress response in patients with tinnitus, resulting in changes in the neuroendocrine system and biological factors such as intestinal flora in susceptible populations. These changes subsequently lead to abnormal immune system responses.<sup>[2]</sup>

Sleep disorders affect performance in multiple domains of functioning, including, but not restricted to cognitive, emotional, metabolic, and immunological. Sleep disorders are a major problem associated with tinnitus, especially in cases of acute exacerbation. The more serious a sleep disturbance is, the worse tinnitus is. The prevalence of disturbed sleep in persons with tinnitus is reported to be in



**Figure 1:** The decision analysis model shows the influence mode of fatigue, stress, negative emotions, and sleep disorders on tinnitus. Squares indicate a decision node; circles indicate a chance node (events occurring or not); triangles indicate an endpoint node. Numbers indicate the proportions of acute exacerbations of tinnitus in all chronic tinnitus patients under different models.

the range of 25% to 60%.<sup>[3]</sup> Tinnitus patients with disturbed sleep often experience headaches and memory deficits, and the occurrence of a simultaneous migraine is thought to be closely related to the aggravation of tinnitus by sleep disorders. Insomnia and tinnitus in sleep-disturbed tinnitus patients can be treated with hypnotics, insomnia-specific psychotherapy, or cognitive behavior therapy.

Most patients with tinnitus have no serious emotional problems. However, anxiety is common in patients with tinnitus, and patients with anxiety often have certain personality traits such as introversion and dysfunctional cognition. Many aspects of dysfunctional cognition are also frequently found in tinnitus patients; the dysfunction may be the result of the patient's own thought processes or outside influences. For example, helping a patient to realize that tinnitus beyond their control can promote the fear that the tinnitus will get worse. Thus, concurrent treatment of anxiety and depression is essential for tinnitus patients exhibiting these symptoms. Treatment options include medications such as antidepressants and psychotherapeutic approaches. As shown in Figure 1, a key finding of this study is that the coexistence of fatigue, stress, and negative emotions is the main model of worsening tinnitus. This finding also confirms the close relation between tinnitus and the limbic system. For example, the study of tinnitus from the perspective of the limbic system has suggested that stimulation of the hippocampus may have a regulatory effect on the auditory cortex.<sup>[4]</sup>

Our results suggested that patients with worsening tinnitus may have experienced increased noise exposure. It is thought that damage to the cochlea caused by heightened noise leads to abnormal neural activity in the brain and the false perception of sounds (*ie*, tinnitus). Prolonged exposure to noisy environments causes neural degeneration in the central nervous system and can change the balance of excitation and inhibition in auditory pathways, eventually resulting in tinnitus. Based on these findings, Jiang *et al*<sup>[5]</sup> proposed a new hypothesis named "bionic active noise reduction" by considering the innate structures in the auditory system that may contribute to noise suppression. If this hypothesis can be verified, it may have significant implications for noise protection in social medical services, especially to prevent the occurrence and aggravation of tinnitus. The study also found that abrupt changes in barometric pressure, such as those which occur during diving in water or during a flight, can also cause acute exacerbation of chronic tinnitus. Barotrauma may cause an aggravation of tinnitus because of changes in the cochlear fluids. Aggravated tinnitus may either be temporary or persistent.

Patients with tinnitus frequently have headaches, but the relation between these two disorders is not always causal. Current research suggests that headaches and tinnitus may be symptoms of the same disease. Both cause a high degree of disability, and both are often accompanied by psychiatric disorders. Additionally, headaches and tinnitus share some common mechanisms in relation to their tendency to become chronic. However, regrettably, we did not evaluate headaches in the current study. In the face of

an exacerbation of chronic subjective tinnitus, we not only need to think about the problem from the perspective of hearing loss-tinnitus, but also understand the possible causes of disease aggravation from the perspectives of social support, a patient's work and leisure life, and social psychological stress. It is important to analyze the intrinsic relations between incentives and diseases, help patients rebuild good living habits, and improve their social and interpersonal relationships and their ability to cope with stressors. Only when all of these factors are considered can tinnitus prognosis maintenance be improved.

We conclude that fatigue, stress, negative emotions, and sleep disorders are the main manifestations of aggravated chronic tinnitus, and these four factors often coexist and affect each other. To prevent acute exacerbations of chronic tinnitus, it is necessary to help patients to rebuild good living habits and to improve their social interpersonal communication and ability to respond to stressors.

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### Conflicts of interest

None.

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