Review Article

The Effects of the Early-onset Otitis Media on Cognitive Skills in Children: A Systematic Review

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ABSTRACT

Objectives: Some children are at risk of middle ear infections; however, the impact of the fluctuating hearing sensations on cognitive systems and immature central auditory is not fully recognized. Therefore, we reviewed and discussed the impact of early-otitis media on the cognitive skills of affected school-aged children.

Methods: A computerized search of the databases was conducted between January 2000 and December 2020 using the following keywords, including “otitis media” and “cognition” or “attention” or “memory” or “working memory” or “short term memory”.

Results: After applying inclusion and exclusion criteria and appraising the quality, seven studies were included and the data were extracted. Some of the articles reported a relationship between otitis media with effusion (OME) and cognitive deficits in 5 years old children and the other studies did not yield significant association.

Discussion: It seems that children with OME experience difficulties in attention and memory; though, the relationship between early childhood OME and cognitive skills in children at school ages is not yet definitive and need more comprehensive and well-organized studies.

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Highlights

• The impact of fluctuating hearing sensations due to middle ear infections, as a common pediatric inflammatory disease, is not well recognized on immature central auditory and cognitive systems in children.

• This paper systematically reviewed the studies that investigated the role of early otitis media in the cognitive skills of affected school-aged children.

• Despite the controversial results of studies, it seems that children with Otitis Media with Effusion (OME) experience difficulties with attention and memory.

Plain Language Summary

Some children are prone to a middle ear infection called Otitis Media (OM). OM can cause temporary and mild or moderate hearing loss. However, the impacts of the fluctuating hearing sensations on immature central auditory and cognitive systems in affected children are not fully understood. This study was designed to review studies and discuss the impact of early-onset otitis media on the cognitive skills of affected children at school. Seven high-quality studies in this field were identified by a comprehensive computerized or hand search in published literature. The results show that some of the articles reported a relationship between Otitis Media with Effusion (OME) and cognitive deficits at age 5 and the other studies did not have a significant relationship. Therefore, the relationship between early childhood OME and cognitive skills in school-aged children is not yet definitive and needs more comprehensive and well-organized studies.

1. Introduction

Otitis media (OM) is a prevalent inflammatory disease in children that results in the accumulation of infectious or non-infectious effusion in the middle ear [1]. The peak prevalence of this condition is commonly reported in the first three years of life in Europe and North America [1]. The frequency of OM decreases with age [2]. OM has different subtypes based on time sequence, inception, and associated symptoms. Upper respiratory tract infections, cough, pain, fever, otorrhea, nasal congestion, and discharge are among the symptoms of early acute OM [2]. During otitis media with effusion (OME) fluid accumulates in the middle ear, but no sign of acute infection exists. This condition is usually associated with temporary and mild-to-moderate hearing loss as a common early childhood disease [3-6]. Children are also at risk of recurrent OM (ROM) which is commonly complemented by OME, and recurrent acute otitis media (RAOM) afflict approximately 30% of children in the early years of life [2, 7-9].

Any type of OM can cause conductive hearing loss of about 20-30 dB, and asymmetric OM negatively affects interaural time and level difference cues cooperating binaural sound localization [10, 11]. Hearing loss is independently associated with poorer cognitive functioning, and the affected children are at risk for deficits in cognitive skills (such as attention, memory, etc.), behavior, language, and learning [12-14]. However, it is not clear whether fluctuating hearing losses due to early childhood OME can affect children's later cognitive performances or not [15]. Some studies have reported substantial relations between early childhood OME and cognitive or behavioral problems [16-23]. Some studies showed difficulties in auditory attention regulation in children suffering from OM [17, 21, 24-27]. Selective maintenance of attention and inhibition of involuntary orientation to environmental happenings has been proven to be crucial for language learning and speech processing [28]. Involuntary attention explains the recognition and selection of information about events that are possibly meaningful but unassociated with the current task [29]. However, no significant association between attention or behavior and OME was observed in other studies [30-35]. Unlikely, some of the studies in the field have methodological problems, (e.g., reviewing and study design) affected by imprecise OME detection methods, recall bias, and mere presentation of the teacher or parent's reports on behavior and attention [15, 18, 19, 30, 32, 34].

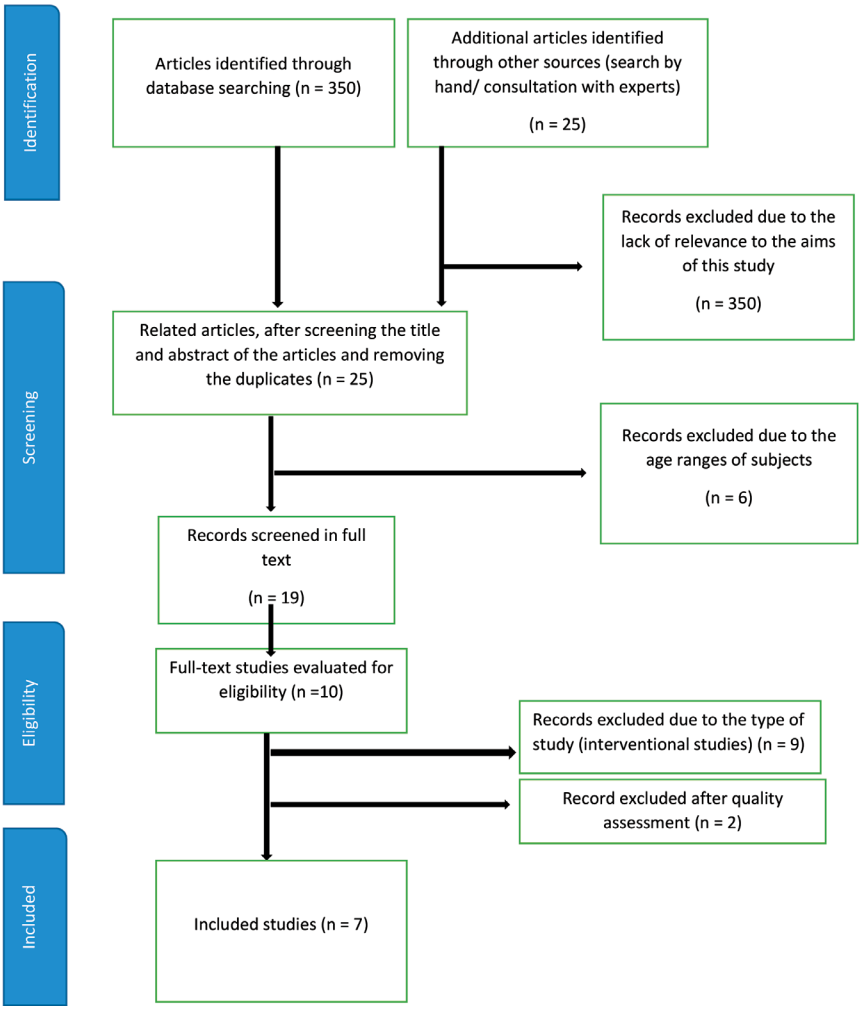

Figure 1. Study selection flow

The performances of school-aged children with a history of OM in dichotic listening tasks revealed that these children experience some deficits in selective auditory attention [24, 25, 27]. Similarly, they needed more time to reorient in behavioral attention tasks [26], and in some studies, teachers or parent's reports suggested that they were not task-oriented [12, 21].

Few studies on toddlers in this regard can be attributed to the poor co-operation of these children [17]. However, based on the questionnaire and mothers' ratings, toddlers suffering from chronic OM showed less attention in book reading during middle ear effusion [17]. The neural mechanisms of these results have remained undetermined up to this date [28]. In language-demanding environments (elementary school and preschool), the effects on attention is presented by not paying attention to directions, unfinished school assignments, behavioral noncompliance, and unpredictable working habits [36]. Some reconsidering and probable studies have provided evidence about the association of OME with the subsequent estimation of cognitive skills [16, 17, 19, 21, 22, 24, 27, 37-39]. Based on the results of some prospective studies, children with early OME scored lower on the measures of overall attention, indicated by behavioral ratings conducted by teachers or parents, classroom performance, and dichotic listening [17, 21, 24]. However, other studies have defined no significant relationships [15, 30, 32-35, 40].

According to previous studies, it seems that any type of otitis media and the resulting hearing loss can negatively affect cognitive skills, including memory, attention, as well as behavior, and language. These side effects can result in long-term adverse effects up to school age and even, involve affected persons in older generations. However, as mentioned, the results of studies are contradictory, and the impacts of this disorder are not definite. No systematic study exists to review previous studies and their consequences. In this

study, we focused on studies investigating the impact of early OM on the cognitive skills of affected school-age children.

2. Methods and Materials

Literature search strategy

A comprehensive search was conducted on published articles in databases including EMBASE, Scopus, Medline (via PubMed), Google Scholar, ProQuest, and Cochrane between January 2000 and December 2020, based on systematic reviews. The keywords and search strategies in different databases were "otitis media", "cognition", "attention", "memory", "working memory", "phonological working memory" or "behavior". In addition to the comprehensive search in databases, the reference lists of the searched articles were reviewed, and the experts in this field were consulted to introduce related studies.

Inclusion and Exclusion Criteria

The following inclusion criteria were met in the included studies:

• Contained selected keywords in the title or abstract

• Published between January 2000 and December 2020 and

• Published in the English language

Based on the inclusion criteria, a total of 375 articles were included. Two authors reviewed the abstracts of all included studies independently. A total of 366 articles were excluded based on the following exclusion criteria:

• Both authors agreed on the lack of relevance of the article to the aims of the study (Studying cognitive skills of school-aged children who had a history of OME between the ages of 2 and 5) (350 articles).

• Conducted on adolescent/adult participants (6 articles).

• The type of the study was not observational (experimental studies were excluded) (9 articles)

Hence, 9 articles remained that were fully downloaded and appraised for quality (Figure 1).

Study selection and eligibility criteria

The quality of the remaining 9 studies, all of which were cross-sectional, were apprised based on the Newcastle Ottawa scale checklist, which rates articles in terms of sample selection (4 questions), comparability of the subjects (1 question), and statistical methods and outcomes (2 questions). According to the scoring protocol of this scale, studies scored above 7 are of good quality, while the quality of studies scored below 4 are considered poor. The quality of studies with scores of 5-6 is satisfactory. To confirm the quality of included articles, two raters independently completed the quality assessment scale for each article. Finally, 7 studies that received scores of 5 to 10 from both raters were included and reviewed thoroughly. Figure 1 showed a detailed description of the inclusion and exclusion processes.

3. Results

This review included seven studies (Table 1). These articles study the effect of PM on the cognitive skills of 3 American, 1 African, 1 European, 1 Italian, and 1 Belgian children and races [12, 28, 35, 36, 40-62].

Tools used in studies

In this study, 4 studies focused on different types of attention [12, 28, 36, 62] and 3 studies examined memory [35, 40, 59].

Pneumatic otoscopy and conventional tympanometry were used in almost all studies to diagnose OM and assess the participants' hearing status every 1 to 3 months. Among included studies, three studies used both otoscopy and tympanometry [12, 28, 36], and 4 studies used tympanometry alone [28, 40-62]. In only one study, in addition to these tools, visual reinforcement audiometry (VRA) at the age of 6 months-2.5 years and play audiometry (PLAY) at the age of 2.5- 4 years were applied every three months to assess hearing sensitivity [36]. Also, only in one study, transiently evoked otoacoustic emissions (TEOAEs) were specifically used for hearing screening [28].

Different tests were used to assess children's cognitive skills in each study. Two studies used standardized measures to assess children's cognitive skills [33, 35], and only one study used parental reports to determine [40]. Although these three studies performed only one type of evaluation, the other four studies addressed both formal evaluation and parental reporting [12, 28, 36, 59].

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Table 1. Characteristics of included articles

The Effects of Otitis Media on Cognitive Skills in Older Ages (Up to 8 Years Old)	Tools Used to Examine Cognitive Variables	The Variables Examined in the Study	Clinical Scales for Diagnosis of OM	Age of Diagnosis of OME	Participants	Otitis Media Type	Reference
Little effects	McCarthy scales of children's abilities (norm-referenced tests of developmental assessment to assess cognitive skills) (McCarthy, 1972) (receptive vocabulary and the ability to produce lexical items were also examined by Peabody picture vocabulary test-revised (PPVT-R) (Okalidou, Syrika, Beckman, and Edwards, 2011), and conversational sample analysis, respectively)	Language, cognition and psychological development	Pneumatic otoscopy and tympanometry	Two months of age	A total of 241 healthy Western Pennsylvania neonates were diagnosed with OM. The condition of the participants' middle ear was continuously examined in 1, 2, and 3 years of age	Middle ear effusion(MEE)	Paradise et al., 1999 [34]
Not effective	1. Behaviour rating scale of the Bayley scales of infant development, second edition at one, two, and three years old (Provost et al., 2004). 2. The parenting stress index (PSI) (Pérez-Padilla, Menéndez, and Lozano, 2015) 3. Social skills rating system (SSRS) (Eslami, Mazaheri, Mostafavi, Abbasi, and Noroozi, 2014) 4. Hyperactivity index of the Conners' teacher/parent rating scale (Purpura and Lonigan, 2009)	Attention and behavior	Pneumatic otoscopy and routine tympanometry	The first four years of life	Eighty-five black children aged 6 to 12 months were selected, and their hearing status up to 4 years of age was assessed and monitored.	OME	(Minter et al., 2001) [11]
No significant effects were found	Multiple measures of attention including direct assessment, and behavioral observations were evaluated from kindergarten to the second grade (Alexander, 2003; Davis and Matthews, 2010; Elardo and Bradley, 1981; Mueller, Brozovich, and Johnson, 1999; Salcedo et al., 2018; Tinius, 2003).	Attention (selective/sustained attention)	Otoscopy and tympanometry	Six to forty-eight months	Seventy-four African-American neonates in the age range of 6 - 12 months were admitted.	OME	(Hooper et al., 2006) [35]

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Effective	Event-related potentials (ERPs) (with passive multi-feature paradigm with repeating standard and deviant syllable stimuli) (Shtyrov, Kimppa, Pulvermüller, and Kujala, 2011), P3a (eP3a and lP3a) and the late negativity with electroencephalography (EEG) recording	Involuntary change in selective auditory attention	Tympanometry and transiently evoked otoacoustic emissions (TEOAEs) for hearing screening	Aged 22 to 26 months	Eighteen children aged 22-26 months with recurrent acute otitis media were compared to 19 healthy children.	RAOM	Haapala et al., 2016 [27]
Effective at age 3 but not at age 5.	1. The standard progressive matrices (SPM) (Raven, 1938) 2. Measurement of the home environment The AIRE instrument (Gattshall, Shoup, Marshall, Crane, and Estabrooks, 2008) 3. Measurement of socioeconomic characteristic The socioeconomic status (SES) index (Saif-Ur-Rahman et al., 2018) 4. The Bayley scales of infant and Toddler development (the third edition) Wechsler pre-school and Primary scale of intelligence (at age 4) (Gordon, 2004), as well as Wechsler intelligence scale for children, the third edition (at age eight) (Wechsler and Kodama, 1949)	Attention, intelligence scores, The effects of OME on cognitive functions in this study was evaluated by considering the role of moderators such as the child's characteristics and socio-economic status)	Tympanometry	Infants with OME	Six hundred and ninety-eight healthy infants.	OME	Hall et al., 2014 [58]
Not effective	The online measure of phonological processing (Conway, 2003)	Auditory verbal short-term memory (AVSTM)	Tympanometry	Up to three years old.	Eighty-seven kindergarten children.	OME	Majerus et al., 2005 [38]
Effective	Child behavioral checklist (Schmeck et al., 2001) Parental report and clinical examination	Behavioral developmental delays	Tympanometry	Between the ages of three and five	Two hundred and ninety-nine children with OM between 3-5 years old.	OM	Da Costa et al., 2018 [61]

RAOM: Recurrent Acute Otitis Media; OME: Otitis Media With Effusion; OM: Otitis media.

In total, most studies included behavioral tests/measures, including parent-centered questionnaires/parent reports [12, 36, 48, 52, 59], standardized measures [12, 28, 35, 40, 41, 45], and informal researcher-made tests [33, 35]. Only in one study [28], brain function monitoring method, i.e., electroencephalography (EEG) and specifically early and later phase of the late negativity and the P3a (eP3a and lP3a) has been used to investigate the involuntary attention switch (Table 1).

Selection and size of samples

The sample size was significantly different among included studies ranging from 19 to 698 participants between six months to five years of age.

Only one study examined neonates in the age range of 22-26 months. This study included 19 neonates with OM (who were randomly selected and a tympanostomy tube was placed with the parent's consent) [28].

Two studies [35, 59] examined children who developed OM in the first 3 years of life. The total number of samples in these studies was 939 children with OM (samples were randomly selected to insert a tympanostomy tube with the parent's consent) [59].

Two of the seven included studies [12, 36] examined children who developed OM before they were four years old. The sample size was 159 children with OM who were randomly selected for tympanostomy tube placement.

Two other studies examined children who developed OM before they were four years old. The sample size of the mentioned studies was 386 children with OM that were randomly selected to insert a tympanostomy tube [40, 62].

Except for one study out of seven that examined a small sample size, the rest of the studies had sufficient sample sizes. Despite a small sample size, this study was the only study with a control group of healthy infants to compare with infants with OM [28].

4. Discussion

This study aimed to review the studies that investigated one of the main reasons for concern about early-onset OME, i.e., its side effects on cognitive skills in older children. Fluctuating hearing sensations due to repetitive middle ear infections are common in young children, but their impact on the immature central auditory system is not well determined [28]. A hypothesis is that children with sustained or repetitive OME became inattentive, specifically in noisy states, leading to attention difficulties for auditory-based information. School-age children with OME are believed to suffer from selective auditory attention deficits and present increased reorientation time of attention during behavioral tasks [24-27]. Haapala et al. pointed to the long-term effects of early-onset OME on the immature central nervous system [27]. This study aimed to investigate the impact of early-onset OME on the cognitive skills of affected school-aged children.

As mentioned in the result section, although some studies highlighted the adverse effects of OM on cognitive skills of children and proposed that if OME is persistent enough in early life, it may adversely affect children's cognitive development later in life, some studies have produced conflicting results [35, 40].

Cognition encompasses different aspects of intellectual functions and processes, including attention, learning, memory, perception and thought [12, 34]. Children with OME appear to experience difficulties in at least two critical areas of cognition, i.e., attention, and memory and these problems can also lead to behavioral problems in childhood; however, the results of the studies are controversial.

Attention

Among the four studies that examined the effect of OME on attention, Haapala et al. focused on the effect of OM on involuntary change in selective auditory attention by a non-invasive method of brain function measurement, i.e., ERP, which has proven to be a valuable technique for testing theories of perception and attention [27]. These authors conducted their study on a low number of subjects (18 participants with OME compared to 19 healthy participants) by visualizing the cognitive processing via P3a and LN and proposed that RAOM has destructive effects on neural mechanisms of involuntary attention which causes a delay in attention reorientation [28]. The results of the study conducted by Haapala were consistent with the results obtained in Da Costa's et al. study, which was conducted on a large number of subjects (299 participants) using both formal assessment and a parent report showed the correlation of OME with hyperactivity and attention difficulties in children [61].

Contrary to these two studies, the Hooper's et al. study was conducted on 74 participants and used both standardized tests and the parent's report to evaluate the effects of OME on different types of attention (se-

lective/sustained attention) during the early years of children's life [35]. The second-grade auditory attention component of the auditory attention and response set subtest of a developmental neuropsychological assessment (NEPSY) was used to measure selective auditory attention. The integrated visual and auditory continuous performance test (IVA) and the child symptom inventory (CSI) were also used to assess the selective/focus attention and the rating of attention behaviors in children, respectively. The hyperactivity index of the Conners' scale, the attention/engagement scale from the observational ratings of classrooms, and the home observation measurement of the environment were used to investigate the classroom engagement and home environment. The results demonstrated that early-onset OME and hearing loss had no significant relationship with any cross-sectional or longitudinal scores of selective/sustained attention [36]. The findings of the Hooper's study confirmed the results reported by Minter et al., which was performed on 85 participants and used formal tests, and they concluded that no relationship was observed among the early-onset OME and attention scores [35, 45, 48].

Memory

Among the included studies, three studies evaluated the impacts of OME on children's memory [34, 40, 59]. Paradise et al. examined the effect of early OM on cognition and psychological development in a large group of children (241 participants) using formal (general cognitive index (GCI) to assess memory) and informal assessments and found that persistent OME in early childhood caused limited cognitive impairments in children [34]. Consistent with their results, Majerus et al. found no relationship between OME and auditory-verbal short-term memory skills in a group of 87 kindergarten children [39]; however, Hall et al.'s study was performed on a higher sample (698 participants) and used rigorous evaluation tests to investigate the relationship between OME with transient hearing loss and attention in infants indicated that long-term OME was significantly associated with decreased intelligence quotient (IQ) (working memory index) and attention at age 3 and hearing loss at age 2 was significantly associated with lower memory scores at age 5 [59].

In sum, in this study, some of the findings indicated that persistent OME actually caused slight, limited cognitive impairments in certain groups of children and was not significantly associated. Still, as mentioned, others had conflicting results. The source of these discrepancies in the results of studies can be differences in the sample size, differences in target variables to assess cognition, variability in tests used to determine and differences in the accuracy of these tests in diagnosing cognitive problems, age of subjects to otitis media and the time since the onset of this complication in the study.

Based on the current studies on the relationship between the presence of OME history and language development, as a cognitive function, it seems that both intrinsic and environmental factors as well as the interaction of these factors may affect this relationship. Some risk factors are involved here, including a child's poor phonemic awareness skills, low-education levels of parents, and, specifically the mother's noisy child-care environment [29, 38]. Although some studies have not found significant relevance, parents of children with otitis media, audiologists, teachers, and those associated with these children should be concerned about the cognitive status of children with OM and evaluate or even provide early intervention for their child. The next point is that most studies only focus on a subset of cognitive skills, including attention or memory [34], so it is suggested that another subset of cognition be considered in the future.

5. Conclusions

Overall, according to the results of the 7 selected articles, relatively some of the articles reported a significant association between OME and cognitive skills (memory, attention, etc.) at the age of 5, while other studies did not have significant results. Therefore, the relationship between early childhood OME and cognitive skills in school-aged children is not yet definitive, and further studies are required in this field.

Ethical Considerations

Compliance with ethical guidelines

This article is a systematic review with no human or animal sample.

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Authors' contributions

Investigating and writing the original draft: Shamim Ghazi; Conceptualization, methodology, validation, project administration, reviewing, and editing: Fatemeh Haresabadi; Investigating, validating, conceptualizing, supervision, methodology, reviewing, and editing: Toktam Maleki Shahmahmood.

Conflict of interest

The authors declared no conflict of interest.

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