Association of Chronic Subjective Tinnitus with Neuro-Cognitive Performance

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Abstract

Introduction: Chronic subjective tinnitus is associated with cognitive disruptions affecting perception, thinking, language, reasoning, problem solving, memory, visual tasks (reading) and attention. Objective: To evaluate existence of any association between tinnitus parameters and neuropsychological performance to explain cognitive processing. Materials and Methods: Study design was prospective, consisting 25 patients with idiopathic chronic subjective tinnitus and gave informed consent before planning their treatment. Neuropsychological profile included (i) performance on verbal information, comprehension, arithmetic and digit span; (ii) non-verbal performance for visual pattern completion analogies; (iii) memory performance for long-term, recent, delayed-recall, immediate-recall, verbal-retention, visual-retention, visual recognition; (iv) reception, interpretation and execution for visual motor gestalt. Correlation between tinnitus onset duration/ loudness perception with neuropsychological profile was assessed by calculating Spearman’s coefficient. Results: Findings suggest that tinnitus may interfere with cognitive processing especially performance on digit span, verbal comprehension, mental balance, attention & concentration, immediate recall, visual recognition and visual-motor gestalt subtests. Negative correlation between neurocognitive tasks with tinnitus loudness and onset duration indicated their association. Positive correlation between tinnitus and visual-motor gestalt performance indicated the brain dysfunction. Conclusion: Tinnitus association with non-auditory processing of verbal, visual and visuo-spatial information suggested neuropsychological changes that need to be targeted in cognitive rehabilitation.

Keywords: loudness, onset, nonauditory, visuomotor, working-memory.
INTRODUCTION

Subjective tinnitus is the phantom auditory sensation\(^1,^2\) in absence of any external or internal physical sound source\(^3\). It is conscious perception due to the multiple, parallel and overlapping brain networks\(^4\). Chronic tinnitus is maladaptive neuronal plasticity and subsequent hyperactivity in primary and secondary auditory pathways, higher-order association areas and parts of the limbic system\(^2,^3,^5,^7\). Tinnitus might be associated with hyperacusis, sound distortion, sleep disturbances and psychological symptoms such as affective disorders, phonophobia, and/or depression\(^2,^5,^8\). It is also associated with cognitive processing affecting perception, attention, thinking, memory, language, reasoning, processing speed, problem solving, and visual tasks (reading)\(^7,^8^\,^11\).

Most of the clinical neuro-psychological studies have been conducted with self-report methodology or rating scale handicap inventories and very few have targeted clinical performance on the cognitive tests\(^9,^12\). The impaired cognitive functioning that has been observed are the concentration problems\(^13,^14\), processing speed\(^9\) and everyday cognitive failures\(^12\). The patient performance worsens on cognitive tests\(^9,^15\) as tinnitus distracts from the task\(^14\). Attentional deficits due to thalamocortical functions were reported by scalp-recorded auditory-evoked responses (P50 potential) but no correlations of sleep disturbance or tinnitus severity with reaction-time\(^16\) have been found. It has been reported that tinnitus and cognition are inseparable\(^7\) as neurobiological model involving (i) brain areas (nucleus accumbens/ limbic/ sympathetic); (ii) modified GABAergic, serotonergic, adrenergic and cholinergic afferents (iii) sensory perception\(^5,^13,^17\), and (iv) heterogenous multimodal processing that affects the patients’ quality of life\(^13,^18\) so should be taken into account in diagnosis and rehabilitation\(^7,^9\). Thus, objective of the present study was to find any association of auditory phantom sensation (subjective tinnitus) with cognitive performance of patients to enhance the knowledge for planning focused, targeted and cost effective management.

METHODS

This was a prospective non-randomized clinical study, that included 25 patients with idiopathic non-pulsatile chronic subjective tinnitus, who were attending out-door patient (OPD) services in the Department of Otorhinolaryngology at the institute. The study was approved by institute’s ethical committee (IEC; histopath/14/2860). Research was conducted in accordance with the Helsinki declaration and each participant was informed the purpose of investigation. Patients had chief complaint of tinnitus and were seeking treatment for it. Inclusion criteria for selection in the study were: patients with consistent idiopathic subjective tinnitus, tinnitus onset since 10 weeks or more (≥ 2.5 months), and those who gave their written consent for the study, before starting their tinnitus management. Onset duration ≥ 2.5 months was considered as chronic tinnitus in concordance with neuro-cognitive studies\(^19,^20\) and chronic pain definition in ICD10. Exclusion criteria were: patients having any external or middle ear pathology, suspected of Meniere’s disease or otosclerosis, having acoustic neuroma or vestibular schwannoma, with history of ototoxicity, sudden hearing loss, ear trauma, noise induced hearing loss, having any systemic disorders, and/or any other organic neurological or psychiatric disease. The patients having any cognitive dysfunction due to tumor, head injury, dementia or taking any medication that could affect cognitive functioning (i.e. drugs inducing drowsiness, confusion or agitation) were also excluded from the study.

Assessments included in the study were: clinical examination, audiological, and neuro-psychological where clinical evaluation was detailed general physical, systemic and otorhinolaryngological examinations done by medical professional. Audiological assessment consisted of pure tone audiometry [PTA- conventional audiometry, high frequency audiometry (HFA), extended high frequency audiometry (EHA)], speech audiometry [speech reception threshold (SRT), speech discrimination score (SDS), most comfortable level (MCL) and uncomfortable level (UCL)], tinnitus matching (pitch, loudness) and residual inhibition (RI) using Madsen Orbiter 922 clinical audiometer.

All the patients were subjected to a detailed evaluation to understand the different domains of neuropsychological functioning that began with subjective scaling (5-point scale) of annoyance and sleep disturbance due to tinnitus. Subjective rating was also done by the patients on hearing handicap inventory (HII)\(^21\) and tinnitus handicap questionnaire (THQ Hindi version)\(^22\). The formal neuro-psychological battery included performance on verbal intellectual capacity or verbal comprehension index\(^23\) assessed with Verbal Adult Intelligence Scale (VAIS\(^24\)), Standardized local version of Wechsler Adult Intelligence Scale, WAIS with test-retest reliability of 0.87 to 0.98. Non-verbal performance (visual reasoning) was evaluated by using Standard Progressive Matrices (Raven’s Standard Progressive Matrices, SPM\(^25\); standardized on local population with age range of 11 to 65 years normative matched according to age and gender\(^26\)). Different aspects of memory were assessed with Post Graduate Institute Memory Scale (PGIMS\(^26,^27\); consisting of ten subtests with local population standardization normative). Perceptual and visual motor functioning involving reception, interpretation (gestalt reorganization or formation) and execution were assessed with Bender Visual Motor Gestalt Test (BVMG, Bender Gestalt Test\(^28,^29\); standardized version on local population). The errors committed in copying the black-and-white drawings were indicative of brain-dysfunction measured by the visuo-spatial working memory and executive control instead of visual memory or imagery\(^30\). The complete neuropsychological battery was administered in 2-3 visits,
Table 1 shows that 48% of the subjects were in the age range of 41 to 45 years, 56% of the subjects were male, and 76% of the subjects had educational status of 10 to 10+ standard. Mean of age was found to be approximately 90 to 120 minutes on each visit because the task completion took longer time in tinnitus patients (slower performance speed) (total time taken 190-270 minutes) as compared to the normative administration time (VAIS- 15 to 20 minutes; SPM- 45 to 60; BVMG- 10 to 15 minutes; PGI memory scale-20 to 25 minutes; total- 90 to 120) of the tests.

Statistical analysis of the data was done using SPSS software (version SPSS.Statistics.17.0), computed the descriptive values of mean and median for central tendency and standard deviation (SD) for variability. Spearman’s correlation coefficient (rho) was calculated between the parameters of tinnitus and neuro-psychological profile. Student-Newman-Keuls test was used to compare the sub-groups of tinnitus ear (right, left, and both) for homogeneity. All significance tests were two-tailed and conducted at or above the 95% significance level.

RESULTS

The 25 patients with consistent tinnitus were included in the study, age ranging 20 to 45 years with mean age of 37.12 years ± SD 8.57 with 56% of male patients and 44% of female patients. The educational status of the patients (76%) was either tenth standard or higher, as shown in Table 1.

Table 1. Demographic Characteristics of Tinnitus Patients in terms of age, gender, and education (N=25).

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Frequency (No. of Subjects)</th>
<th>Percentage (%)</th>
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<tbody>
<tr>
<td>20-25</td>
<td>5</td>
<td>20</td>
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<tr>
<td>26-30</td>
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<td>12</td>
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<td>41-45</td>
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<td>56</td>
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<tr>
<td>Female</td>
<td>11</td>
<td>44</td>
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<tr>
<th>Education (Standard)</th>
<th>Frequency (No. of Subjects)</th>
<th>Percentage (%)</th>
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<tbody>
<tr>
<td>0-5</td>
<td>4</td>
<td>16</td>
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<td>6-9</td>
<td>2</td>
<td>8</td>
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<td>10-10+</td>
<td>19</td>
<td>76</td>
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Table 1 shows that 48% of the subjects were in the age range of 41 to 45 years, 56% of the subjects were male, and 76% of the subjects had educational status of 10 to 10+ standard. Mean of age was found to be 37.12 years ± SD 8.57.

On high frequency audiometry (average of 4000, 8000 & 10000 Hz) patients had moderate hearing loss (mean 50.28 ± 27.52 SD, 41.84 ± 25.16 for right and left ear respectively), and on extended high frequency (average of 12000, 14000 & 16000 Hz) had moderate to severe hearing loss (mean 57.69 ± 16.96 SD, 55.65 dB ± 21.66 SD for right and left ear respectively). The speech reception threshold (SRT) for both the ears was either < 28 dBHL (72% of the patients) or 28 dBHL to 35 dBHL (26% of the patients) and good speech discrimination score (SDS) i.e. > 80% for both the ears and almost all the patients (96%). The uncomfortable level of auditory stimulus (UCL) testing showed UCL was ≥ 90 dBHL in both the ears and all the patients (100%). None of the patients reported hyperacusis and/or phonophobia predominance. Mean subjective reporting by the patients was ‘no handicap’ (Mean 6.43 ± 7.95 SD) on hearing handicap inventory. Most (76%) of the patients reported ‘no handicap’ (i.e. 0-8 raw score on HHI), 24% of them scored as ‘mild-moderate handicap’ (10-24 raw score) and none of them subjectively reported ‘severe hearing handicap’. Neuro-psychological assessment

The mean score of patient’s self-reporting on tinnitus handicap questionnaire (THI) was 28.00 ± 5.55 SD where total score reflects the sum of all responses, averaged to give a global score out of 100 and higher.
scores indicate higher levels of tinnitus handicap. Frequency of global scores was: 'no handicap' (0-15% global score) observed in 4% (one) of the patient, ‘mild handicap’ (16-40% global score) in 88% whereas 8% (two) of the patients rated their tinnitus as ‘moderate handicap’ (45% global score) and none of the patients reported higher to moderate handicap (> 45% global score) on THQ. The level of annoyance was subjectively rated by the tinnitus patients on 5-point scale as 0 = no annoyance, 1 = little annoyance, 2 = average annoyance, 3 = high-annoyance, and 4 = intolerable. All the patients reported level of annoyance as average or more than average i.e. ≥ 2. The sleep disturbance due to tinnitus was rated on 5-point scale as 0 = never affected, 1 = rarely affected, 2 = sometimes affected, 3 = mostly affected, 4 = always affected. Twenty-two patients reported sleep disturbance as rarely affected due to tinnitus, two of the patients reported as sometimes (since < 6 weeks) and one as mostly affected (since 2 weeks).

The formal tests were carried in comfortable and least distraction conditions for the patients to minimize the external interferences. The patients with hearing loss used hearing aid during neuro-psychological assessments.

**Verbal performance (Verbal Adult Intelligence Scale, VAIS)**

Performance of the tinnitus patients on VAIS was scored as raw scores, which was converted to test quotient (TQ) value given by Indian standards matching the subject’s age, gender and education. The mean information TQ of patients was 99.84 ± 22.62 SD; mean TQ of the patients for digit span was 86.64 ± 11.50 SD; mean arithmetic TQ was 92.20 ± 17.41 SD; mean comprehension TQ 97.80 ± 19.25 SD; and VAIS average TQ of the patients was 94.12 ± 13.84 SD. The occurrence of low performance was the number of patients who performed poorer (< 90). 60% of the patients had low TQ for digit span subtest and 40% performed poorly on comprehension task (Table 2a). The total time taken (20-30 minutes; mean 26 ± 7.24) by the tinnitus patients was longer (longer reaction time) than normative administration time of the test (15 minutes).

**Non-verbal performance (Standard Progressive Matrices, SPM)**

The test is designed to provide a reliable estimate of person’s capacity for observation and clear thinking to grasp the visual-spatial recognition, form comparison and reasoning analogy for completing the missing pattern (Raven 1958). The performance of tinnitus patients as mean and SD were 91.68 ± 8.46 SD indicating normal performance on SPM. In Table 2a, the number of patients was classified according to their score on SPM. Most of the patients scored in normal range (≥ 90). The low performance was categorized to be scored as < 90 on SPM and 36% of the patients performed poorly (< 90 score).

**Post Graduate Institute Memory Scale (PGIMS)**

The mean memory performance in tinnitus patients was: (i) remote memory (subtest I) as 5.44 ± 0.65 SD, (ii) recent memory 4.80 ± 0.65 SD, (iii) mental balance 5.96 ± 2.42 SD, and (iv) attention & concentration 8.56 ± 2.14 SD, (v) delayed recall was 8.56 ± 1.36 SD, (vi) immediate recall 7.08 ± 1.44 SD, (vii) retention of similar pairs 4.24 ± 1.16 SD, (viii) retention of dissimilar pairs 9.52 ± 4.46 SD, (ix) visual retention 9.48 ± 2.55 SD, and (x) mean of visual recognition was 8.62 ± 1.32 SD. The low performance on PGI memory scale has been summarized in Table 2b.
more than 40% of the patients had performance lower than 50th percentile for subtests remote memory (44%); mental balance (72%); attention & concentration (52%); immediate recall (68%); retention of dissimilar pairs (44%); and on visual recognition (40%).

**Bender Visual-Motor Gestalt Test (BVMGT)**

The signs or errors observed were distortion (in 24% of the patients), perseverations (inter- or intra-perseverations in 24%), rotation of design (in 28%), macro-designs observed (in 20% of the tinnitus patients), along with other signs like closure, point of contact, added angles, reduction of angles, micro-designs, embellishment etc. on BVMGT. The mean raw score of the tinnitus patients was 8.20 ± 3.33 SD, with dysfunction rate of 2.12 ± 0.78 SD, indicating moderate level of brain-dysfunction of tinnitus patients. The occurrence of brain-dysfunction is summarized in Table 2c indicating majority (64%) of the tinnitus patients’ performance was affected to moderate level.

**Correlation of onset duration and neuro-psychological profile & correlation of loudness and neuro-psychological profile of tinnitus patients**

The correlation of duration and loudness with Subtests of PGI memory scale were not statistically significant, thus values are not presented here. Table 3 shows values of correlation coefficient (rs) between subtests of verbal scale (VAIS) with duration and loudness. Negative correlation of duration with subtest digit-span (r = 0.414, p < 0.05) and arithmetic (r = 0.433, p < 0.05), suggest that as the tinnitus duration increases the attention, working memory, arithmetic ability and reasoning deteriorates. Similarly, negative correlation of loudness and verbal information processing (r = 0.424, p < 0.05) suggest its association with poor performance.

Correlation between duration & loudness perception of tinnitus with non-verbal (visual) processing are shown in Table 3. It was found that duration had statistically significant (r = 0.532; p<0.01) negative correlation with non-verbal patient performance (on SPM), indicating that the longer tinnitus duration is associated with decreased non-verbal stimulus processing. Majority of the patients (76%) completed the task in one session but the time taken was longer (more than 50 minutes; mean 54 ± 8.65) as compared to normative administration time of test and rest of the 24% (6) subjects were not willing to finish the test in one session as they were unable to concentrate on the patterns, so rest of the test was completed in next session (these patients were not same as 36% who scored < 90, mentioned in non-verbal performance).

Table 3 also shows that duration had statistically significant positive correlation (r = 0.490; p < 0.05) with performance of subjects on BVMGT, suggesting that increase in duration of tinnitus is associated with the poor visual-motor gestalt skills of the patient.

**Correlation of subjective rating of tinnitus-handicap and hearing-handicap with neuro-psychological profile**

It was observed that patient’s self-rating on tinnitus handicap questionnaire (THQ) was positively correlated (r = 0.451; p < 0.05) with brain-dysfunction based on visual motor gestalt performance (BVMG scores). No significant correlation was observed between self-hearing handicap rating and any of the neuropsychological performance.

### DISCUSSION

Neuropsychological investigation for subjective tinnitus is an accessible approach towards highly complex neurobiological process. Impact of tinnitus on quality of life is better defined by identifying cognitive impairments thus essential for optimal rehabilitation. Non-auditory cortical regions (nucleus accumbens, hippocampus and limbic system) are believed to be key sites for neuroplastic habituation and normal auditory analysis. Assessments of attention, working memory, symbolic (verbal) processing, visual perception, visuospatial judgment, problem solving, and processing speed are important aspects in neuropsychological battery. The results of the present study on these cognitive tasks suggest that tinnitus interferes with the nonauditory processing, as the patients performed poorly on digit span, verbal comprehension, mental balance, attention & concentration, immediate recall, visual recognition and visual-motor gestalt subtests. The correlation between different cognitive performances with tinnitus loudness and onset duration, indicated their association as hypothesized in other studies.

The study involved a sample of 25 patients; the
highest numbers (48%) of the patients were in age group of 41 to 45 years that is in concordance with tinnitus prevalence in earlier studies. The majority of the patients matched their tinnitus loudness above 30 dBHL in contralateral ear by hearing level units (HL) before defining the minimum masking level in ipsilateral ear by sensation level units (SL) for treatment plan. The level of annoyance reported by all the patients was an average or more than an average (≥ 2 on self-rating scale). This level of annoyance was responsible for bringing them to super-speciality hospital for the treatment. Normal speech reception threshold (less than, equal to 25 dBHL) and speech discrimination score (more than 80%) was found in all of the patients (96% or 24 subjects) in both ears. The patients with hearing loss used hearing aid during the assessments. Hence, it was ensured that verbal assessments for neuro-psychological profile were not affected due to poor audibility of the stimuli. Majority of participants (76%) in the present study had educational status of 10th or higher than 10th Standard (≥ 10th Std.). The knowledge regarding educational status was integral as the norms of neuro-psychological battery had been standardized according to age, gender and education.

Performance on VAIS was included to evaluate the verbal symbolic processing and 40% of patients scored poorly (< 90 Test Quotient) on comprehension task. In present study 60% of the tinnitus patients performed below 50th percentile on digit-span. This might be due to interference and/or inability to shift attention from tinnitus leading to cognitive inefficiency. Observed negative correlation of onset-duration and loudness with performance on VAIS shows that longer the duration, poorer the performance similarly greater the tinnitus loudness poorer the performance, especially for information subtest. This association indicates that the subjective tinnitus loudness and/or duration might have influenced cortical modifications, also associated with deviated functional connectivity between frontal-temporal-occipital cortices in the tinnitus group.

Visuo-perceptual and visuo-spatial judgments were assessed with non-verbal subtest (non-verbal intelligence scale, SPM) and the performance was observed poorer as the duration of tinnitus increased; similarly the performance deteriorated when loudness increased but was not statistically significant, although all the subjects reported level of tinnitus annoyance as an average or more than an average. Andersson and McKenna reported that tinnitus had an interfering effect on cognitive functions, observed in those subjects who attend to the tinnitus (Andersson and McKenna, 2006), association of non-verbal performance with the duration further in present study emphasize the non-auditory areas modification. It was also suggested by fronto-occipital cortical areas (functional) connectivity in the tinnitus patients. The performance of the tinnitus patients on memory test (PGIMS) was affected on subtests: mental balance (72% patients), attention & concentration (52%), immediate recall (68%), remote memory (44%), retention of dissimilar pairs (44%) and visual recognition of pictures (40%). The performance might be altered due to deviated attention for auditory and nonauditory sensory processing, poor working memory, word recall, plan execution, remote memory or/and autobiographical memory. It can be hypothesized that in tinnitus patients due the reduction of gray matter in the ventromedial prefrontal cortex that participates in auditory gating there is disruption in the processing of information and working memory system, the attention is focused to tinnitus leading to cognitive inefficiency.

Visual sensory motor skills were evaluated with visual-motor gestalt task where most of the tinnitus patients (92%) showed dysfunction on BVMG (moderate level in 64% and severe level in 28% of the patients). Although the test targets the visual-motor perception but the performance was linked with auditory phantom sensation (tinnitus) as observed with positive correlation, the different signs or errors observed indicated the greater probability of organic changes at cortical level. The visuo-spatial planning time and execution is processed in right prefrontal cortex and bilateral dorsolateral prefrontal cortex, the areas also responsible for auditory and linguistic working memory or recall. It is also reported that there is higher activity in right frontal and cingulate (limbic system) in tinnitus patients responsible for processing emotions, attention and executive functions. On BVMG the performance was poorer with increase in tinnitus onset duration (Correlation coefficient 0.490, p < 0.05) leading to moderate level dysfunction rate (dysfunction rate ≥ 2). It indicates that tinnitus chronicity was associated with poor performance that might be due to changes in supplementary motor area (BA6), dorsal anterior cingulate (BA24 and BA32), insula (BA13), auditory cortex (BA21 and BA22), hippocampus and parahippocampus resulting in modified global visual workspace. The positive correlation of tinnitus handicap with BVMG scores in present study further suggest that patients’ perceived tinnitus impact was associated with visual-motor executive ability. Non-concordance with previous study findings might be due to difference in cognitive tasks.

Tinnitus interferes with attentional orientation and executive control leading to longer processing time (slower processing speed). Similar was observed in present study that tinnitus patients took longer time to complete the task for all the subtests as compared to normative administration time.

Despite our best efforts and sound methodology, the study had limitations which should be considered while interpreting the results. The time bound nature limited the sample size and comparison of results with clinical normative data rather than control (non-tinnitus) group profile. Inclusion of functional neuro-imaging like functional magnetic resonance imaging (fMRI) would
have added to the validity of the changes due to tinnitus. Correlation between time taken for task performance and tinnitus duration or loudness would have further elaborated on processing speed. The study had been limited to the subjects of 16 to 45 years age range, to exclude the possibility of hearing or cognitive changes due to ageing although the prevalence of tinnitus increases with age.

### CONCLUSION

Performance of verbal and non-verbal tests indicates that subjective tinnitus was associated with modified neuro-cognitive processing. In majority of the tinnitus patients, performance was poor (i.e. < 50th percentile) on mental balance, attention & concentration and immediate recall subtests of PGI-memory scale, suggesting that tinnitus interferes with not just auditory decoding but also encoding and accessing stored information. Most of the tinnitus patients (92%) showed moderate or severe brain dysfunction on Bender visual-motor gestalt test that may attribute organic changes at cortical level. Tinnitus chronicity is also associated with modified coordinated functioning of auditory, visual and visuo-spatial information as observed from negative correlation with digit span, arithmetic and non-verbal performance, also positive correlation with Bender visual-motor gestalt (BVMG) test suggesting modification in cortical areas.

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### Conflict of interest

None

### ICMJE-Recommendations

ICMJE recommendations had been carefully read and followed during the study as well as manuscript writing.

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