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Smartphone Usage and Its Influence On Brainstem Auditory Evoked Potentials in Young Adult Population: A Systematic Review

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ABSTRACT

Background: Smartphones are radiotransmitters that emit electromagnetic radiation. The increase in mobile phone usage in the modern era could lead to various health problems. The human auditory system lies close to the source of radiation and is hence at greater risk of absorbing a relatively more significant amount of radiation. The brainstem auditory evoked responses (BERA), being a non-invasive tool allows quantification of the activity and functions of the auditory system. **Materials and methods:** The systematic review was conducted using the scientific information published from January 2002 to June 2022 using the keywords "smartphone", "auditory evoked potentials" and "adult population" in different databases to find relevant articles. The review was conducted in adherence to the PRISMA statement. Out of 977 articles screened, 8 articles were selected for review. **Results:** Out of the 8 studies considered for review, 5 showed that BERA was significantly altered in subjects with prolonged mobile phone usage. In the rest of the studies, though statistically significant results were not produced, latency was prolonged and amplitude was decreased in study groups with prolonged mobile phone usage. **Conclusion:** Young adults are prone to developing auditory disturbances as they are exposed to the maximum amount of electromagnetic radiation owing to the longer duration of mobile phone usage. Our study concludes that prolonged mobile phone usage has negative consequences on the auditory functions quantified using BERA.

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Keywords: *Adult population, Brain stem auditory evoked potential (BERA), Electromagnetic field (EMF), Smartphone.*

INTRODUCTION

Mobile phones are widely used throughout the world. For the past few decades, mobile technologies and services have been benefiting the world by helping with economic growth[1] and also improving social bonding in a busy world. The increase in mobile phone usage in the modern era has led to various concerns related to its effects on human health. The benefits of a mobile phone are numerous. But at the same time, these devices function as radiotransmitters that emit electromagnetic radiation that might cause health problems. The microwave radiation from mobile phones oscillates between frequencies of 900 MHz and 1,800 MHz, which causes some organic molecules and water molecules to rotate [1].

The WHO report claims that smartphones could be used by 55% of the total population by 2023, growing from 610.9 million in 2018 at a rate of 5% compounded annually. Currently, there are 929.37 million mobile phone users in India, compared to 31.53 million fixed-line subscribers. Internet and mobile usage in India is all set to cross the 1 billion mark by 2023, with nearly two-thirds of the population estimated to have internet access and a mobile device [2]. The increasing usage and dependability of mobile phones have undoubtedly become the most impactful innovations of this time. Indian mobile users speak for 330 minutes per month on average, or 11 minutes per day [3]. This is on par with most of the averages in other countries.

Though rapid use of modern telecommunication is useful in the time of emergency, mobile phone users have been suffering from a lot of possible adverse health effects.Due to the widespread usage of mobile phones, concerns have been raised about the electromagnetic waves these devices produce, which could harm the human auditory system. The human auditory system lies close to the source of radiation. Hence, the tissues are at greater risk of absorbing a relatively more significant amount of radiation. Negative health effects from electromagnetic field (EMF) radiation may include headache, sleep issues, memory loss, inability to focus, dizziness, an increase in the frequency of seizures in children with epilepsy, brain tumours, and high blood pressure [4].

Mobile phones are typically held close to the ear while being used, which raises the brain's specific absorption rate (SAR) of EMFs, which could impact the auditory system. Though the SAR levels are being monitored and controlled in an optimum range, there is a concern as to whether or not chronic exposure to this radiation on a day-to-day basis affects the auditory system in the long run. Early adopters have reported of health issues like fatigue, headache, cognitive dysfunction and stress [5]. Reduced finger muscle strength can occur in those subjects who send short message service (SMS) frequently. In today's hectic environment, headphones for listening to music to unwind have become common. The body of the recipient absorbs invisible ionised electromagnetic radiation (EMR) from telecommunications networks, which modifies the electrical activity of the brain, causes earburn or heat sensations, alters the blood-brain barrier, and reduces cerebral blood flow in the affected area [6,7]. Long-term mobile phone use causes damage to the cochlea, including the auditory cortex [8].

The brainstem auditory evoked responses (BERA) may allow quantification of the auditory organ's activity and functions, including the auditory nerve and sub-cortical centes. These potentials were captured from the ear and vertex in response to brief auditory stimulation to determine how well conduction travelled along the auditory pathway all the way to the midbrain [9]. In response to transient sound stimulation, the neurological system produces electrical potentials known as BERA. The primary auditory cortex up to the thalamic medial geniculate body is tested for structural integrity. The source of these activities is the summation of the action potentials generated by the afferent tracts and the electrical fields or activities of the synaptic discharges or post-synaptic potentials on those tracts [9].

The recording of BERA is a noninvasive technique. The resulting waveform shows voltage (amplitude) as a function of time (latency). The components are labeled according to their sequence by polarity. The latency studies the conduction velocity of nerve impulses, and the amplitude studies the number of nerve cells that are stimulated [10].

Since dependency on the mobile phone is growing at an alarming pace due to the COVID-19 pandemic and the present situation of multiple lockdown of long duration. Biological effects resulting from exposure to electromagnetic waves (EMW) emitted from MP have also been demonstrated in various research studies focusing on the aspects of brain physiology and the auditory system affected by exposure to EMW by causing damage to nerves around the ears and also to the blood-brain barrier (BBB). As stated above, though various research studies have been done to study the effects of mobile phone radiation exposure on the auditory system, variable results have been obtained regarding the subjective and objective effects of exposure to this radiation. Hence, this systematic review focused on the effects of mobile phone electromagnetic radiation on the auditory system, spotlighting the brain stem auditory evoked potential.

MATERIALS AND METHODS

Study design and setting

This review was conducted in adherence to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement [20].The present systematic review was conducted using the scientific information published from January 2002 to June 2022 and aimed at collecting information on changes in brainstem auditory evoked potential in the young population with prolonged smartphone usage. To that end, the keywords "smartphone", "auditory evoked potentials" and "adult population" were searched in different databases to find relevant articles. The PRISMA statement [20] was used to report 977 articles, which were found on the Web of Science (54), Scopus (4), PubMed (6) and Google Scholar (913). Searching for resources was done electronically in the above-mentioned scientific databases. Based on the preliminary investigations, all the articles relevant to the present work were extracted.

Information sources and search

The search strategy was defined by merging the keywords “smartphone”, “auditory evoked potentials” and “adult population” using the operators AND (between word groups) and OR (within each word group). A manual search was also applied to find other reports and documents.

Search strategy

The researchers searched all the articles under Medical Subject Headings (MeSH). The following keywords and terms were accordingly searched. The operators (AND and OR) were used in a database.

Search concepts and keywords in the PubMed database

((("smartphone"[MeSH Terms] OR "smartphone"[All Fields] OR ("smart"[All Fields] AND "phone"[All Fields]) OR "smart phone"[All Fields] OR ("cell phone"[MeSH Terms] OR ("cell"[All Fields] AND "phone"[All Fields]) OR "cell phone"[All Fields])) AND ("evoked potentials, auditory, brain stem"[MeSH Terms] OR ("evoked"[All Fields] AND "potentials"[All Fields] AND "auditory"[All Fields] AND "brain"[All Fields] AND "stem"[All Fields]) OR "brain stem auditory evoked potentials"[All Fields] OR ("brainstem"[All Fields] AND "auditory"[All Fields] AND "evoked"[All Fields] AND "potential"[All Fields]) OR "brainstem auditory evoked potential"[All Fields])) OR ("evoked potentials, auditory"[MeSH Terms] OR ("evoked"[All Fields] AND "potentials"[All Fields] AND "auditory"[All Fields]) OR "auditory evoked potentials"[All Fields] OR ("auditory"[All Fields] AND "evoked"[All Fields] AND "potential"[All Fields]) OR "auditory evoked potential"[All Fields])) AND ((y_10[Filter]) AND (ffrft[Filter]))

Selection of studies

Three investigators independently selected and reviewed fair and good-quality studies. The search for keywords in various databases yielded a total of 977 documents. Using manual methods, duplicates were removed, and 689 documents remained after eliminating 288 duplicate studies. Following this, the title and abstract were studied to identify documents that were eligible to be included in the study.80 articles were selected in the process of title/abstract screening. The next step was to carefully study the full text of the articles to determine their relevance to the purpose of the research, and in this process, 72 articles were removed. Finally, 8 articles were included in this study (Figure 1).

Inclusion and exclusion criteria

Articles published between January 2002 and June 2022 in the English language, describing the effects produced due to prolonged mobile phone usage on brainstem auditory evoked potential in the adult population were included in the study. Narrative reviews, meta-analysis, case reports, grey literature (conference paper), and animal studies were excluded. If the subjects of the study were less than 18 years of age, more than 60 years of age and/or if they suffered from chronic disorders,

metabolic conditions, or co-morbidities, those studies were excluded. If merely the effect of mobile phone usage on auditory function was studied without measuring auditory evoked potential, those studies were excluded. Studies that are not accessible in full text were excluded from the present study.

Extracting the data

The articles were reviewed by five researchers independently. The title and abstract were initially reviewed, taking into consideration the inclusion and exclusion criteria. After the title/abstract screening process, full-text articles were reviewed by the investigators. If the articles were rejected in this review process, the reason was mentioned, and in the case of disagreement between the investigators, these studies were judged by an expert. Data extraction was performed using a checklist.

Quality assessment of articles

Two reviewers assessed the methodological quality of the selected studies. The Agency for Healthcare Research and Quality Methods Reference Guide for Effectiveness and Comparative Effectiveness Reviews was used to perform quality assessments of the studies. The criteria include information on the sampling method, outcome measurement, intervention, and reporting of biases and limitations. A summary of these criteria is presented in Table 1.

RESULTS

Out of 977 studies that were reviewed, 8 articles were recognized as eligible and thus analyzed. The results of the studies are summarized in Table 2. Out of the 8 studies considered for review, 5 showed that BERA was significantly altered in subjects with prolonged mobile phone usage. In the rest of the studies, though statistically significant results were not produced, latency was prolonged and amplitude was decreased in study groups with prolonged mobile phone usage

DISCUSSION

Mobile phones are becoming more and more common and practically essential in contemporary life. It is among the modern era's technological advancements with the quickest rate of growth. The public's worry over the potential health consequences of electromagnetic field (EMF) exposure from mobile phones is growing, though.The organic tissues will absorb radio frequency electromagnetic radiation from mobile phone antennas and turn it into heat.High quantities of EMF radiation will be deposited in the user's ear as a result of a mobile phone antenna being close to the ear [1].

Brainstem auditory evoked potential (BERA) constitutes an objective hearing test. These potentials were captured from the scalp and ear after a brief auditory stimulus. The evoked potentials that appear following the transduction of acoustic stimulus by the hair cells create an electrical signal that is carried through the auditory pathway to the brainstem and from there to the cerebral cortex.

When the signal travels, it generates action potential in all the fibers. These action potentials can be recorded at several points along the auditory pathway and even from the surface of the body. BERA assesses the conduction of the impulse through the auditory pathway upto the midbrain [11].

The changes in the brainstem auditory evoked potentials have been correlated with diseases at different levels of the auditory pathway. BERA is usually helpful in localizing the lesions in the brainstem. It is useful in diagnosing various diseases affecting the brainstem [12]. Numerous studies have investigated the electrophysiological effects of EMF due to mobile phone usage on auditory brainstem evoked responses (ABR). But there are disparities inthe results published among those studies. Hence, our systematic review focused on the studies concerning mobile phone radiation and listed out the findings, including the controversial results as well.

A study carried out by Bortkiewicz in 2001 [13] demonstrated that headaches, weariness, overall bad health, muscular pains, and nausea are among the most common complaints among mobile phone users. There could be a number of biological impacts caused by the electromagnetic field (EMF) of microwave frequencies as well as the frequency emitted by mobile phones. The investigation involved exposing the head to the EMFs produced by a GSM mobile phone for 15 minutes while tracking the delay in the fifth wave's latency.

The extent of harmful biological consequences from mobile phone microwave radiation relies on a variety of factors, including the length of exposure, individual immunological and central nervous system traits, and other factors like the rate of EMF energy absorption and distribution of EMF energy by different tissues of the body [14,15].

Chandra Selvi et al., in 2014 [16] concluded that longer-term mobile phone users (17-29 yrs) may experience aberrant conduction at various levels of the auditory pathway, as well as difficulties paying attention, cognition, and engaging in intellectual activity.

Conversely, a study done by Aria et al., in 2003 [17] discovered no impacts from a 30-minute mobile phone radiation exposure on ABR (I, II, and III) waves. Also, the studies of Oysu et al., 2005 and Sievert et al., 2005 [18,19] suggest that exposure to mobile phone microwaves has no influence on the activity of cochlear outer hair cells or of cochlear nerve electrical conduction, both in vivo and in vitro. These uncertain findings need future studies to better understand the effect of mobile phone electromagnetic radiation on the auditory systems. Any adverse effect that may eventually be found should be promptly reported; it is a health issue of interest to billions of users worldwide. As they are most exposed to EMRs, the younger population is more vulnerable to earlier otological problems. Both physiological and psychological behaviours could be improved by avoiding mobile phones for a longer duration, as young adults are the stepping stones of the future. Therefore, since this technology has become an integral part of human life and the uncertain findings from our review imply future studies for the exposure of the probable harmful effects on the auditory system by mobile phone electromagnetic radiation.

Limitations and Recommendations

One of the limitations of the present study was the limited scope of search and the lack of an adequate number of studies conducted in this field. Out of the 8 studies considered for review, 5 studies have shown a significant association between prolonged mobile phone usage and BERA

parameters. In the rest of the studies, though statistically significant results were not produced, latency was prolonged and amplitude was decreased in study groups with prolonged mobile phone usage. Hence, to validate the results further, several studies should be conducted in this regard.

CONCLUSION

Young adults are prone to developing auditory disturbances as they are exposed to the maximum amount of electromagnetic radiation owing to the longer duration of mobile phone usage. Our study concludes that prolonged mobile phone usage has negative consequences for the auditory functions quantified using BERA.

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Conflicts of interest: There are no conflicts of interest

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FIGURES:

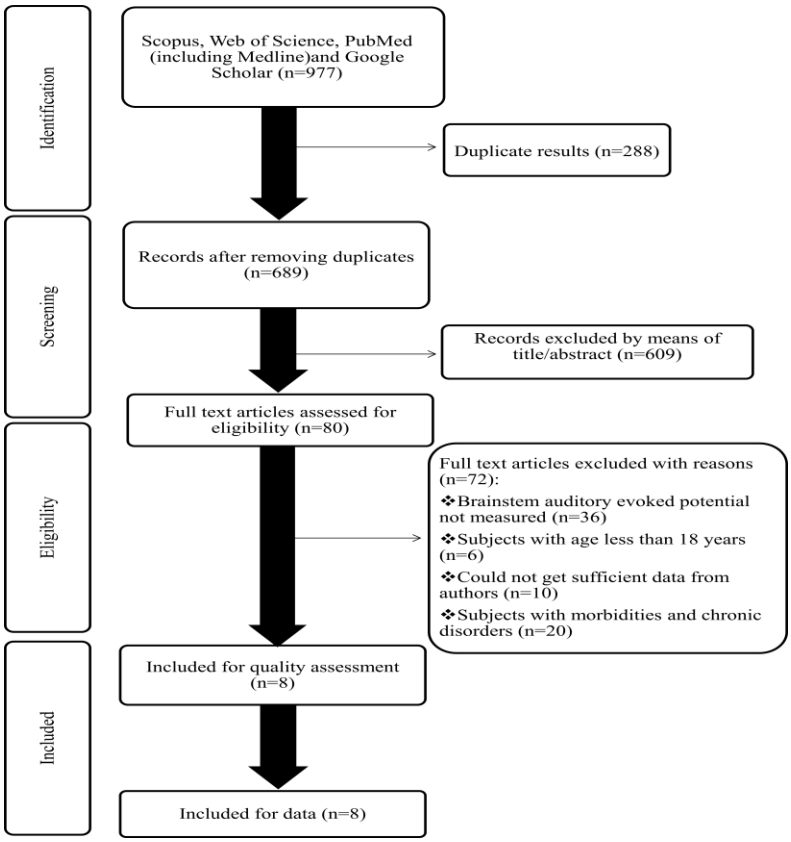

Figure 1: Flow diagram of the final article selection process

TABLES:

Table 1: Titles and specifications of articles included in the study for the final review

Source & study design	Methods	Participants	Assessment
Gupta N et al [21] Cross-sectional study	Depending on how often they used their mobile phones, the subjects were split into two groups. Subjects in Group A had used their cell phones for more than a year. Subjects in Group B were those who had never used a mobile	100 normal healthy volunteers (69 women and 31 men) between the ages of 18 and 30 years with no clinical evidence of hearing disorder.	In order to determine the effects of electromagnetic exposure, changes in both participants' ears were observed in both groups and tested for auditory brainstem evoked responses (ABR).

	phone.		
Selvi EC et al [16] Cross-sectional study	Subjects were dividedintothree groups based on age as follows: Group I (17-19yrs), Group II (20-29 yrs) and Group III (30-39yrs).	173 healthy Mobile phone users formore than 3 years, aged around 17-39 yrs (both sexes), were included. Group I (n-60), II (n-70), and III (n-43). **Exclusion criteria:**subjects with otological diseases, family/own history of diabetes mellitus, hypertension, familial hearing disorder, exposure tosevere noise, or consumption of alcohol or drugs 24 hours before testing.	The respondent completed the questionnaire to provide a thorough history of their usage of mobile phones, including the model of their phone for frequency variation and how long they had been using it (in hours, days, and years). Conduction deafness: auditory brainstem responses in both ears were assessed.
Priya AJ et al [22] Cross-sectional study	Middle latency auditory-evoked potential(MLAEP) recordings were performed on 20 short- and long-term mobile users, defined as less than and more than 1 year of mobile phone usage,respectively. Further, the group was categorized based on the duration of usage per day.	40 subjects were included in the study in the age group between 18 and 30 years. Twenty individuals had a history of mobile phone usage for more than 1 year (long-term users) and twenty individuals had a history of mobile phone usage for <1 year (short-term users). Further, the forty individuals were divided into two other groups based on the duration of mobile phone usage per day: Group A: <60 min usage/day (29 individuals) and Group B: >60 min usage/day (11 individuals). **Inclusion criteria:** Healthy with normal hearing, and no history of ear disease. GSM (global system for mobile communication) mobile phones with SAR <2 W/kg. **Exclusion criteria1**: Head/ear trauma, occupational noise exposure, familial history of hearing loss, history of any underlying condition affecting neurological system, tobacco chewing, chronic alcoholism, or cigarette smoking, consumption of ototoxic drugs or any affecting nervous system, and history of any ear surgery, radiotherapy, or chemotherapy.	History of mobile phone usage was obtained, regarding the years of usage, the duration of attending calls each day, the preferred ear while attending a mobile phone call, the mobile phone model, the years since the purchase of the current mobile, and the frequency of changing mobile phones. An ear, nose, and throat specialist used otoscopy and tuning fork tests to examine the ear. Audiometry was done to rule out conductive hearing loss. The peak latencies of the Na, Pa, and Nb components of MLAEP were recorded using the Galileo NT machine using silver disc surface electrodes which were placed according to the 10–20 International System of Electrode Placement.
Sharma G et al [10] Cross-sectional study	Subjects were grouped into non-user participants (not currently usingmobile phones OR only seldom	**Inclusion criteria:**30 non-user participants and 60 user participants of the age group of 18-40 years. **Exclusion criteria:** Subjects with	The information regarding the use of hands-free devices, duration ofuse and exposure time per

	using mobile phones, i.e., less than 10min per day for less than one year) and user participants (who use mobile phones for more than 1 hour for more than 2years). User participants were further sub-divided into Group A (which uses mobilephones for more than 1 hour for more than 2 years but less than 5 years) and Group B (who uses mobile phones formore than 1 hour and more than 5 years).	diabetes, hypertension, and psychiatric disorders. History of otalgia, discharging ear, ear surgery. Subjects diagnosed with head and neck tumour or any other known otological conditions and prolonged usage of ototoxic drugs.	day, use of which ear predominantly (leftear or right ear), and medical and/or otological morbidities were recorded. The duration for which the hands-free set was used was deductedfrom the total duration of usage. Eligiblesubjects fulfilling theinclusion criteria were then subjected to BERA using the Neuroperfect apparatus byMedicaid India (Chandigarh). Latencies of waves I, III, V and inter-peak latency of I-V were recorded in users andnon-users.
MaghbooliM et al [23] Cross-sectional study	A random consecutive sampling method was used to recruit participants. Subjects were divided into three groups as low (less than 30 minutes), moderate (30-60 minutes), and high (greater than 60 minutes) based on mobile phone usage per day. According to the years of use, the participants were divided into three groups: under 6 years, 7-9 years, and more than 10 years.	96 subjects **Inclusion criteria:** people in the age range of 18 – 45 years who were able to participate in hearing tests in terms of awareness level. **Exclusion criteria:**Tele communications antennas near home or workplace, typical use of hands-free during calls (in over 20% of calls), hearing disorders in first-degree family members, history of severe head trauma, prolonged loss of consciousness, ear surgery, ear drainage, long-term exposure to loud noises or sudden contact with a loud noise, ototoxic drug usage within the last month, meniere, anemia, diabetes mellitus, multiple sclerosis (MS), cerebrovascular accident (CVA), and transient ischemic attack (TIA), hyperthyroidism or hypothyroidism, history of barotraumas, inflammation or accumulation of fluid behind the eardrum, the presence of wax, torn eardrum, and proved hearing loss after PTA test. In terms of the average daily use of	The subjects were evaluated for demographic information, average daily use of mobile phones, the total duration of use in years, the dominant ear of use, and neural and auditory complaints. Subsequently, auditory brainstem evoked responses (ABR) were conducted.

		mobile phones, 96 participants in the study were divided into three groups (32 users in each): low (less than 30 minutes), moderate (30-60 minutes), and high (greater than 60 minutes). Moreover, in another classification according to the years of use, the participants were divided into three groups: under 6 years, 7-9 years, and more than 10 years.	
Kothari R et al [24] Cross-sectional study	In the test group, subjects were split into two groups based on how long they used their mobile devices. (who utilized mobile devices for >30 min/day for theduration of 1 year) and control group (who utilized mobile devices for <30 min/day for theduration of 1 year).	The study population consisted of 50 subjects (age >18years) categorized into test and control groups with 25 subjects each. **Inclusion criteria:** Hearing-normal controls with no history of hearing loss or ear conditions in the past or present. Regular mobile phone users using the Global System for Mobile (GSM) mobile phones for >1 year. **Exclusion criteria:** Ear discharge and hearing loss following ear surgery, prolonged loud noise exposure, using an ototoxic medication and suffering a brain injury, hereditary hearing impairment or deafness, brain injury, hypertension, or diabetes mellitus, People who refused to participate in the study were not included	General physical examination, audiological examination, and history by a consultant otolaryngologist to rule out diseases. BERA was performed by RMS EMG (EP MARKII)
Manhas M et al [25] Cross-sectional study	On the basis of how often they used their mobile phones, the subjects were split into three groups.Group A consists of control participants, Group B consists of people who used mobile phones for 30 minutes per day for 4 years, and Group C consists of subjects who used mobile phones for 30 minutes per dayfor 4 to 8 years.	The study involved 60 subjects of either gender divided into three groups of 20 each, based on the usage of mobile phones. The subjects were selected from amongst the volunteers and patients attending ENT OPD. **Inclusion Criteria:** Subjects between the ages of 18-30 years of either sex, using GSM phones only for the past 4 years (for group B) and for 8 years (for groupC) with normal hearing **Exclusion Criteria:** Subjects with the history of ear discharge, hearing loss, or ear surgery, metabolic disorders known	Medical history and complete systemic examinations before recording the ABRs was taken. Examination of the external ear was done to rule out any hearing loss The auditory threshold was determined using pure tone audiometry (PTA). Along with this, a complete history of mobile phone usage was taken from the subjects: the number of years they have been using a mobile phone and the average

		to affect hearing, • ototoxic drugs (aminoglycosides, diuretics, analgesics), history of chronic smoking and/or alcohol abuse, noise-induced hearing loss and any hormonal imbalance e.g., thyroid, acromegaly	duration of use per day (for groups B and C). ABRs were recorded using a computerized evoked potential recording system (EB Neuro, Italy).
Latha R et al [26] Cross-sectional study	The study participants were dividedinto 2 groups. Group 1 (Headphone users <3hrs/day) and Group 2 (Headphone users > 3hrs/day)	A convenient sampling method selected 30 subjects aged between 18 and 21 years old. Subjects with a history of systemic diseases like diabetes mellitus, hypertension, and presbycusis were excluded.	A complete ENT examination including Rinne's test, Weber's test, absolute bone conduction test, and PTA was carried out to rule out ear pathology. BERA was recorded in the morning at a pleasant temperature in a quiet air-conditioned room using Physiopac PP4.

Table 2: Results of the studies included for the final review

Source & study design	Results
Gupta N et al [21] Cross-sectional study	Latencies, interpeak latencies, and amplitudes of ABR waves between groups A and B did not differ significantly ($p>0.05$).
Selvi EC et al [16] Cross-sectional study	A significant difference was observed among the three groups in their duration of mobile phone use. The latency of waves in three groups showed a significant differenceIn contrast to Group I and Group III, Group II was shown to have a longer average latency (both right and left ear) for waves I–V. Interpeak latencies I-V and I-III showed differences among the three groups. Though subjects used mobile phones for fewer years in Group I (17-19 yrs) and Group II (20-29 yrs), their usage per day was found to be higher.
Priya AJ et al [22] Cross-sectional study	The mean latencies of MLAEP waveforms in both ears were found to be significantly increased in long-term mobile phone users and in individuals who use mobile phones for more than 1 h per day.
Sharma G et al [10] Cross-sectional study	There was a significant change in the latencies of BERA potentials of waves I and III in users compared to non-users.
Maghbooli M et al [23] Cross-sectional study	A significant correlation was found between mobile phone use and wave Ⅲ ($P=0.04$) and wave Ⅴ ($P=0.03$) latencies in the right ear.

Kothari R et al [24] Cross-sectional study	When compared to controls, the test group's I-V waves' average latency (both in the right and left ear) and interpeak latencies (IPLs) I-III, III-V, and I-V waves were found to be prolonged (P > 0.001).In the test group, the mean latencies of the left ear were significantly (P 0.05) longer than those of the right ear.
Manhas M et al [25] Cross-sectional study	There was statistically no significant difference in ABR parametersi.e., latencies of waves and interpeak latencies among groups A, B and C.
Latha R et al [26] Cross-sectional study	They concluded that prolonged headphone usage had a negative influence on brain stem auditory evoked potentials, but there was no remarkable difference between the genders (There was no significant difference in peak latencies of waves I to V and inter-peak latencies between genders on the rightand left ear of headphone users, except wave V ($p<0.01$)on the left ear of headphone users, with latency being more in males than in females).