



## Review Article

## Neurocognitive outcomes after pediatric adenotonsillectomy for obstructive sleep apnea: A systematic review and meta-analysis

Sungjin A. Song<sup>a,\*</sup>, Anthony M. Tolisano<sup>a</sup>, Benjamin B. Cable<sup>a</sup>, Macario Camacho<sup>a,b</sup><sup>a</sup> Department of Otolaryngology-Head & Neck Surgery, Tripler Army Medical Center, Honolulu, HI, USA<sup>b</sup> Department of Psychiatry and Behavioral Sciences, Sleep Medicine Division, Stanford Hospital and Clinics, Stanford, CA, USA

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## ABSTRACT

**Objective:** To provide an up-to-date systematic review and critical appraisal of prospectively performed studies evaluating neurocognitive function in children treated with adenotonsillectomy.**Data sources:** PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library.**Review methods:** Searches were performed from inception through September 2, 2015.**Results:** Nineteen prospective studies (898 adenotonsillectomy patients) met criteria and reported neurocognitive outcomes. The average age of children was  $6.6 \pm 2.3$  years (range 2.5–14 years) and 51.1% were male. Pre- and post-operative data utilizing the Neuropsychological Developmental Assessment score demonstrated an increase from a means  $\pm$  standard deviations of  $101.5 \pm 14.7$  [95% CI 100.0, 103.0] to  $108.8 \pm 13.4$  [95% CI 107.4, 110.2],  $p$ -value  $<0.0001$  (375 children, three studies). Pre- and post-operative data utilizing the Stanford-Binet Intelligence Scales (IQ) demonstrated an increase in IQ scores from a means  $\pm$  standard deviations of  $97.1 \pm 13.8$  [95% CI 91.6, 95.4] to  $100.7 \pm 11.1$  [95% CI 100.4, 103.4],  $p$ -value  $<0.0001$  (254 children, three studies). The mean pre- and post-adenotonsillectomy apnea-hypopnea index (AHI) decreased from 8.0 to 1.8 (274 children, six studies).**Conclusions:** This meta-analysis found an improvement in neurocognitive function and IQ after pediatric adenotonsillectomy, especially in pre-school aged children. However, this must be interpreted with caution as only three studies were performed in pre-school aged children. The decreased effectiveness in older children suggests possibly a threshold age when neurocognitive deficits become irreversible.

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\* Corresponding author at: Tripler Army Medical Center, c/o Department of Otolaryngology-Head & Neck Surgery, 1 Jarrett White Road, Honolulu, HI 96859-5000, USA.  
Tel.: +1 808 433 3712; fax: +1 808 433 9033.

E-mail address: [Sungjin.a.song.mil@mail.mil](mailto:Sungjin.a.song.mil@mail.mil) (S.A. Song).

## 1. Introduction

Neurobehavioral deficits related to childhood obstructive sleep apnea (OSA) are well established, with recent studies identifying impairment of cognitive functions and behavior in children across all severities of sleep disordered breathing (SDB) from primary snoring to OSA [1]. The various dimensions of cognition include attention, executive functions, language, sensorimotor, visuospatial, and memory and learning versus behavioral components of hyperactivity, anxiety, depression, and aggression. Psychologists obtain neurocognitive measures directly from the child being tested, whereas behavioral instruments are validated questionnaires generally completed by caregivers and are subjective. Testing cognitive processes requires a systematic and comprehensive approach. The Neuropsychological Developmental Assessment (NEPSY) measures these complex cognitive processes by specific subtests to delineate the primary deficit in the chain of subprocesses. The NEPSY has been developed and revised to form a standardized test for ages 3–12 and now consists of 27 subtests divided into five functional domains [2]. NEPSY and Stanford-Binet Intelligence Scale 5th edition (SB-5 IQ) are both normed and well-validated instruments with robust validity and reliability [3]. NEPSY and SB-5 IQ have normal populations means of 100 and the standard deviations are 15 [4].

In 1976, Guilleminault et al. [5] reported improvement in neurocognitive function in children with SDB treated with adenotonsillectomy, citing improved school performance in eight children after surgery. Subsequent studies by Gozal et al. [6] in 1998 and Goldstein et al. [7] in 2000 demonstrated that poor academic performance and impaired neurocognitive functions improved following adenotonsillectomy, respectively. However, more recent studies conflict with these earlier findings, demonstrating persistence of cognitive deficits [8,9]. The most comprehensive study to date, Childhood Adenotonsillectomy (CHAT) [8], showed no difference between the adenotonsillectomy and control groups.

In an attempt to better understand the role of adenotonsillectomy on neurocognitive outcomes in children, a systematic review of the literature is warranted. The earliest systematic reviews demonstrated a paucity of high-quality evidence [10–12]. Moreover, the most recent systematic review [13] is now over five years old, and conflicting neurocognitive outcomes were identified in the two studies meeting inclusion criteria [3,14]. In the last five years, additional prospective studies (including a randomized, controlled trial) have been performed [8,9,11,15,16] that have added to the body of evidence evaluating the efficacy of adenotonsillectomy in the management of OSA. The objective of this study is to provide an up-to-date systematic review and critical appraisal of prospectively performed studies evaluating neurocognitive function data in pediatric patients treated with adenotonsillectomy.

## 2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [17] was followed as closely as possible throughout this review.

### 2.1. Search strategy

Authors S.S. and M.C. independently searched PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library from inception through September 2, 2015. MeSH terms, keywords and phrases searched included: “adenotonsillectomy,” “tonsillectomy,” “neurocognitive,” “neuro\*,” “cognition,” “snoring,” “sleep apnea,” “sleep disordered breathing,” “surgical,” “surgery,” “sleep apnea syndrome,” and “obstructive sleep apnea.” An example of a

PubMed/MEDLINE search strategy is: ((tonsil\*) OR (adenotonsillectomy\*) OR (“Adenoidectomy”[MeSH]) OR (“Tonsillectomy”[MeSH])) AND ((neurocognitive) OR (intelligence) OR (IQ) OR (cognit\*) OR (“Neuropsychological Tests”[MeSH]) OR (“Aptitude Tests”[MeSH]) OR (“Cognition/physiology”[MeSH])). All potentially relevant studies were cataloged. The full-text versions of the articles were then downloaded and reviewed for determination of inclusion in this review. The references of each study were also scanned, and any potentially relevant study was cataloged, downloaded, and reviewed. The “cited by” function on Google Scholar<sup>®</sup> was used by inputting each of the articles included in this review to attempt to identify any additional studies.

### 2.2. Study selection

For a study to be included in this review, the following inclusion criteria had to be met (using PICOS): (1) *Patients*: subjects had to be pediatric patients (<18 years old) (2) *Intervention*: who underwent tonsillectomy with or without adenoidectomy, (3) *Comparison*: pre- and post-operative data, (4) *Outcomes*: quantitative outcomes for neurocognitive function had to be reported, and (5) *Study design*: prospective studies in any languages. We excluded studies involving adults (age  $\geq 18$ ), retrospective studies, review articles, studies reporting qualitative data only, and those studies not using validated neurocognitive tests.

### 2.3. Data abstractions and study quality assessment

After the systematic search, authors S.S. and M.C. subsequently came to a consensus as to which studies met the above inclusion criteria. Full-text articles were digitally stored. Data collected from the studies included patient demographics, polysomnography (PSG) data, and neurocognitive function testing outcomes. Authors of studies not reporting sufficient data were contacted via email at least twice in an attempt to obtain further information. The National Institute for Health and Clinical Excellence (NICE) quality assessment tool was used to evaluate the quality of the included studies [18,19].

The Cochrane Collaboration’s Review Manager Software (REV-MAN) version 5.3 was used to combine data across studies. REVMAN was used to calculate the mean differences (MD), 95% confidence intervals [95% CI], and standardized mean differences (SMD). Two-tailed, unpaired *t*-tests were used for comparing means and standard deviations between studies. A *p*-value <0.05 was considered statistically significant.

## 3. Results

Two-hundred and six potentially relevant studies on the topic of pediatric adenotonsillectomy with neurocognitive function data were screened for relevance, and twenty-seven were downloaded for detailed evaluation. Four review articles, one case report, and seven studies without neurocognitive function data reported were excluded. An additional four studies were added after reviewing references. A total of 19 full-text articles met criteria for inclusion in this study (Fig. 1). There were 898 patients, ages  $6.6 \pm 2.3$  years (range 2.5–14 years), and 51.1% male.

### 3.1. Methodological quality of included studies

The studies included in this review were all prospective studies (Table 1). The Childhood Adenotonsillectomy (CHAT) study [8] was the only multi-centered, randomized, controlled study. Most studies were from a single institution and did not state that patients were consecutive. Most included studies (83%) were high quality and satisfied at least 6 of the 8 items on the NICE quality assessment tool categories.

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