



## Changes in tinnitus and physiological biomarkers of stress in response to short-term broadband noise and sounds of nature



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### ARTICLE INFO

#### Keywords:

Tinnitus  
Sound therapy  
Stress  
Biomarker

### ABSTRACT

**Background:** Tinnitus is the perception of sound when no external sound source is present. In some cases, this perception coincides with, or results in, stress. Tinnitus-related distress has been associated with increased levels of cortisol and elevated levels of sympathetic tone. Our primary hypothesis was that short-term sound exposure would reduce tinnitus perception and various physiological measures of stress. A secondary hypothesis was that a self-selected nature sound would reduce physiological markers of stress more than broadband noise.

**Methods:** Twenty-one participants with constant bothersome tinnitus underwent an audiological assessment. Measurements of blood pressure, heart rate, salivary cortisol and cortisone concentrations, and tinnitus ratings were carried out three times: prior to and, in a counterbalance order, after 30 min of broadband noise and after 30 min of a self-selected nature sound (from: ocean waves, stream, rain or shower sounds).

**Results:** Findings revealed significant reductions in blood pressure measurements following broadband noise. None of the other stress measures demonstrated a statistically significant change. Both broadband noise and nature sounds elicited significant improvements in ratings of tinnitus.

**Conclusions:** While both sound types had a positive impact on many dimensions of tinnitus, only the broadband noise was associated with a reduction in blood pressure. These results are consistent with a complex interaction between sound and tinnitus and suggest a multifactorial basis to sound therapy that includes a reduction in arousal.

### 1. Introduction

Stress can be defined as the sum of physiological or biochemical ‘responses’ elicited by any stimulus that poses a risk to an organism’s homeostasis.<sup>1</sup> Distress occurs when stress is severe and prolonged, resulting in disequilibrium.<sup>2</sup> Tinnitus is the perception of sound in the absence of a sound source. Tinnitus and stress have been linked.<sup>3,4</sup> The emphasis of research in this area has been on the effects of stress on the onset, maintenance and progression from tinnitus to distressing tinnitus.<sup>5</sup> Significant and strong correlations have been found between stress-related mood disorders, e.g. anxiety and depression and tinnitus.<sup>6</sup> Constant and unrelenting exposure to tinnitus may also result in stress.<sup>4</sup> But the direction of the relationship between stress and tinnitus has not been explored extensively.

Although the mechanisms generating tinnitus are uncertain, tinnitus usually begins following auditory pathology and establishment of neural networks creating the dysfunctional perception.<sup>50</sup> For the

majority of the population tinnitus is just the experience of a sound sensation, it does not significantly disrupt quality of life. For a minority it is associated with handicap and reduced function.<sup>7,8</sup> Notably, the psychoacoustic characteristics of tinnitus (loudness and pitch) are often very similar in these two sub-populations<sup>9</sup> and little correlation has been found between tinnitus loudness and tinnitus-related distress.<sup>10</sup> Tinnitus lies in a continuum between barely noticeable to preventing daily activities.<sup>11</sup> Previous experience and emotional state have profound impacts on arousal, recognition and attentiveness.<sup>7,12,13</sup> Stress is also a possible candidate affecting the perception of tinnitus.<sup>3</sup> According to Lazarus’s transactional appraisal approach, psychological stress occurs when an individual makes a subjective judgement (appraisal) that internal or external demands exceed their available resources and ability to cope with the stressor.<sup>14</sup> From this perspective, tinnitus may act as a psychological stressor that exceeds one’s coping skills. One important determinant of a stressor is its uncontrollability.<sup>15</sup> Uncontrollability may lead to further stress, learned helplessness and

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<https://doi.org/10.1016/j.ctim.2019.07.018>

Received 24 April 2019; Received in revised form 9 June 2019; Accepted 24 July 2019

Available online 25 July 2019

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adopting maladaptive coping strategies that are unlikely to facilitate adaptation to tinnitus.<sup>13</sup> Tinnitus sufferers report exacerbation and heightened loudness during stressful periods<sup>51</sup> and there is an increased prevalence of depression and anxiety disorders with tinnitus.<sup>52</sup> It has been reported that when present concurrently, psychological disorders and tinnitus tend to exacerbate one another.<sup>5</sup> Tinnitus onset may be associated with a stressful situation.<sup>16</sup> The context of a traumatic event is likely to heighten the tinnitus experience feeding into a vicious cycle of perception and stress.<sup>17</sup>

Sound is used by audiologists to complement counselling or cognition behavioural therapy in a number of ways; these various approaches are known as “sound therapy”.<sup>18</sup> However the benefits of sound and mechanisms of sound therapy are not universally accepted.<sup>19</sup> Tinnitus may be affected by sound secondary to its effect on stress. Physiological mechanisms underlying stress and tinnitus interaction are likely to be multifaceted and complex.<sup>4</sup> Non-auditory systems, especially the limbic system, make important contributions to tinnitus in many tinnitus models<sup>12</sup> and a key role has been attributed to the amygdala for mediating tinnitus and stress.<sup>20</sup> The amygdala is responsible for the emotional interpretation of sensory stimulation and for controlling the physiologic output systems such as the autonomic nervous system.<sup>53</sup> Temporary suppression of tinnitus following transient inactivation of the amygdala further supports this hypothesis.<sup>21</sup> Involvement of emotion-related areas has also been identified with synchronised alpha activity, using continuous scalp recordings, from areas such as the subcallosal anterior cingulate cortex, the insula and the amygdala of patients with serious tinnitus-related distress.<sup>22</sup>

Standardised questionnaires have often been used in clinical practice to probe the relationship between subjective stress and tinnitus severity. For example, in a study by Gomaa et al.<sup>23</sup> using the Depression Anxiety and Stress Scale,<sup>54</sup> most individuals with tinnitus (75%) reported stress levels changing from mild-to-moderate to severe-to-extreme, compared to no stress reported by individuals without tinnitus. In another study, Zirke et al.<sup>6</sup> used the Perceived Stress Questionnaire<sup>55</sup> to analyse the subjective impairment and prevalence of psychological comorbidity in the chronic tinnitus population. Their results revealed that those patients with the most annoying tinnitus were more frequently accompanied by neurotic, stress related and somatoform disorders significantly higher than those who were only annoyed in quiet situations and when under stress.<sup>6</sup> Further, a retrospective study showed significantly higher scores using self-reported questionnaires in the lives of patients with sudden hearing loss and tinnitus compared to a control group.<sup>24</sup> This study also found that depression and poor well-being at the onset of tinnitus were strong predictors of tinnitus severity.<sup>24</sup>

Under physiological conditions, a reduced sympathetic tonus is consistent with typical cardiovascular symptoms at the periphery, such as lower heart rate and reduced blood pressure.<sup>25</sup> It is for this reason that both parameters were hypothesized to change following sound exposure in this study. Few studies have used blood pressure as a marker of autonomic nervous system reactivity in tinnitus patients, Değirmenci et al.<sup>26</sup> reported significantly lower mean heart rate in tinnitus compared to controls, using 24-h ambulatory blood pressure monitoring.<sup>56</sup> reported a lower increase in heart rate in a tinnitus group compared to controls to a mental arithmetic stress task and suggested that their result indicated an attenuated stress response and maladaptive autonomic nervous system reactivity in tinnitus patients.<sup>56</sup> Manufacturing noise has been linked to increased systolic blood pressure<sup>27</sup> and strong associations have been found between long term aircraft noise exposure and risk of hypertension (sustained blood pressure elevation).<sup>28</sup> Long term exposure to persistent stressors can cause hypertension.<sup>29</sup> Although listed among the risk factors for hypertension,<sup>30</sup> how stress causes sustained blood pressure elevation over time is not well understood. Suggested mechanisms are: 1) repeated activation of the sympathetic nervous system, 2) impaired cardiovascular recovery following stressful

events and 3) failure to habituate to repeated stressful stimulus, or some combination of these factors.<sup>31</sup>

Measurements of stress hormone levels in the tinnitus population have also been performed in order to discover a physical correlate to tinnitus. Upon appraisal of a stressor, sensory information is modulated by the limbic system and conveyed to the hypothalamus.<sup>57</sup> The neurosecretory cells in the hypothalamus release corticotropin-releasing factor (CRF) into the hypothalamic-hypophyseal portal circulation system.<sup>32</sup> The CRF promotes the secretion of adrenocorticotrophic hormone (ACTH) from the pituitary gland which in turn stimulates the adrenal cortex to release the mineralocorticoid hormone aldosterone, and glucocorticoid hormones, cortisol and cortisone, to the circulation.<sup>57,58</sup> Since the preliminary work by Shannon and Prigmore,<sup>33</sup> salivary cortisol has become increasingly popular for the determination of the condition of the adrenocortical system because it has been shown that salivary cortisol reliably reflects free plasma cortisol levels.<sup>34,59</sup> Hébert et al.<sup>3</sup> studied the levels of stress hormones in a tinnitus population and found that individuals with high tinnitus-related distress had higher cortisol levels than both a low tinnitus-related distress group and controls, indicating arousal of the hypothalamic-pituitary-adrenal axis in distressing tinnitus.<sup>3</sup> The hypothalamic-pituitary-adrenal axis was found to be activated to a lesser degree and at a later stage, in tinnitus patients than those of the controls in a more recent study.<sup>35</sup> This difference is most likely reflects the existence of two separate feedback loops: 1) controlling the basal cortisol secretion for maintenance of physiologic activities and 2) regulating acute stress stimulated cortisol response.<sup>36</sup> Another possible explanation may be the difference in duration of tinnitus in two studies, as it was longer in the acute stress exposure study (14.7 years on average)<sup>35</sup> than in the basal cortisol study (7.2 years on average).<sup>3</sup> The hypothalamic-pituitary-adrenal axis could be exhausted after prolonged elevation of basal cortisol levels in the acute stress group.<sup>37</sup> In support of this hypothesis, when a low-dose dexamethasone suppression test was used to examine if there was hypothalamic-pituitary-adrenal axis dysregulation, an almost complete cortisol suppression was observed.<sup>38</sup> Such suppression is indicative of chronic exhaustion of the hypothalamic-pituitary-adrenal axis in the tinnitus population.<sup>38</sup> Another study that aimed to probe the diagnostic and clinical values of several stress hormones found significantly higher levels of norepinephrine and 5-hydroxyindoleacetic acid (a serotonin metabolite) in a tinnitus group compared to non-tinnitus controls, but the levels of cortisol did not differ between the groups.<sup>39</sup> Kim and co-workers only took one cortisol sample per individual, which may have been insufficient considering the diurnal secretion pattern of cortisol<sup>36</sup> and no exclusion criteria for disorders or medications that can interfere with hypothalamic-pituitary-adrenal axis were mentioned. However,<sup>60</sup> also failed to show any significant correlations between several biochemical measures of stress (various immunological markers, adrenocorticotrophic hormone, cortisol and urinary catecholamines) and psychological distress.

It is generally accepted that there is both the tinnitus sound and reaction to this sound.<sup>40</sup> The reaction to tinnitus may create stress or be modified by stress. In this study we evaluated the effects of common sounds used to complement counselling in tinnitus therapy in an attempt to ascertain whether one of one mode of action of action might be via stress reduction pathway. We hypothesized that: 1. Sound will reduce tinnitus perception and various physiological measures of stress (heart rate, blood pressure, salivary cortisol and cortisone concentrations). 2. A preferred nature sound would reduce physiological markers of stress more than broadband noise.

## 2. Methods

This study was approved by The University of Auckland Human Participants Ethics Committee.

## 2.1. Participants

A total of 21 participants (12 males and 9 females) with bothersome tinnitus were recruited through the University of Auckland Hearing and Tinnitus Clinic. A power analysis calculation was undertaken to determine the sample size for an ANOVA with 3 repeated measures. For an effect size of 0.7 (moderate-large) an alpha of 0.05 and power 0.8 a sample size of 21.2 was calculated (<http://psychstat.org/rmanova>).

The age of the participants ranged from 22 to 69 years with a mean age of 47.2 years (SD = 13.7). Participants were required to meet the following criteria: Not having physical sickness on the day of testing. Not taking steroid-based medications (e.g. corticosteroids or had steroid injections). Not taking medications to reduce high blood pressure (e.g. beta-blockers). Not having any endocrine disease (e.g., diabetes, uncontrolled hypo- or hypertension, lupus). Not having jet lag or having undergone surgery in the past six months. Non-smoking. Body Mass Index (BMI) of 29 or less. Additional to these criteria, participants were asked to have a light lunch around 12 pm and all assessments were conducted at 2 pm, in order to avoid the fluctuations that occur in cortisol levels after food intake. Participants were also instructed to avoid food, coffee and caffeinated beverages or fruit juices after 1 pm and during the appointment. They were notified about the potential effects of caffeinated drinks on heart rate and blood pressure and the importance of following this schedule for obtaining meaningful results.

## 2.2. Procedure

### 2.2.1. Audiometry

Pure-tone audiometry was performed in a sound-treated room (ISO 8253–1:2010) using a Grason-Stadler 61 (GSI-61) audiometer. The modified Hughson-Westlake method<sup>41</sup> was used for obtaining hearing thresholds of participants. Pure-tone audiometry was performed from 250 Hz to 8 kHz. Pure-tones were presented via either ER-3A insert earphones or TDH50 supra-aural headphones for air conduction testing and Radioear B-71 for bone conduction testing. Tympanometry was performed using a Grason Stadler GSI Tymptstar using a 226 Hz probe tone.

### 2.2.2. Questionnaires

Participants completed the Tinnitus Functional Index (TFI)<sup>61</sup> and the Hospital Anxiety and Depression Scale (HADS)<sup>62</sup> as baseline measures of tinnitus and psychological wellbeing. Rating scales of the how great a problem the tinnitus was (1–5) and loudness, comfort, annoyance, ability to ignore and comfort (1–10) were completed at three separate times. The first ratings were obtained before the first half of the sound therapy session, as a baseline measurement, the second and third ratings were completed following presentations of a broadband noise and a nature sound (counterbalanced) (Fig. 1).

### 2.2.3. Sounds

The nature sounds (self-selected from rain, ocean, stream, shower or ocean waves [[www.tinnitustunes.com](http://www.tinnitustunes.com)]) and broadband noise were

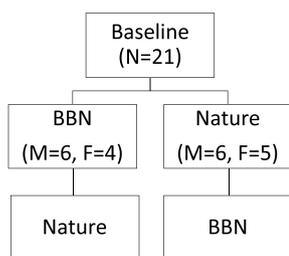


Fig. 1. Participant allocation. Participants were allocated to two groups, either BBN or nature sounds first. Tinnitus ratings and physiological measures were undertaken at each time.

used for two 30-minute listening sessions.

The participants were randomly separated into two groups. Half of the participants were asked to listen to one of the nature sounds first and the other half listened to the broadband noise first. The loudness of sounds was adjusted according to participants preference and their comfort. Sounds were presented using a pair of Bragi Dash earbuds. The Dash earbuds were controlled by manufacturer’s app downloaded to the researcher’s Android mobile phone. The sound tracks were uploaded to the Android device and streamed to the Dash via Bluetooth. All participants were instructed on how to make volume adjustments to set the volume of the sounds at a comfortable level.

### 2.2.4. Blood pressure and heart rate measurements

Participants were seated on a comfortable chair and rested for at least 10 min prior to initial measurements. Blood pressure was measured on the left arm using a commercially available digital sphygmomanometer (Omron Heartsure Blood Pressure Monitor BP100) and expressed in terms of systolic blood pressure over diastolic blood pressure. Participants were instructed to remain seated during the whole session to prevent fluctuations in blood pressure due to postural changes.<sup>42</sup> Heart rate was measured using the palpitation method by counting the pulse on the left radial artery for 1 min using a stopwatch. Both measurements were obtained three times: prior to, after broadband noise and after the nature sound.

### 2.2.5. Saliva collection: salivary cortisol and cortisone assays

Saliva sampling was also performed: prior to, after broadband noise and after the nature sound. The samples were obtained via passive drooling technique as described by Granger et al.<sup>43</sup> In order to stimulate saliva flow, participants were asked to imagine they were chewing their favourite food and then to slowly force the saliva into a transparent plastic test tube. The procedure continued until the level of saliva was well above the 1 mL mark on the test tube to ensure sufficient amount of sample was collected for cortisol assay. Saliva samples were collected and stored in 5.0 mL polypropylene micro-centrifuge tubes with locking caps (Interlab Ltd., Wellington, New Zealand). The samples were frozen immediately at –20 °C. All samples were transferred frozen to the research laboratory. Saliva analysis was performed at the Liggins Institute of the University of Auckland. Salivary cortisol assays were performed by liquid chromatography and tandem mass spectrometry (LC–MS/MS) as described in detail by McKinlay et al.<sup>63</sup>

## 2.3. Data and statistical analysis

All data was recorded in Microsoft Excel 2016 and analysed using repeated measures analysis of variance (ANOVA) with IBM Statistical Package for the Social Sciences (SPSS) Version 23 software. The data was normally distributed.

## 3. Results

### 3.1. Audiometry

The mean pure tone audiometric thresholds from 250 Hz to 8000 Hz showed a slight high frequency hearing loss slightly worst in the left ear (Fig. 2).

### 3.2. Questionnaire outcomes

The TFI was measured at the beginning of the session. The average TFI score was 33.1 ± 15.1, consistent with mild to moderate severity.<sup>61</sup> The mean HADS total score for the participant sample was 9.76 out of a possible 42 points. On average, this score suggested a low level of emotional distress. The average score for the anxiety subscale was 6.19 and for the depression subscale was 3.57. Both subscales

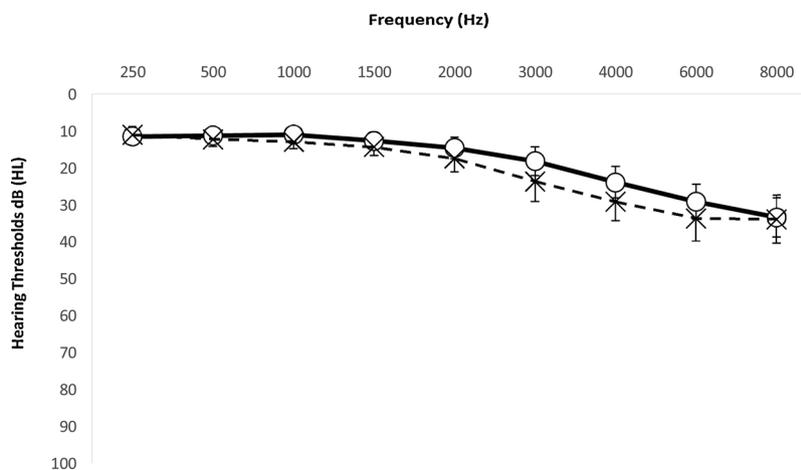


Fig. 2. Mean hearing thresholds ± SEM of the study participants (o right, x left; n = 21).

indicated a ‘normal’ level of anxiety and depression among the participant sample.<sup>62</sup>

### 3.3. Effects of sound on tinnitus ratings

The sound stimuli were counterbalanced. A repeated measure of ANOVA was applied. Mauchly’s test of sphericity indicated that the assumption of sphericity was met therefore, no adjustments were made to the degrees of freedom for either the time or error effect. No effect of presentation order was found for any of the measures obtained. Improvements were found between the mean TSNS scores of baseline, broadband noise and nature sounds,  $F(2, 40) = 14.47$ ,  $p < 0.0005$  (Fig. 3). Both sounds had a similar effect on each of the rating scales.

### 3.4. Blood pressure and heart rate

Mauchly’s test of sphericity indicated that the assumption of sphericity was met therefore, no adjustments have been made to the degrees of freedom for either the time or error effect. Sound therapy elicited statistically significant effects on mean systolic blood pressure measurements,  $F(2,40) = 7.490$ ,  $p = .002$  (Fig. 4A). Multiple paired-samples *t*-tests with a Bonferroni adjustment for multiple comparisons were run. There was a decrease in systolic blood pressure from baseline ( $M = 124.8 \pm 2.6$  mm/Hg) to broadband noise ( $M = 117.61 \pm 3.04$  mm/Hg), a statistically significant mean reduction of 7.19 mm/Hg,

95% CI [2.77, 11.6],  $p = 0.001$ . A significant effect of intervention was observed on diastolic blood pressure,  $F(2,40) = 6.72$ ,  $p = 0.003$ . Multiple paired-samples *t*-tests with a Bonferroni adjustment revealed that the mean decrease of 6.28 mm/Hg in diastolic blood pressure from baseline ( $M 73.85 \pm 1.98$  mm/Hg) to broadband noise ( $M 67.57 \pm 2.61$  mm/Hg) was statistically significant, 95% CI [1.53, 11.03],  $p = 0.008$  (Fig. 4B). A one-way repeated measures of variance (ANOVA) was conducted to determine whether there was a statistically significant difference in mean (*M*) heart rate for the different experimental conditions. Non-statistically significant changes in heart rate from baseline ( $M = 67.19 \pm 2.5$  bpm) to BBN ( $M = 64.38 \pm 2.5$  bpm) and to nature sounds ( $M = 64.9 \pm 2.8$  bpm) were obtained.

### 3.5. Cortisol and cortisone concentrations

Changes in cortisol and cortisone concentrations were not statistically significant (Fig. 5). Variation between participants was high. Salivary cortisol concentrations decreased from baseline ( $M = 1.04 \pm 0.1321$  nmol/L) to BBN ( $M = 0.9981 \pm 0.2236$  nmol/L) and increased to nature sound condition ( $M = 1.0976 \pm 0.2416$  nmol/L). Cortisone concentrations decreased from Baseline ( $M = 6.75 \pm 0.58$  nmol/L) with BBN ( $M = 6.30 \pm 0.69$  nmol/L) and the nature sound ( $M = 6.47 \pm 0.8$  nmol/L).

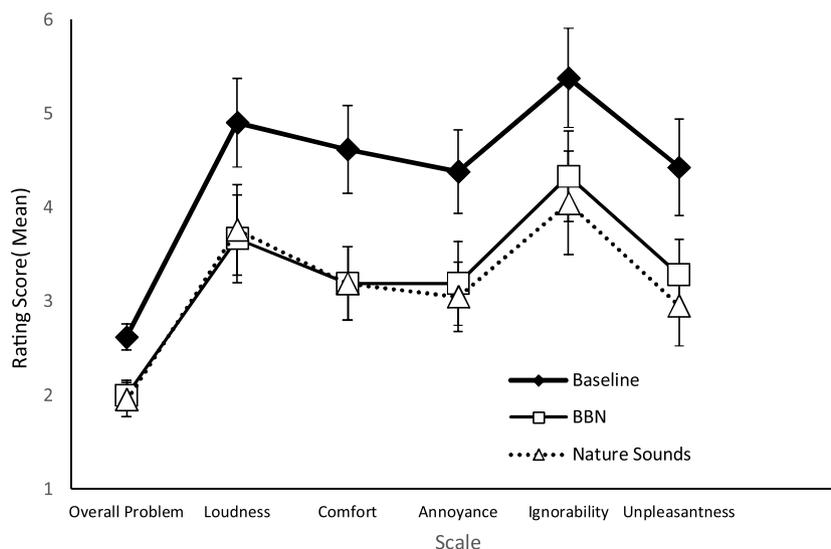


Fig. 3. Summary of participants’ mean tinnitus ratings baseline and following both sound stimuli error bars are ± SEM. Overall problem scale 1–5 all others 1–10.

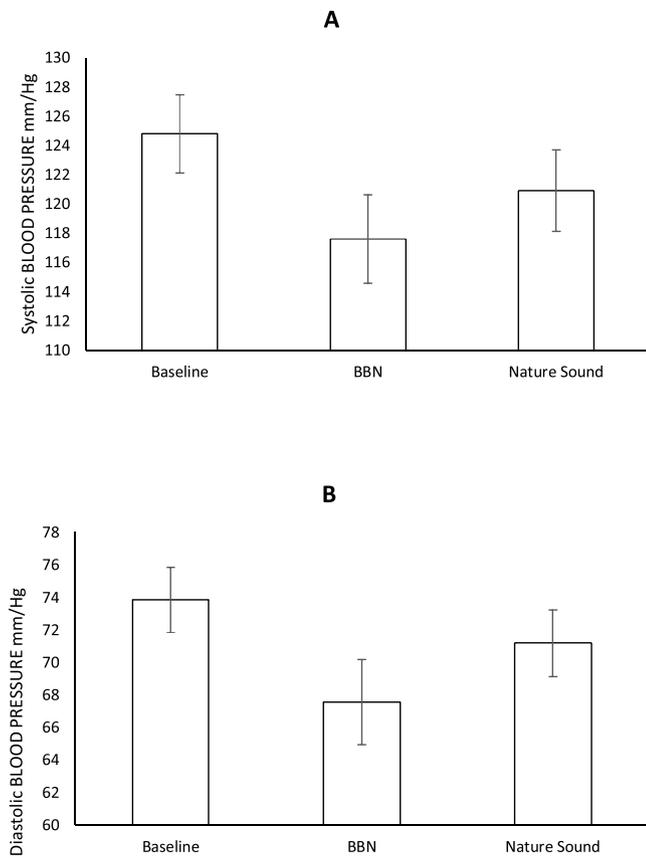


Fig. 4. A. Systolic blood pressure measurements. B. Diastolic blood pressure (n = 21) at baseline, broadband noise and nature sound conditions error bars are ± SEM.

#### 4. Discussion

In this study we were able to demonstrate that sound reduced one objective measure of stress, blood pressure, in a group of tinnitus sufferers. The effect was achieved without counselling. The result lends support to the belief that appropriate sound use is complementary to counselling.<sup>18</sup>

A baseline measurement of the stress markers of interest was undertaken and this was repeated for two sound conditions (broadband noise and nature sounds). The stress markers used were heart rate, blood pressure and the concentrations of cortisol and cortisone in saliva. Rating scales were also administered to examine the changes in subjective tinnitus ratings and to compare physiological findings with self-perceived dimensions of tinnitus. It was hypothesized that in comparison to baseline ratings, sound would elicit reductions in the participants' subjective ratings of tinnitus perception. This hypothesis was supported as both sounds reduced ratings of tinnitus. It was hypothesized that the sound would decrease elevated levels of arousal, that in turn would reduce activation of sympathetic nervous system measured by reductions in blood pressure, heart rate and salivary cortisol and cortisone concentrations. The only statistically significant change in stress measures was in blood pressure and in response to broadband noise. The other measures showed similar patterns of change but appeared less sensitive to the effect of sound. Compared to baseline measurements, significant reductions were observed in both systolic and diastolic blood pressure immediately after broadband noise. It has been suggested that broadband noise may achieve its effect through a presence of sound pathway, its fairly constant temporal structure and wide frequency content resulting in it being an effective masker.<sup>64</sup> Nature sounds also would elicit some reduction in the audibility of tinnitus, however these sounds are also thought to have an

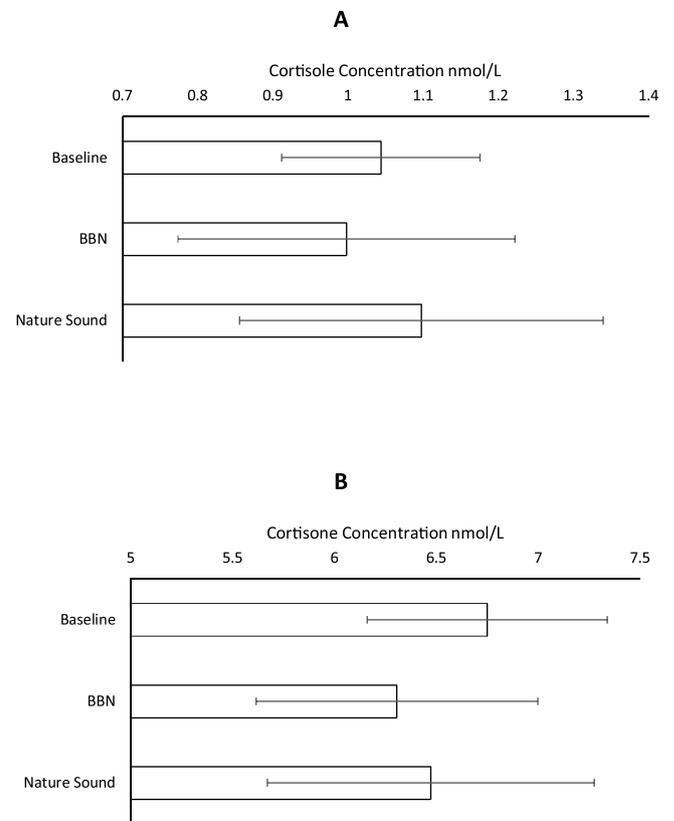


Fig. 5. The mean salivary A. cortisol and B. cortisone concentrations ± SEM (n = 21) at baseline, broadband noise and nature sound conditions.

emotional benefit, and may also act on a context pathway in which attention is captured by the temporal fluctuations in the sound.<sup>64</sup> In a meta-analysis, stress management treatments,<sup>44</sup> meditation<sup>45</sup> and relaxing music<sup>65</sup> have been found to be effective in lowering blood pressure. An explanation for the absence of stress related effects of the nature sounds in our study is that nature sounds may have engaged attention away from tinnitus but in doing so may also have raised limbic system activity. Masking of tinnitus with broadband noise may have eliminated its perception, removing it as a stressor.<sup>66</sup>

We found no differences in heart rate, cortisone or cortisol across conditions. A reduction in the sympathetic tone has been shown after suppression of tinnitus.<sup>67</sup> Since the heart is innervated by both divisions of the autonomic nervous system,<sup>68</sup> it was hypothesized that sound therapy would reduce activation of the sympathetic nervous system, increase parasympathetic tone and subsequently decrease heart rate. No significant change between repeated measurements of heart rate was observed. It is theoretically possible that following the presentation of both sound stimuli, the decreases in blood pressure might have caused a compensatory baroreflex gain for heart rate that would otherwise decreased.<sup>46</sup> Another possible explanation could be simply that exposure to sound did not evoke a strong enough parasympathetic response to reduce heart rate. Our participants had low scores on the HADS questionnaire. The average TFI was 33.1, consistent with mild to moderate tinnitus distress.<sup>61</sup> No behavioural measure of stress was used to quantify how stressed participants were. If participants with higher levels of anxiety and tinnitus-related severity were included, more informative data may have been obtained on the mode of effect of sound, because stress is believed to be one of the major determinants of arousal and attentiveness to tinnitus. We chose to use the HADS and TFI as intake questionnaires as they are regularly used in audiology-based tinnitus clinics and in the case of the TFI have been validated in our clinic population.<sup>47</sup> Alternative measures to have used at baseline would have been a questionnaire of stress or the Tinnitus Primary

Function Questionnaire (TPFQ,<sup>48</sup>). In the case of the TPFQ the thoughts and emotions subscales might have provided insight into aspects of tinnitus related stress.<sup>48</sup>

No significant change in salivary cortisol and cortisone concentrations was observed between the measurements at baseline and immediately after broadband noise and nature sound. It was assumed that salivary cortisol and cortisone concentrations would be good indicators of the short-term sound exposure because cortisol has been used as an objective measure of tinnitus-related distress previously<sup>3</sup> showed that high tinnitus-related distress was characterized by chronically elevated levels of salivary cortisol compared to non-tinnitus controls. However in a low tinnitus-related distress group basal cortisol levels were not elevated.<sup>3</sup> Therefore, in our study, the non-significant salivary biomarker results could be due to relatively lower tinnitus severity of the sample population. Our result partially supports past observations made by Monzani et al.<sup>9</sup> in which a decrease in tinnitus perception was not always related to a reduction in the perceived severity of the tinnitus. The levels of salivary cortisol and cortisone were not affected by the temporary reduction in tinnitus. Chronic tinnitus distress has been associated with delayed and blunted cortisol response, which was thought to occur because of a dysregulation of the hypothalamic-pituitary-adrenal axis due to chronic stress.<sup>35</sup> The underlying physiological mechanism of this dysregulation is still being investigated. Current evidence suggests that prolonged high levels of cortisol down-regulate the glucocorticoid receptors in the hypothalamus and pituitary gland, to which cortisol levels fail to decrease despite alleviation of stress.<sup>69</sup>

It is possible that the effects seen would differ in another sample. The sample was recruited from our clinic population. A general population sample might have different levels of stress or responds to sound in a different way. Our sample had better hearing than many clients of our clinic.<sup>49</sup> This is probably due to the average age of the sample being relatively young (47 years); this in turn being a consequence of our exclusion criteria regarding blood pressure, medication etc. The younger sample would reflect the reduced likelihood of presbycusis.

## 5. Conclusion

This study investigated the effects of sound on tinnitus ratings, blood pressure, heart rate, salivary cortisol and cortisone concentrations in individuals with bothersome tinnitus. No counselling was provided. Subjective changes in tinnitus perception were found with both broadband noise and nature sounds. Significant reductions in blood pressure measurements were observed following broadband noise. None of the other stress measures demonstrated a statistically significant change. These results are consistent with a complex interaction between sound and tinnitus and suggest a multifactorial basis to the effects of sound on tinnitus.

## Funding

This research was supported by a University of Auckland School of Population Health student grant to Nihal Aydin.

## Declaration of Competing Interest

G D Searchfield is director of the University of Auckland's Hearing and Tinnitus Clinic and Tinnitus Tunes an online subscription-based tinnitus resource. The other author has no conflicts of interest to report.

## References

1. Selye H. *Stress in Health and Disease*. Boston: Butterworths; 1976c1976.
2. National Research Council. *Recognition and Alleviation of Pain in Laboratory Animals*. Vol. 1. National Academies Press; 2010.
3. Hébert S, Paiement P, Lupien SJ. A physiological correlate for the intolerance to both internal and external sounds. *Hear Res*. 2004;190(1):1–9.
4. Mazurek B, Szczepek AJ, Hébert S. Stress and tinnitus. *HNO*. 2015;63(4):258–265.

<https://doi.org/10.1007/s00106-014-2973-7>.

5. Baguley D, Andersson G, McFerran D, McKenna L. *Tinnitus: A Multidisciplinary Approach*. West Sussex, UK: John Wiley & Sons, Ltd; 2013.
6. Zirke N, Seydel C, Szczepek A, Olze H, Haupt H, Mazurek B. Psychological comorbidity in patients with chronic tinnitus: analysis and comparison with chronic pain, asthma or atopic dermatitis patients. *Qual Life Res*. 2013;22(2):263–272.
7. Dobie RA. Overview: suffering from tinnitus. In: Snow JB, ed. *Tinnitus: Theory and Management*. Ontario: BC Decker Inc; 2004:1–7.
8. Tyler RS, Baker LJ. Difficulties experienced by tinnitus sufferers. *J Speech Hear Disord*. 1983;48(2):150–154.
9. Monzani D, Genovese E, Marrara A, et al. Validity of the Italian adaptation of the Tinnitus Handicap Inventory; focus on quality of life and psychological distress in tinnitus-sufferers. *Acta Otorhinolaryngol Ital*. 2008;28(3):126.
10. Ward LM, Baumann M. Measuring tinnitus loudness using constrained psychophysical scaling. *Am J Audiol*. 2009;18(2):119–128. [https://doi.org/10.1044/1059-0889\(2009/07-0033\)](https://doi.org/10.1044/1059-0889(2009/07-0033)).
11. Kaltenbach JA. Insights on the origins of tinnitus: an overview of recent research. *Hear J*. 2009;62(2):26–29. <https://doi.org/10.1097/01.HJ.0000345991.57291.9b>.
12. Jastreboff PJ. Phantom auditory perception (tinnitus): mechanisms of generation and perception. *Neurosci Res*. 1990;8(4):221–254.
13. Searchfield G. Tinnitus what and where: an ecological framework. *Front Neurol*. 2014;5. <https://doi.org/10.3389/fneur.2014.00271>.
14. Lazarus RS. *Psychological stress in the workplace. Occupational Stress: A Handbook*. 1. 1995; 1995:3–14.
15. Peters ML, Godaert GL, Ballieux RE, et al. Immune responses to experimental stress: effects of mental effort and uncontrollability. *Psychosom Med*. 1999;61(4):513–524.
16. Kreuzer PM, Landgrebe M, Schecklmann M, Staudinger S, Langguth B. Trauma-associated tinnitus: audiological, demographic and clinical characteristics. *PLoS One*. 2012;7(9):e45599.
17. Fagelson MA. The association between tinnitus and posttraumatic stress disorder. *Am J Audiol*. 2007;16(2):107–117.
18. Searchfield GD, Linford T, Durai M. Sound therapy and aural rehabilitation for tinnitus: a person centred therapy framework based on an ecological model of tinnitus. *Disabil Rehabil*. 2018:1–8.
19. McKenna L, Irwin R. Sound therapy for tinnitus—Sacred cow or idol worship?: An investigation of the evidence. *Audiol Med*. 2008;6(1):16–24.
20. Rauschecker JP, Leaver AM, Mühlau M. Tuning out the noise: limbic-auditory interactions in tinnitus. *Neuron*. 2010;66(6):819–826.
21. De Ridder D, Franssen H, Francois O, Snaert S, Kovacs S, Van De Heyning P. Amygdalohippocampal involvement in tinnitus and auditory memory. *Acta Otolaryngol*. 2006;126(sup556):50–53.
22. 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(2):470–480.
23. Goma MAM, Elmagd MHA, Elbadry MM, Kader RMA. Depression, Anxiety and Stress Scale in patients with tinnitus and hearing loss. *Eur Arch Oto-Rhino-Laryngol*. 2014;271(8):2177–2184.
24. Schmitt C, Patak M, Kröner-Herwig B. Stress and the onset of sudden hearing loss. *Int Tinnitus J*. 2000;6:41–49.
25. Sapolsky RM, Romero LM, Munck AU. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocr Rev*. 2000;21(1):55–89. <https://doi.org/10.1210/edrv.21.1.0389>.
26. Değirmenci H, Bakırcı EM, Salcan İ, et al. Determination of correlation among heart rate variability, left atrium global strain, and nighttime blood pressure among patients with tinnitus. *Med Sci Monitor*. 2014;20:1714.
27. Ismaila SO, Odusote A. Noise exposure as a factor in the increase of blood pressure of workers in a sack manufacturing industry. *Beni-Suef Univ J Basic Appl Sci*. 2014;3(2):116–121.
28. Eriksson C, Rosenlund M, Pershagen G, Hilding A, Östenson C-G, Bluhm G. Aircraft noise and incidence of hypertension. *Epidemiology*. 2007;18(6):716–721.
29. Goldstein CM, Josephson R, Xie S, Hughes JW. Current perspectives on the use of meditation to reduce blood pressure. *Int J Hypertens*. 2012;2012.
30. World Health Organization. *A Global Brief on Hypertension, Silent Killer, Global Public Health Crisis*. [Press release]. 2013; 2013.
31. McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med*. 1998;338(3):171–179.
32. Green J, Harris G. Observation of the hypophysiportal vessels of the living rat. *J Physiol*. 1949;108(3):359–361.
33. Shannon IL, Prigmore JR. Parotid fluid as a medium for the determination of human adrenocortical status. *Oral Surg Oral Med Oral Pathol*. 1960;13(7):878–882. [https://doi.org/10.1016/0030-4220\(60\)90019-0](https://doi.org/10.1016/0030-4220(60)90019-0).
34. Aardal E, Holm A-C. Cortisol in saliva-reference ranges and relation to cortisol in serum. *Clin Chem Lab Med*. 1995;33(12):927–932.
35. Hébert S, Lupien SJ. The sound of stress: blunted cortisol reactivity to psychosocial stress in tinnitus sufferers. *Neurosci Lett*. 2007;411(2):138–142.
36. Lightman SL, Conway-Campbell BL. The crucial role of pulsatile activity of the HPA axis for continuous dynamic equilibration. *Nature reviews. Neuroscience*. 2010;11(10):710.
37. Tsigos C, Chrousos GP. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress. *J Psychosom Res*. 2002;53(4):865–871.
38. Simoons VL, Hébert S. Cortisol suppression and hearing thresholds in tinnitus after low-dose dexamethasone challenge. *BMC Ear Nose Throat Disord*. 2012;12(1):4.
39. Kim D-K, Chung D, Bae S, Park K-H, Yeo S, Park S-N. Diagnostic value and clinical significance of stress hormones in patients with tinnitus. *Eur Arch Oto-Rhino-Laryngol*. 2014;271(11):2915–2921.
40. Tyler RS, Aran JM, Dauman R. Recent advances in tinnitus. *Am J Audiol*. 1992;1:36–44.

41. Carhart R, Jerger J. Preferred method for clinical determination of pure-tone thresholds. *J Speech Hear Disord.* 1959.
42. Olufsen MS, Ottesen JT, Tran HT, Ellwein LM, Lipsitz LA, Novak V. Blood pressure and blood flow variation during postural change from sitting to standing: model development and validation. *J Appl Physiol (Bethesda, Md.: 1985).* 2005;99(4):1523. <https://doi.org/10.1152/japplphysiol.00177.2005>.
43. Granger DA, Kivlighan KT, Fortunato C, et al. Integration of salivary biomarkers into developmental and behaviorally-oriented research: Problems and solutions for collecting specimens. *Physiol Behav.* 2007;92(4):583–590. <https://doi.org/10.1016/j.physbeh.2007.05.004>.
44. Linden W, Chambers L. Clinical effectiveness of non-drug treatment for hypertension: a meta-analysis. *Ann Behav Med.* 1994;16(1):35–45.
45. Rainforth MV, Schneider RH, Nidich SI, Gaylord-King C, Salerno JW, Anderson JW. Stress reduction programs in patients with elevated blood pressure: a systematic review and meta-analysis. *Curr Hypertens Rep.* 2007;9(6):520–528.
46. Tank J, Diedrich A, Szczech E, Luft FC, Jordan J. Baroreflex regulation of heart rate and sympathetic vasomotor tone in women and men. *Hypertension.* 2005;45(6):1159–1164.
47. Chandra N, Lee A, Shekhawat GS, Searchfield GD. Psychometric validity, reliability and responsiveness of the Tinnitus Functional Index. *J Acad Audiol.* 2016;29(7):609–625.
48. Tyler R, Ji H, Perreau A, Witt S, Noble W, Coelho C. Development and validation of the tinnitus primary function questionnaire. *Am J Audiol.* 2014;23(3):260–272.
49. Shekhawat GS, Searchfield GD, Stinear CM. The relationship between tinnitus pitch and hearing sensitivity. *Eur Arch Otorhinolaryngol.* 2014;271(1):41–48. <https://doi.org/10.1007/s00405-013-2375-6>.
50. Eggermont JJ, Roberts LE. Tinnitus: animal models and findings in humans. *Cell and Tissue Res.* 2015;361(1):311–336.
51. Tyler R. The psychoacoustical measurement of tinnitus. In: Tyler R, ed. *Tinnitus Handbook.* San Diego, CA, USA: Singular Publishing Group; 2000:149–179.
52. Møller AR. Pathophysiology of tinnitus. *Otolaryngol Clin of North Am.* 2003;36(2):249–266.
53. Møller AR. Anatomy and physiology of the auditory system. In: Møller AR, ed. *Textbook of Tinnitus.* New York: Springer; 2011:51–68.
54. Lovibond SH, Lovibond PF. *Manual for the Depression Anxiety Stress Scales.* Sydney: Psychology Foundation of Australia; 1995.
55. Levenstein S, Prantera C, Varvo V, Scribano ML, Berto E, Luzi C, Andreoli A. Development of the Perceived Stress Questionnaire: a new tool for psychosomatic research. *J Psychosomatic Res.* 1993;37(1):19–32.
56. Betz LT, Mühlberger A, Langguth B, Schecklmann M. Stress reactivity in chronic tinnitus. *Sci Rep.* 2017;7:41521.
57. Aguilera G. The hypothalamic–pituitary–adrenal axis and neuroendocrine responses to stress. In: Fink G, Pfaff DW, Levine J, eds. *Handbook of Neuroendocrinology.* San Diego: Academic Press; 2012:175–196.
58. Everly GS, Lating JM. *The anatomy and physiology of the human stress response. In a Clinical Guide to the Treatment of the Human Stress Response.* 17–51: Springer; 2013.
59. Hellhammer DH, Wüst S, Kudielka BM. Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinology.* 2009;34(2):163–171.
60. Savastano M, Aita M, Barlani F. Psychological, neural, endocrine, and immune study of stress in tinnitus patients: any correlation between psychometric and biochemical measures? *Annals of Otol Rhinol Laryngol.* 2007;116(2):100–106.
61. Meikle MB, Henry JA, Griest SE, Stewart BJ, Abrams HB, McArdle R, Turk DC. The tinnitus functional index: Development of a new clinical measure for chronic, intrusive tinnitus. *Ear and Hearing.* 2012;33(2):153–176.
62. Zigmund AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica.* 1983;67(6):361–370.
63. McKinlay C, Thorstensen E, Cutfield W, Battin M, Dalziel S, Harding J. Effect of Collection Methods on Salivary Cortisol. *J Diagn Tech Biomed Analysis.* 2017;6(2) <https://doi.org/10.4172/2469-5653.1000126>.
64. Searchfield GD, Durai M, Linford T. A state-of-the-art review: Personalization of tinnitus sound therapy. *Front Psychol.* 2017;8:1599.
65. Steelman VM. Intraoperative music therapy: Effects on anxiety, blood pressure. *AORN J.* 1990;52(5):1026–1034.
66. Searchfield G, Kobayashi K, Sanders M. An adaptation level theory of tinnitus audibility. *Front Syst Neurosci.* 2012;6:46.
67. Datzov E, Danev S, Haralanov H, Naidenova V, Sachanska T, Savov A. Tinnitus, heart rate variability, and some biochemical indicators. *Int Tinnitus J.* 1999;5(1):2023.
68. Hall J. *Guyton and Hall Textbook of Medical Physiology E-Book.* 13th ed. Elsevier Health Sciences; 2015.
69. Cleare AJ. The neuroendocrinology of chronic fatigue syndrome. *Endocr Rev.* 2003;24(2):236–252.