A SYSTEMATIC REVIEW ON AUDITORY PROCESSING ABILITIES IN CHILDREN WITH NONSYNDROMIC CLEFT LIP/AND PALATE

BANUMATHI

20AUD007

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This Dissertation is submitted as part of

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ALL INDIA INSTITUTE OF SPEECH AND HEARING

Manasagangothri, Mysuru 570 006

August 2022

CERTIFICATE

This is to certify that this dissertation entitled **'A systematic review on auditory processing abilities in children with nonsyndromic cleft lip/and palate'** is a bonafide work submitted as a part for the fulfilment for the degree of Master of Science (Audiology) of the student Registration Number: 20AUD007. This has been carried out under the guidance of the faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru
August, 2022

Dr. M. Pushpavathi
Director
All India Institute of Speech & hearing
Manasagangothri, Mysuru - 570006

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Mysuru
August 2022

Guide

Dr. Chandni Jain
Associate Professor in Audiology,
Department of Audiology,
All India Institute of Speech and Hearing
Manasagangothri, Mysuru 570 006

DECLARATION

This is to certify that this dissertation entitled **'A systematic review on auditory processing abilities in children with nonsyndromic cleft lip/and palate'** is the result of my own study under the guidance of **Dr. Chandni Jain**, Associate Professor, Department of Audiology, All India Institute of Speech and Hearing, Mysore and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysuru **Registration Number: 20AUD007**

August 2022

This Dissertation is dedicated to My parents and My sister

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ABSTRACT

The present systematic review aims to understand auditory processing abilities in children with nonsyndromic cleft lip and/or palate (NSCL/P). The review summarizes questionnaire, behavioral and electrophysiological findings of auditory processing abilities in children with NSCL/P. The study used a literature search of electronic databases (e.g., Pub Med, Google Scholar, Research Gate, Science direct) and the AIISH repository from 2000 to 2021. The retrieved articles were assessed in two stages: title and abstract screening, followed by a full-length article review. Thirteen articles were selected after the full-length review of 17 shortlisted articles. All selected studies used cohort design. The review showed that the speech perception in noise and temporal processing are majorly affected processing abilities in children with NSCL/P. The review also showed that cleft palate children are more prone to auditory pro cessing deficits than other cleft subgroups. These auditory processing deficits in NSCL/P children may cause delayed speech and language skills, reading, and learning disabilities, which are highly reported in these children. To conclude, auditory processing evaluation should be a part of the audiological test battery for these children to promote early diagnosis and management

Chapter 1

INTRODUCTION

Cleft lip and palate (CL/P) disorders are the most prevalent congenital deformities that account for many human birth problems. CL/P have a global prevalence of 1 in 1000-1500 births, with wide variations between different populations and studies (World health Organization, WHO, 2020; Salari et al., 2021). According to Allagh et al. (2015), the overall birth prevalence of clefts in India is 1.3 per 1000 total births. The majority of cleft patients (70%) are classified as having a nonsyndromic cleft lip and/or palate (NSCL/P), which refers to an isolated cleft that is not accompanied by any other abnormalities (Stanier & Moore, 2004). According to studies, peripheral hearing loss is common in children with NSCL/P due to direct or indirect effects of Eustachian tube dysfunction (Bluestone & Doyle, 1988b; Sheer et al., 2012). It has been reported that hearing loss in children with NSCL/P is often mild to severe, bilateral, and fluctuating (Yang & McPherson, 2007).

Children with NSCL/P have also been linked to a higher degree of reading disability, learning disability, and academic underachievement (Chollet et al., 2014; Roberts et al., 2012; van der Plas et al., 2012). Children with NSCL/P scored significantly lower on reading and related skills tasks which could be attributable to a higher prevalence of hearing problems (Chollet et al., 2014). However, recurrent middle ear infection or a history of conductive hearing loss does not justify or fully explain the amount of language delay, learning, and reading difficulties reported in children with NSCL/P (Chollet et al., 2014; Jocelyn et al., 1996). Another potential contributing cause to learning and language delay is auditory processing disorder (APD), which has recently been flagged as an additional hearing deficit in children with NSCL/P. APD is a perceptual condition hypothesized to be caused by a dysfunction of the brainstem and cortical functions (American Speech-Language-Hearing Association, ASHA,

2005). APD is defined as " Deficits or poor performance in one or more of the following listening skills: Auditory pattern recognition; auditory performance with competing acoustic signals and degraded acoustic signals; auditory localization and lateralization; auditory discrimination; temporal aspects of audition; auditory pattern recognition" (ASHA, 2005).

Auditory processing difficulties most commonly exhibit themselves in the situation of normal hearing, although they can also develop in children with recurrent middle ear infections. Several studies have found that children with NSCL/P are more likely to develop glue ears because the palate and Eustachian tube share muscles (Bluestone & Doyle, 1988a) Mucus and debris from the middle ear are drained through the Eustachian tube. A cleft in the palate causes aberrant alignment of muscles and tendons in children with NSCL/P. Consequently, the Eustachian tube fails to drain waste from the middle ear, leading to fluid collection and middle ear infection (Sharma & Nanda, 2009). Recurrent otitis media in NSCL/P children is likely to damage auditory system processing capacities due to disruptions in binaural hearing and possible auditory system neuronal changes which could slow or stop normal central nervous system development (Roberts et al., 2012).

The cerebral architecture of people with NSCL/P has also been shown to differ from those of their craniofacial normal counterparts (Nopoulos et al.,2002). Compared to craniofacial normal individuals, young men with NSCL/P have radiologically abnormal cortical regions, with significant differences in the left temporal lobe, which showed grey and white matter volume reductions (Nopoulos et al., 2000, 2002; Shriver et al., 2006). Infants with NSCL/P have been shown to have reduced volume and thickness in the left superior temporal plane and other developmental abnormalities in the cortical area (Yang & McPherson, 2007). As a result of these variances, the auditory cortex's functional capacities may be affected in children with

NSCL/P. These factors could be the reason for auditory processing deficits in children with CL/P.

Questionnaires have been recommended as useful screening tools before formal diagnosis in a comprehensive test battery for APD because they can save time and costs spent due to improper referrals (Musiek & Chermak, 2007). The FISHER checklist was administered to NSCL/P children by (Minardi et al., 2004), and the results revealed that 100% of NSCL/P children had auditory processing disorder-related behaviors. Various electrophysiological studies on NSCL/P children have assessed their auditory processing abilities. (Cheour et al., 1999) studied MMN between normal children and children with CL/P. They found a significant difference in the mean amplitudes of responses to infrequent tones between healthy and cleft palate neonates. APD assessment using behavioral tests also showed that children with CL/P had poorer auditory processing abilities than their craniofacial normal counterparts (Ma et al., 2015, 2016a, 2016b). This is true even for children with NSCL/P who have never had a middle ear problem.

APD may negatively affect children's development of speech and language, communication skills, and learning capacity. Studies have reported that NSCL/P children have poorer language, communication, and learning skills than their typical peers (Ma et al., 2015, 2016a, 2016b). Given the high risk of APD in NSCL/P children, a part of speech, language, and academic achievement might be related to APD. Studies have also shown that hearing impairments might affect children's lives if left untreated and hence should not be underestimated. Therefore, assessing different aspects of auditory processing in NSCL/P children and providing appropriate auditory training is necessary.

1.1 Need for the Study

Children with nonsyndromic cleft lip and/or palate are at greater risk of having auditory processing disorder (Ma et al., 2015, 2016a). APD has a detrimental impact on young children's academic achievement, linguistic skills, cognitive capacities, and quality of life (Cacace & McFarland, 1998). As a result, auditory processing abilities in children with NSCL/P should not be overlooked. Auditory processing assessment measures should be considered when making an auditory evaluation and diagnosis for this population.

Hence, there is a need to understand auditory processing abilities in children with CL/P, as many studies have identified auditory processing deficiency in CL/P in various domains. Thus, this review will provide insight into children's auditory processing abilities with NSCL/P. It will provide evidence to the audiologist, which will help them in early diagnosis and management and improve the quality of life for these children.

1.2 Aim of the Study

The present study aims to summarise and disseminate the existing material on auditory processing in the NSCL/P population and identify any research gaps.

1.3 Research questions

1. Do the nonsyndromic cleft lip/palate individuals' questionnaire and behavioral auditory processing test findings differ from craniofacial normal peers?
2. Do the nonsyndromic cleft lip/palate individuals' electrophysiological test findings differ from craniofacial normal peers?
3. If affected, which auditory processes are majorly affected in nonsyndromic cleft lip/and palate individuals?
4. Does the auditory processing deficit vary across cleft types?

Chapter 2

METHODS

2.1 Research Design

The Preferred Reporting Items for Systematic Reviews and Meta-analyses statement (PRISMA statement) was followed in this systematic review (Page et al., 2021). A comprehensive review of peer-reviewed studies published between 2000 and 2021 was conducted.

2.2 Information sources

The following databases and search engines were extensively searched: Science Direct, Medline/PubMed, Google Scholar, and Com-Disdome (ProQuest), and SpyNet. Lists of references and citations were searched manually for further relevant studies.

2.3 Search strategy

The search was carried out using key terms, related search phrases, derivatives, and MeSH words relevant to the study combined with Boolean operators such as 'AND,' 'OR,' 'NOT.

The keywords used were "cleft lip and palate" OR "oral cleft “AND "auditory processing " OR "CAPD" OR "P300" OR "MMN" OR " speech perception in noise " OR “SPIN” OR ‘'binaural interaction" OR "binaural integration " OR " dichotic listening" OR "temporal processing " OR " auditory closure".

2.4 Inclusion criteria to select the studies for systematic review

- Articles that have been published in peer-reviewed journals over the past twenty years (2000 and 2021) were included.
- Studies were selected based on the quality of the method, data, and outcome.
- Each study should have a minimum of ten participants.
- Original articles containing human subjects with appropriate samples and relevant statistics were only considered.
- Articles published in the English language were considered for the review.
- The selection was based on PECOS criteria (Methley et al., 2014).

  Participant- Nonsyndromic cleft lip/and palate

  Exposure- APD tests (behavioral and electrophysiological)/Questionnaires

  Control- Craniofacially normal peers

  Outcome-Results on APD tests/Questionnaires

  Study design – Cohort, case-control, retrospective, and prospective studies.

Exclusion Criteria

- Articles with poor methodological quality or published in a language other than English were rejected.
- Case reports, letters to editors, systematic reviews, and editorials were excluded.
- Articles with syndromic cleft lip / and palate participants were excluded.

2.5 Data extraction

Rayyan QCRI (Qatar Computing Research Institute) was used to compile all articles and remove the duplicates. Mendeley desktop reference manager system was used for referencing.

The articles which met the inclusion criteria were selected by screening the titles and abstracts retrieved from the search strategies. After that, the full text of the potential studies was retrieved and matched to see if they were eligible. The extracted data included: article title, author details with their affiliation, year of publication, research design, study population, sample size, age group, comparison group, and method of outcome measures.

2.6 Quality assessment

The studies included in the systematic review were subjected to a methodological quality assessment . We used the National Institute of Health (NIH) quality assessment tool for Cohort studies. The following criteria: Design, research population, sample bias, information gathering, variables, blinding, and dropouts were all covered by the NIH quality assessment tool for Cohort studies. Based on the above parameters, an overall rating of 'good,' 'fair,' or 'poor' was given. All studies were rated individually.

Chapter 3

RESULTS

A total of 11,339 articles were identified using database searches, with 468 duplicates eliminated. A total of 10,871 articles were included in the title/abstract screening. Seventeen articles were selected for the full-length article screening. Thirteen articles matched the inclusion criteria of the study. The remaining four articles were excluded because of lesser participants and irrelevant study design. A detailed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart for the selection of the study is shown in Figure 3.1

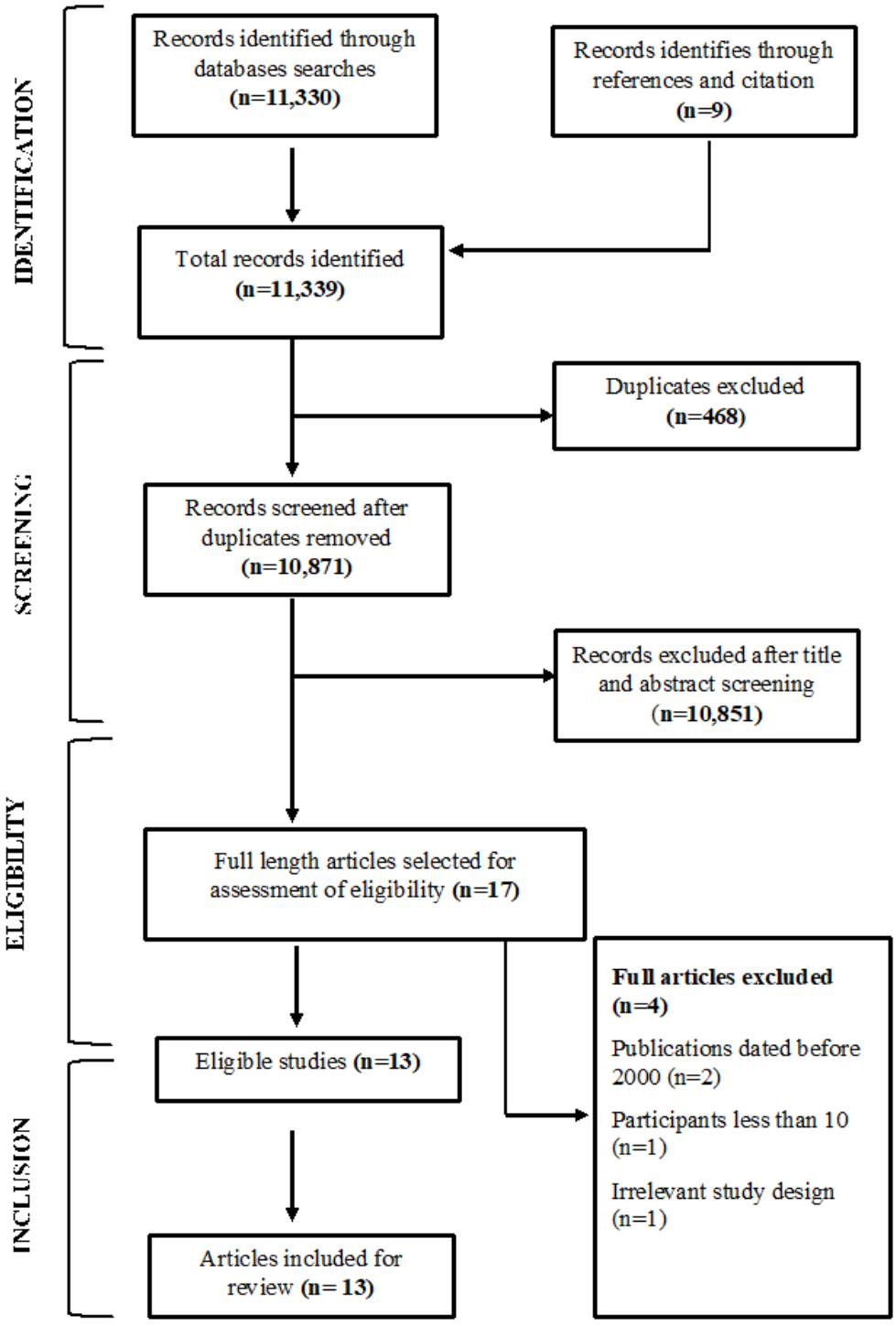

Figure 3.1

PRISMA flowchart for the selection process of articles included in the review.

3.1 Study characteristics

Population: The participants in the included studies NSCL/P children aged 6 to 16 years. All the studies had CL/P children as participants without any associated problems like intellectual disability, attention deficit hyperactive disorder, autism spectrum disorder, etc. All studies included some basic or detailed audiological evaluation before auditory processing testing, and all participants had normal peripheral hearing and no active middle ear infections during the investigation.

Exposure: In this study, the exposure of interest was auditory processing tests. All the selected articles assessed auditory processing abilities in various modalities. Out of thirteen studies selected, APD was assessed using a questionnaire in one study (Ma et al., 2016a) and nine studies used behavioral tests for evaluating APD (Ma et al., 2016 b; F. F. Yang et al., 2012) The remaining three studies used electrophysiological measures for auditory processing assessment (Ma et al., 2016 b; Yang et al., 2012 ; Čeponiene et al., 2007).

Comparators: Craniofacial normal children were taken as a control group in eight studies (Zarei et al.,2021; Feng & Lu, 2016; Lemos et al., 2008; Amaral et al., 2010; Ma et al., 2016; Ma et al., 2015; Yang et al.,2012; Ceponiene et al., 2000) and five of the included studies had no control group (Maximino et al., 2021; MacDonald et al., 2019; Amaral et al., 2010; Boscariol et al., 2009; Martin et al., 2021).

Outcomes: Auditory processing ability in NSCL/P was the primary outcome of interest in all the selected articles. All results were based on behavioral and electrophysiological measures, except for one study using a questionnaire (Ma et al., 2016a).

3.2 Results of Data Extraction

Table 3.1 shows the aim of the study, details of the participants, the testing method/questionnaire (behavioral) used in the study, and the results for each study included in the systematic review. Table 3.2 shows the aim of the study, details of the participants, the testing method (electrophysiological**)** used in the study, and the results for each study included in the systematic review.

Table 3.1

The details of participants, behavioral tests, and results of auditory processing abilities in NSCL/P children in studies included for systematic review.

Title and author	Aim of the study	Population type	Testing method/questionnaire	Results
Assessment of auditory processing in children with nonsyndromic cleft lip and/or palate (Zarei et al., 2021)	The study aimed to assess temporal resolution, binaural processing and perception of speech in noise abilities in NSCL/P individuals	Study group- 23 NSCL/P children Age: 8 to 12 years (mean=6.9 years) Control group– 30 craniofacially normal individuals. Age: 8-12 years (mean =9.5 years)	Children with bilateral normal peripheral hearing were taken for the study. APD tests included were: Monaural selective auditory attention tests (m SAAT), Gaps in noise (GIN), Dichotic Digits (DD)	In children with NSCL/P, the average score of dichotic digits in the right ear was higher than that of children without a cleft. Between the NSCLP and normal children there was no significant difference noted in the DD score of the left ear. GIN and mSAAT scores of the NSCL/P children were significantly lower than those of the control

				group without craniofacial anomalies.
Auditory processing and perception in children and adolescents with cleft palates (Hofer-Martini et al., 2021)	This study aimed to look into auditory processing disorders in NSCL/P children with various cleft manifestations.	**Study group**-48 children with NSCL/P (girls-20, boys -28) **Age**:5 to 16 years **Control group** – no control group.	All participants were NSCLP and normal bilateral hearing at the time of examination The protocol included for evaluation were Otoscopic examination, Pure tone audiometry, A parental questionnaire (DGPP-AVWS-FB), Dichotic speech discrimination, Speech intelligibility in noise and Auditory short-term memory.	The majority of caregivers did not report any issues in the parental questionnaire. Only 16.7 percent of participants had suspicious results in auditory short-term memory and dichotic speech discrimination, while 69 percent had questionable results in speech intelligibility in noise. The results of both tests revealed that younger children had the most difficulty.

				NSCLP showed a deficit in hearing in background noise.
Auditory and language skills in children with cleft lip and palate (Maximino et al., 2021)	The study investigated language and auditory skills in repaired CL/P children.	Study group- 22 repaired CL/P children and without any associated issue. (male =11, female =11) Age: 7 to 9 years (mean=6.9 years) Control group – 30 craniofacially normal individuals. Age: 8-12 years (mean =9.5 years)	Four central auditory processing tests were used for assessing processing skills. Random Gap Detection Test (RGDT), DDT Sustained Auditory Attention Ability Test (SAAAT) Dichotic Non-Verbal Test.	The tests results revealed that one child performed adequately in all skills examined, five children performed inadequately in all skills, and 16 displayed deteriorations in one to three auditory skills. The result also highlighted that the most affected processes was temporal processing (81 percent)
Spatial processing disorder in children with cleft palate	This study aimed to investigate the prevalence of Spatial	Study group- 20 children with NSCL/P	All participants had a normal hearing threshold from 0.5 to 4kHz, normal otoscopy, and immittance	Using the LiSN-S, eight (40%) of the 20 children were found to have SPD.

(MacDonald et al., 2019)	Processing Disorder (SPD) in children with cleft palate (with or without cleft lip), describe their spatial processing ability, and investigate the possibility of SPD rehabilitation using an established remediation program.	Age :6 to 16 years NSCLP with associated problems like ID, ANSD, and ADHD were excluded. Control group -No control group	results in both ears. The LiSN-S test was administered, and the signal-to-noise ratio (SNR) required to identify 50% of the words in target sentences was determined in four conditions that differ in terms of the virtual location of the noise source and the speaker's vocal quality. High-cue condition (competition is a different voice at 90 degrees azimuth). Only spatial separation (competition is the same voice at 90° azimuth). Condition of different voices (competition has a different voice at 0° azimuth). Low-cue (competition is the same voice at 0° azimuth).	Four children had signal-to-noise ratio losses greater than 2 dB from the mean, indicating a significant loss in speech intelligibility. Three children received remediation through the Listening in Spatialized Noise and Learning Program, and all benefited significantly.

Behavioral signs of (central) auditory processing disorder in children with nonsyndromic cleft lip and/or palate: a parental questionnaire approach (Ma et al., 2016)	Study aims to determine the prevalence of typical (C)APD-related behaviors in cleft lip and/or palate children using a questionnaire.	Study group - 147 NSCL/P children (49 girls and 98 boys) (CL= 37, CP= 27 and CLP= 83) Age - 6 to 15 years (mean age-10.06 years). Control group - Craniofacially normal children	Children with puretone thresholds less than 25dBHL and 'A' type tympanogram with present reflexes were taken for the study. FISHER Checklist was administered on caregivers of CLP children.	Signs of (C)APD -related behaviors were substantially higher in the CP children. The NSCL/P group's most typical characteristics were a short attention span, a lack of willingness to learn, and hearing difficulties in noisy environments.
Auditory processing impairments under background noise in children with nonsyndromic cleft lip and/or palate (Feng & Lu, 2016)	The study aimed to investigate auditory processing abilities in NSCL/P using a structured behavioral test	Study group – 18 NSCL/P children Age – 7 -15 years (mean =11.33 years) Control group – 18 age and gender	Children with normal peripheral hearing were taken for study. Behavioral tests for APD included were - Hearing in noise test (HINT) DDT GIN	During the DDT test, no significant differences were found between groups, indicating typical binaural separation and integration ability among the children with

		match craniofacially normal peers were taken.		NSCL/P. The cleft group scored much lower than typical peers in the HINT under noisy conditions and in the GIN test. This indicates that NSCL/P children may have reduced temporal resolution and reduced monoaural low redundancy ability.
Behavioral assessment of auditory processing disorder in children with nonsyndromic cleft lip and/or palate (Ma et al., 2015)	The study aimed to compare auditory processing skills between NSCL/P and craniofacially normal school-age children using behavioral speech and non-speech assessment.	Study group – 141 NSCL/P (96 males; 45 females) Age- 6.00 to 15.67 years (mean = 10.16 years) Control group – 60	Children with bilateral normal hearing were enrolled in the study. Behavioral test – Adaptive tests of temporal resolution (ATTR) [Gap detection test] Mandarin pediatric lexical tone and disyllabic-word picture	In the gap detection test, NSCLP children showed significantly poorer than the normal children. SNR-50 percent ratings were significantly lower in the bilateral CL/P subgroup than in the

		craniofacially normal children (25 boys and 35 girls) Age- 6.00 to 15.50 years (mean = 10.16).	identification test in noise (MAPPID-N) [Speech perception in noise test]	control group in the MAPPID-N condition, where speech was spatially separated from noise. In addition, children with a cleft palate showed much smaller spatial separation advantage than the control group for speech recognition in noise.
A study on the hearing of children with nonsyndromic cleft palate/lip (Amaral et al., 2010)	This study aimed to see how children with NSCLP performed on basic audiologic tests and auditory processing screening.	Study group - 44 cleft palate children. (25 males; 19 females) Age - 8-14 years (mean=10.2 years) Control group – No control group	The basic audiological evaluation included- Case history on recurrent otitis media Otoscopy PTA Immittance The following auditory processing	In basic audiological evaluation, 77.27 % had normal hearing, conductive hearing loss in 13.6 %, and rest 2.2 % had mixed hearing loss. A type curve was found in 68.2 %, C type in

			tests were performed - • Sound localization test in five directions. • Non-Verbal Sounds Digits Dichotic Test and • Sequential Memory Test for Verbal	21.2%, B curve in 7.1 %, and an Ad curve in 3.5 % of children with NSCLP. The auditory processing test findings were impaired in 72.7 % of the children, and 45.5 % of them had impaired dichotic listening test results.
Cleft palate children: performance in auditory processing tests (Boscariol et al., 2009)	The study aimed to assess the performance in cleft palate children in behavioral auditory processing tests.	Study group - 20 cleft palate children. Age - 7-11 years (mean – 9.4 years) Control group – No control group	Children with normal middle ear function and peripheral hearing were included in the study. **Diotic tests:** Non-verbal sequential memory test (MSSNV), Verbal sequential memory test (MSSV), Auditory Fusion Test-Revised	Many cleft palate children performed poorly on the AFT-R, DD, SSW, and PSI/SSIMCI The best results were obtained in the sound localization tests , PSI/SSIMCC test and

			(AFT-R) Sound location test (LS) **Monotic tests**: Synthetic Sentences Test with Ipsilateral Competitive Message (SSI/MCI); Pediatric Test of Speech Intelligibility with Ipsilateral Competitive Message (PSI/MCI) **Dichotic tests:** Alternate Disyllable Test (SSW) Synthetic Sentences Test with Contralateral Competitive Message (SSI/MCC) Pediatric Test of Speech Intelligibility with Contralateral Competitive Message (PSI/MCC) Dichotic Digits Test (DD).	verbal and nonverbal sounds for sequential memory test among NSCL/P.
Dichotic listening test (directed	The study aimed to examine NSCLP	Study group - 30 cleft palate	Children with bilateral normal hearing abilities were taken for the	The performance of NSCLP children in

attention mode) in children with cleft lip and palate (Lemos et al., 2008)	performance in the dichotic listening test.	children. (17 males; 13 females) Age – 7 to 7.11 years Control group – 25 Craniofacial normal children (12 males; 13 females) Age – 7 to 7.11 years	study. A dichotic listening test (direct attention mode) was administered for both groups.	dichotic listening test was significantly lower than the control group. NSCLP girls performed poorer than normal girls, with no statistical difference in boys between the study and control group.

*Note***.** ASD- Autism spectrum disorder, ADHD- Attention deficient hyperactive disorder ATTR- Adaptive tests of temporal resolution, CAPD- Central auditory processing disorder, CL- Cleft lip, CLP- Cleft lip and palate, CP-Cleft palate, DD- Dichotic digits, DDT -Dichotic Digit Test, DNVT- Dichotic Non-Verbal Test, GIN- Gaps in noise, HINT – Hearing in noise test, ID- Intellectual disability M- SAAT - Monaural selective auditory attention tests, MAPPID - Mandarin pediatric lexical tone and disyllabic-word picture identification test in noise. NSCL/P- Non-syndromic cleft lip and/or palate, REA - Right ear advantage, RGDT - Random Gap Detection Test, SAAAT- Sustained Auditory Attention Ability Test.

Table 3.2

The details of participants, electrophysiological tests, and outcomes in NSCL/P children in studies included for the systematic review.

Author and year	Aim of the study	Population type	Testing method/questionnaire	Results
Electrophysiological assessment of auditory processing disorder in children with nonsyndromic cleft lip and/or palate (Ma et al., 2016)	Research aimed to study electrophysiological test findings in NSCLP children and also to observe the effect of age and cleft type	Study group- 146 children with NSCL/P (Male=98; females = 48) Participants were divided based on the cleft type: CL= 37 children CP=26 Children CLP= 83 children (CLP further divided into UCLP and BLCP) Age :6 to 15.67 years (mean=10.08 years) Control group – 60 normal (male =25;	Children with bilateral normal hearing were considered for the study. Following electrophysiological tests were administered: ABR ALLR P300	Children with NSCL/P had a longer ABR and N1 wave latency. Compared to the control group, children with clefts had abnormal long-term potentials. However, there was no significant difference between NSCLPs and controls in P300. Compared to other cleft subgroups, unilateral cleft lip and palate children had higher

		female=35) Age: 6-15.5 years (mean =10.16 years)		abnormal results. In contrast, the subgroup with only cleft lip children had robust responses for all tests.
Central auditory nervous system dysfunction in infants with nonsyndromic cleft lip and/or palate (Yang et al., 2012)	The study aimed to investigate obligatory and discriminative potentials in infants with NSCLP	Study group- 34 children NSCL/P Age :6 to 24 months (mean=5.9 months) Control group – 34 age and gender-matched normal. (mean=15.4 months, SD =5.9 months)	Normal hearing children were considered for the study. Following obligatory and discriminative potentials were administered: ABR MLR MMN	All measurement parameters between the NSCLP and normal group did not significantly differ in ABR or MLR. (Including wave, I, III, V absolute peak latencies, I–V inter-peak latency, and amplitude of wave V, recordable components, Na, Pa latencies, and Na–Pa amplitude). Compared to their

				typical controls, infants with NSCLP displayed a significantly decreased MMN response..
Dysfunction of the auditory cortex persists in infants with certain cleft types (Ceponiene et al.,2000)	The study aimed to investigate sensory potentials (MMN) in NSCL/P at birth and six months of age.	Study group- 32 children with NSCL/P (Male=22; females = 10) All participants were divided based on the cleft type CL= 4 children CP=17 Children CLP= 11 children Age: CP, CL, CLP were tested at the mean age of 4 months 20 days to 7 months 6 days soon after the birth. Control group – 12 normal (male = 6; female	MMN component of brain evoked potentials was recorded, indicating preconscious sound discrimination. 'Standard' 1000-Hz sine-wave tones were occasionally substituted by 'deviant' 1100-Hz tones in the oddball paradigm.	Brain reactions to infrequent sounds were weaker in both cleft subgroups than in healthy counterparts during birth and after six months of age. However, in the latency range of 300 to 500 ms, the MMN in babies with cleft palate only (CPO) was smaller. The MMN in CLP infants was comparable to that of healthy infants. Differences in auditory

	= 6) Age: Mean age of 5 days after birth.	discrimination between babies with CLP and CPO, as measured by MMN, were noticeable at birth and remained until early childhood.

Note. CAPD- central auditory processing disorder; CL-icleft lip, CP-cleft palate, NSCL/P- non syndromic cleft lip and/or palate, CLP- cleft lip and palate, MMN-Mismatch negativity, MLR- Middle latency response , LLR-Long latency response.

3.2 Quality assessment

Quality assessment of the selected studies for the systematic review was done using the National Institute of Health (NIH) Quality assessment tool for observational cohort studies. All articles included in the review were cohort studies.

All the selected articles had defined aims and objectives, clearly defined population, clearly stated dependent variables, well-controlled extraneous variables, and overall, the methodological quality ranged from good to fair. However, none of the studies said or explained their sample size. The results of the quality assessment for all of the selected studies are provided in Table 3.3

Table 3.3

Results of the quality assessment for the selected studies

	Zarei et al., (2021)	Hofer-Martini et al.(2021)	Maximino et al. (2021)	MacDonald et al. (2019)	Ma et al., (2016 a)	Feng & Lu, (2016)
1. Was the research question or objective in this paper clearly stated?	YES	YES	YES	YES	YES	YES
2. Was the study population clearly specified and defined?	YES	YES	YES	YES	YES	YES
3. Was the participation rate of eligible persons at least 50%?	YES	YES	YES	YES	YES	YES
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	YES	YES	YES	YES	YES	YES
5. Was a sample size justification, power description, or variance and effect estimates provided?	NO	NO	NO	NO	NO	NO
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	YES	YES	YES	YES	YES	YES
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	YES	YES	YES	YES	YES	YES

8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	YES	NO	NO	NO	NO	NO
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	YES	YES	YES	YES	YES	YES
10. Was the exposure(s) assessed more than once over time?	NA	NA	NA	NA	NA	NA
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	YES	YES	YES	YES	YES	YES
12. Were the outcome assessors blinded to the exposure status of participants?	NO	NO	NO	NO	NO	NO
13. Was loss to follow-up after baseline 20% or less?	NA	NA	NA	NA	NA	NA
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	NA	NA	NA	NA	NA	NA
Quality score (Good, Fair, or poor)	**GOOD**	**FAIR**	**FAIR**	**FAIR**	**FAIR**	**FAIR**

	Ma et al. (2015)	Amaral et al. (2010)	Boscariol et al. (2009)	Lemos et al. (2008)	Ma et al. (2016 b)	Yang et al. (2012)	Ceponiene et al. (2000)
1. Was the research question or objective in this paper clearly stated?	YES	YES	YES	YES	YES	YES	YES
2. Was the study population clearly specified and defined?	YES	YES	YES	YES	YES	YES	YES
3. Was the participation rate of eligible persons at least 50%?	YES	YES	YES	YES	YES	YES	YES
4.Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	YES	YES	YES	YES	YES	YES	YES
5. Was a sample size justification, power description, or variance and effect estimates provided?	NO	NO	NO	NO	NO	NO	NO
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	YES	YES	YES	YES	YES	YES	YES
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	YES	YES	YES	YES	YES	YES	YES

8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	YES	NO	NO	NO	YES	NO	YES
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	YES	YES	YES	YES	YES	YES	YES
10. Was the exposure(s) assessed more than once over time?	NA	NA	NA	NA	NA	NA	NA
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	YES	YES	YES	YES	YES	YES	YES
12. Were the outcome assessors blinded to the exposure status of participants?	NO	NO	NO	NO	NO	NO	NO
13. Was loss to follow-up after baseline 20% or less ?	NA	NA	NA	NA	NA	NA	NA
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	NA	NA	NA	NA	NA	NA	NA
Quality score (Good, Fair, or poor)	**GOOD**	**FAIR**	**FAIR**	**FAIR**	**GOOD**	**FAIR**	**GOOD**

Note. NA – not applicable

Chapter 4

DISCUSSION

The systematic review aimed to compile and disseminate the auditory processing abilities in NSCL/P children from existing research findings. Out of 11,339 articles, 17 research articles were initially selected for this systematic review to fulfill the aim. Based on the selection criteria, 13 studies were shortlisted.

Oral cleft individuals have a greater prospect of middle ear infections because of their malformed palates. Middle ear infections in children's early years cause anatomical as well as functional alterations in the auditory system. Furthermore, because of the interruption of inputs between both ears, recurrent otitis media may have a deleterious impact on binaural and temporal processing. Despite treatment for a middle ear infection, a processing impairment may persist, affecting children's language skills, learning capacities, and academic progress (Khavarghazalani et al., 2016).

The cerebral architecture study on individuals with cleft has shown radiologically abnormal findings cortical regions. Significant structural differences in the left temporal lobe have been observed (Nopoulos et al., 2000, 2002). According to Rita et al. (2002), APD in NSCL/P children is primarily linked to CNS abnormalities resulting from delayed brain development and processing. The cause of facial cleft is multifactorial; genetic factors can also cause facial cleft. These factors can also disrupt the embryological development of brain structures, as the brain and face are formed from the same embryonic tissues. As a result, it appears that auditory processing in NSCL/P children is influenced by a combination of environmental and genetic variables (including repeated middle ear infections). In the present systematic review, we included studies that utilized questionnaires, behavioral methods, and

electrophysiological methods for assessing processing abilities in the NSCL/P population.

4.1 Questionnaire and behavioral auditory processing test findings

Questionnaire-based screening approaches help children with CAPD to get a better diagnosis and treatment (Musiek & Chermak, 2007). Ma et al., (2016a) used the Fisher checklist on NSCLP cases and discovered that the most typically reported difficulties were difficulty hearing in noise, short attention span, and low learning motivation. These findings may help to explain why NSCLP patients have poor academic performance and learning difficulties, as reported in various studies (Broder et al., 1998).The most effective strategy for identifying auditory processing deficits is to use behavioral methods. It is strongly advised that a behavioral test battery encompassing both verbal and nonverbal stimuli be used to investigate problems with various auditory systems (Musiek & Chermak, 2013). Several studies have assessed auditory processing abilities in children with clefts using behavioral methods that tap into different processing.

4.1.1 Auditory *closure*

The ability of the normal listener to utilize extrinsic and intrinsic redundancy to fill in distorted or missing portions of the auditory signal and recognize the whole message is termed as auditory closure (Musiek & Chermak, 2013). Tests such as SPIN, Time compressed speech test with reverberation, SSI-ICM, and filtered speech test have been adopted to assess auditory closure in NSCL/P children. Studies have shown that children with NSCLP have poor performance in mSAAT (Zarei et al., 2021), SPIN test (Hofer-Martini et al., 2021), and HINT test (Feng & Lu, 2016).

These test results indicate that NSCLP children have difficulty perceiving speech in

noisy background or environments. Speech perception in noise necessitates normal cortical function. Thus, as reported by various neuroimaging studies, an auditory cortical deficit in cleft cases would result in poor speech perception in noise (Nopoulos et al., 2002; Shriver et al., 2006; Nopoulos et al., 2000).

4.1.2 *Binaural integration*

Binaural integration is the ability to simultaneously process the children with information being presented to both ears, with the information presented to each ear being different (Chermak & Musiek, 2013). Tests used to assess integration ability in children with NSCL/P are dichotic digit, dichotic CV, dichotic rhyme, and SSW. Zarei et al. (2021) noticed a higher right ear advantage (REA) and a lower left ear score in CL/P children. Amaral et al. (2010) stated that 45.5 % of NSCLP children had impaired dichotic digit performance. Furthermore, Maximino et al. (2021) and Boscariol et al. (2009) also reported poor dichotic digit scores. In contrast to the previously stated findings, Feng and Lu (2016) and Hofer-Martini et al. (2021) observed normal performance in dichotic digit testing in children with clefts.

The deficit in the dichotic test could result from a maturational delay and poor neuronal connectivity, most likely caused by inconsistency in auditory stimulation caused by recurrent otitis media (Borges et al., 2013). The difference in the findings could be attributed to the different tests used across studies to assess binaural integration (Jäncke et al., 1992). Further research is needed to conclude the impact of cleft on binaural integration abilities.

4.1.3 *Temporal processing*

The term temporal refers to the acoustic signal's time-related aspects (Bellis, 2011). The temporal processing is essential for everyday listening situations , including music perception and speech perception (Hirsh, 1959). Studies have used GIN, GDT, RGDT and

AFT-R test to assess temporal processing among children with CL/P . Studies have shown that children with clefts had a significant deficit in the GIN test (Feng & Lu, 2016 ; Zarei et al., 2021). It was also reported that 81% of NSCLP cases had a deficit in the RGDT test (Maximino et al., 2021) and Boscariol et al. (2009) reported poor performance of NSCLP cases in the AFT-R test. These findings suggest that CL/P Children have difficulties perceiving rapid changes in speech related to temporal information. The temporal processing is sensitive to cortical and interhemispheric transfer lesions (Bellis, 2011). Therefore, cortical lesions in children with a cleft can cause deficits in temporal processing abilities (Nopoulos et al., 2002; Nopoulos et al., 2000; Shriver et al., 2006).

4.1.4 *Binaural interaction*

Binaural interaction ability indicated how the two ears interact in listening situation. Localization and lateralization of auditory stimuli, detection of signals in noise, binaural release from masking and binaural fusion are all functions that depends on binaural interaction (Durlach et al., 1981). Macdonald et al. (2019) reported that NSCLP children had spatial processing disorder using the LiSN test, implying that these children have difficulty integrating signals arriving at two ears from different sources that vary in the location in space (Moore et al., 2013). However, few studies on localization abilities in children with CL/P have shown normal findings (Amaral et al., 2010 ; Boscariol et al., 2009). However, very few studies assess interaction abilities in children with cleft, and it is challenging to derive a conclusion from these limited studies.

4.1.5 *Auditory memory*

Memory is the retention of patterns of perception (Burford, 1976). Auditory memory

and sequencing are one of the auditory processes, which is the ability to recall information, directions, events, lists, etc., presented aurally. Studies on auditory memory in children with nonsyndromic craniofacial cleft have shown normal findings (Boscariol et al., 2009; Hofer-Martini et al., 2021; Amaral et al., 2010). It can be concluded from these studies that auditory memory is preserved in children with NSCLP.

4.2 Electrophysiological auditory processing test findings

Electrophysiology assessment offers a window on auditory function by representing neural activity from the different anatomical structures along the auditory pathway and helps to locate lesions in the auditory system (Eggermont, 2007). The electrophysiological tests to assess processing abilities in CL/P children have been utilized in several research (Yang et al., 2012 ; Čeponiene et al., 2000). NSCLP children exhibited a significant ABR latency delay (Ma et al., 2016b) indicating that neuronal transmission between brainstem and the peripheral auditory nerve is slower in craniofacial abnormalities. Yang et al. (2012) observed normal ABR recordings in the CL/P group, in contrast to the findings above.

Yang et al. (2012) found normal Na-Pa latency and amplitude in MLR in the CL/P children. According to Ma et al. (2016b), the auditory long-latency response in children with clefts had a prolonged N1 latency and a reduced P1N1 amplitude. MMN is a pre-attentive index for auditory discrimination abilities. MMN findings have been reported to be abnormal in NSCLP children (Ceponiene et al., 2000; Yang et al., 2012). Further research is required regarding MMN as a clinical tool for auditory assessment. This would help identify children with a possible risk of processing deficit early, and early intervention can be provided. P300 reflects the processing abilities for a signal using auditory attention and memory after stimuli reach the cortex. Normal P300 latency and amplitude have been stated in cleft children (Ma et

al., 2016b).

Thus few electrophysiological studies in children with CL/P indicate processing abnormalities (Ma et al., 2016b; Yang et al., 2012;Čeponiene et al., 2000). Additional research is needed to understand the electrophysiological outcomes in these children and the efficacy of electrophysiological tests in the early detection of processing deficits in cleft children.

4.3 Majorly affected Processes in Children with Cleft Lip and/ or Palate

Auditory closure (HINT, SPIN, mSAAT) and temporal resolution (GDT, RGDT, GIN, AFT-R) are consistently reported to be majorly affected in NSCLP children (Hofer-Martini et al., 2021; Maximino et al., 2021; Zarei et al., 2021). Cortical lesions (Nopoulos et al., 2002; Shriver et al., 2006; Nopoulos et al., 2000) and recurrent middle ear infections in children with a cleft can cause deficits in closure and temporal processing abilities (Khavarghazalan et al., 2016). Lack of perception of normal speech, poor phoneme recognition, reading and language errors, phonemic analysis deficit, and articulation error may be present in children with cleft because they cannot detect short silence intervals due to temporal deficits (Fortenbaugh et al., 2015).

Further, the present review also noted that localization and auditory memory are spared in NSCLP children (Boscariol et al., 2009; Amaral et al., 2010). Further studies on auditory integration abilities in children with NSCLP are needed as studies have reported mixed findings, and it is difficult to derive any conclusion (Boscariol et al., 2009b; MacDonald et al., 2019; Amaral et al., 2010).

4.4 Effect of Cleft Type on Auditory Processing abilities

The type of cleft has been shown to impact auditory processing abilities (Ma et al., 2015, 2016b, 2016a). Ma et al. (2016a) reported that the cleft palate group had significantly poorer scores on Fischer checklist than the cleft lip group. Furthermore, Ma et al. (2015) also found that cleft palate and bilateral cleft lip and palate exhibited a significant deficit in auditory processing compared to the cleft lip group alone. Even in electrophysiological measurements, cleft palate children had a more affected response than other cleft subgroups (Ma et al., 2016b). Thus, it can be concluded that cleft palate children are more prone to auditory processing deficits than other subgroups. This can be attributed to the recurrent middle ear infection in cleft palate children because of the shared palate and middle ear musculature. Furthermore, cleft lip children have no maxillofacial deficit of soft palate and thus have less likelihood of cleft-associated cortical abnormalities.

Thus, NSCL/P children are more likely to develop APD than craniofacially normal children, particularly cleft palate children exhibit higher risk. APD can have a negative impact on children's, communication skills, learning ability, speech and language development. Untreated APD and late diagnosis may affect communication skills, learning ability, linguistic function, and academic accomplishment. Therefore, it is important to consider APD assessment, rehabilitation, and modification of acoustic environments in diagnosing and treating NSCL/P children. Both clinicians and parents should be aware of the potential long-term consequences of middle ear disorders in NSCL/P children. It is critical to intervene early to eliminate the hearing loss caused by middle ear dysfunction and to minimize further effects on auditory processing abilities.

Chapter 5

SUMMARY AND CONCLUSIONS

This systematic review summarizes and disseminates the auditory processing abilities in children with NSCL/P from existing research findings. Based on the selection criteria, 13 studies were shortlisted for systematic review. Studies using questionnaires, electrophysiological measures, and behavioral tests to assess auditory processing abilities in NSCL/P children were considered for the review. The review showed that auditory processing deficits are more prevalent in NSCL/P children because of cortical deformity and recurrent middle ear infections. Speech perception in noise and temporal processing are majorly affected processing abilities in children with NSCLP. Further it was also noted that cleft palate children are more prone to APD than other subgroups of clefts.

To conclude, auditory processing evaluation should be a part of the audiological test battery for these children to promote early diagnosis and management. However, there is limited research on electrophysiological findings in children with CL/P. Therefore, further research is necessary to understand these children's processing abilities.

5.1 Clinical Implication of the Study

- This review provides evidence for the audiologist to understand the processing deficit in children with cleft.
- The review provides evidence to counsel parents on diagnosing and managing APD in children with cleft.
- Caregivers should be advised to get treatment for middle ear infections as soon as possible to limit the consequences on auditory processing abilities.

- An APD screening checklist for all children with CL/P is required. It is advised that diagnostic screening tests be administered for children with cleft palates since they are more prone to processing deficits.
- Children with clefts show more difficulties in listening in a noisy environment; thus, modification of the acoustic environment and assistive listening devices can be recommended to improve SNR in the classroom and other noisy environment.

5.3 Future Direction

- More studies are required to comprehensively understand auditory processing abilities in children with clefts, especially electrophysiological studies.
- Further research should be conducted with bigger sample numbers and data on otitis media, such as the number, duration, and chronicity of occurrences, history of hearing loss, and sensory deprivation time.
- Studies on auditory processing management and outcomes in CL/P children may be included in future studies.
- There is not even one study in the Indian context exploring processing abilities in children with cleft, and these can be considered for future studies for Indian-based researchers.

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