Effect of Maxillary Expansion on Sleep Quality

by

Peter Sulaiman

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This thesis was presented

by

Peter Sulaiman

It was defended on

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and approved by

Dr. Joseph Petrone, Assistant Professor and Director, Department of Orthodontics and Dentofacial Orthopedics

Dr. John Grady, GKG Orthodontics, Pittsburgh PA

Dr. Ryan Soose, Assistant Professor and Director, UPMC Division of Sleep Medicine, Department of Otolaryngology

Dr. Nilesh Shah, Assistant Professor, Department of Dental Public Health

Thesis Advisor/Dissertation Director: Dr. Joseph Petrone, Assistant Professor and Director, Department of Orthodontics and Dentofacial Orthopedics

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Peter Sulaiman, DMD

University of Pittsburgh, 2020

Background

Obstructive sleep apnea (OSA) is a condition characterized by 20-40 second episodes of breathing cessation during sleep. The hard palate serves as both the roof of the oral cavity and the floor of the nasal cavity. Constriction of the palate can have profound effects on the passage of oxygen into the lungs. Polysomnography is the gold standard test for detection of the presence and severity of obstructive sleep apnea. Recently, a home sleep testing device known as the WatchPAT has been implemented as an adjunctive test. This randomized controlled crossover trial will investigate the role of maxillary expansion in children at risk for OSA using the WatchPAT as the diagnostic tool.

Methods

Twelve patients aged 12-16 without any medical syndromes were randomly assigned to either treatment or observation group. Pre-treatment (T1) records were taken on all patients. Treatment group was fitted with bonded type, rapid maxillary expanders and treated for three months according to an expansion protocol utilized by the private practice of GKG Orthodontics. A second WatchPAT study was performed at the completion of the three month period (T2). The treatment group was followed an additional three months without further expansion and a final T3 WatchPAT study was performed. The control group had a T1 WatchPAT study followed by three

months of observation without expansion. A T2 study was performed at the end waiting period and then an expander was placed. The methodology then mirrored that of the treatment group.

Results

Pre treatment AHI was found to be 2.47 episodes per hour for the treatment group. Post-treatment AHI was found to be 2.10 episodes per hour. Pre-treatment snoring frequency was measured at 2.57 percent of the night before expansion therapy and 1.60 percent after treatment.

Conclusions

AHI and snoring as measured by WatchPAT, decreased following expansion. Initial analysis of this pilot study shows a positive effect of rapid maxillary expansion on sleep quality as measured by AHI and other parameters.

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Preface

I would like to thank GKG Orthodontics for their help with this paper. Without the dedication of Dr. John Grady, Melissa Melisko-Herbinko, and Sarah Mantella, this project would never be a reality. Additionally, I would like to thank my wife, Evelyn Sulaiman, for her dedication and support throughout my academic career and specifically with this project.

1.0 Background

1.1 Sleep Architecture

Sleep architecture refers to the basic organization pattern of sleep. There are two distinct forms of sleep; non-rapid eye movement (NREM), and rapid-eye movement (REM) (Loomis, 1937). NREM is further divided into 4 distinct stages; 1, 2, 3, and 4 which denote increasing depth of sleep. NREM sleep constitutes about 80% of total sleep time, with REM sleep making up the last 20%. Each phase of sleep is readily differentiated from the next using electroencephalogram (EEG) recordings of brain activity (Dement, 1957).

Humans do not remain in one stage of sleep for too long. Instead, we cycle from stage 1 through stage 4 and then finally to REM sleep. This pattern repeats itself many times throughout the night and creates what sleep physicians call, a sleep cycle. A sleep cycle takes about 90 – 120 minutes to complete (Zepelin, 2005).

Stage 1 of NREM sleep serves a transitional role in sleep architecture. This stage usually lasts only 1 to 7 minutes and is easily disrupted by a loud noise, bright light, or other physical event. In total, stage 1 sleep only accounts for between 2 and 5 percent of sleep time (Carskadon, 2005).

A single cycle of stage 2 NREM sleep lasts 10-25 minutes during the first cycle and increases in length with each successive cycle; eventually constituting 45-55 percent of total sleep time (Carskadon, 2005). Stage 2 is a deeper level of sleep. Individuals in this stage require more forceful stimuli to be woken.

Stages 3 and 4 are referred to as slow wave sleep due to the high voltage, but slow wave activity present on EEG. Stage 3 sleep usually occurs only in the first third of the night. Cycles last only a few minutes and constitute only 3-8 percent of total sleep time. Sleep cycles in stage 4 last 20-40 minutes and make up 10-15 percent of total sleep time (Carskadon, 2005). As the deepest stage of sleep, stage 4 requires the most extreme stimuli to be aroused.

REM sleep is differentiated by rapid bursts of eye movements. The initial REM cycle only lasts 1-5 minutes; but it lengthens in later periods of the night (Carskadon, 2005). REM sleep is most associated with dreaming, as well as loss of muscle tone reflexes (Dement, 1957).

1.2 Overview of Sleep-Related Breathing Disorders

The International Classification of Sleep Disorders divides sleep related breathing disorders (SRBD) into three groups: central apnea syndromes, obstructive syndromes, and hypoventilation syndromes (AASM, 2005). Obstructive sleep apnea is a sleep disorder that usually results from upper airway obstruction in both children and adults and causes episodes of complete or partial airway obstruction during sleep. It leads to increased respiratory effort, sleep fragmentation, and alterations of gas exchange and is associated with numerous sequelae, primarily involving the cardiovascular, metabolic and neurocognitive systems. Obstructive Sleep Related Breathing Disorders (SRBDs) are a continuum of sleep problems that encompass (in increasing severity);

Primary snoring. Defined as more than 3 nights per week of snoring without any blood gas perfusion symptoms such as apneas, hypopneas, or arousals.

Upper airway resistance syndrome (UARS) includes primary snoring with increased work of breathing and arousals without gas exchange abnormalities.

Obstructive sleep apnea syndrome includes recurrent or partial upper airway obstruction with disruption of normal blood oxygenation and sleep pattern. (Marcus, 2012)

1.3 Epidemiology

Sleep problems rank fifth among the complaints reported to pediatricians by parents (Mindell, 2005). In line with this alarming statistic, it is not surprising to hear that up to 50% of children may experience a sleep problem (Owens, 2000). OSA has a peak incidence around age 2-8, most likely due to the excessive size of the lymphoid tissues in relation to the diameter of the upper airway (Marcus, 2012). Figure 1 summarizes the available epidemiological research concerning OSA among different age groups and populations. Overall, the prevalence of OSA in children varies from 1-5% and is more common in males than females (Li, 2010) Some evidence exists that shows a predilection for Americans of African descent and those with obesity (Redline, 1999).

Author	No. Subjects	Country	Age (Years)	Diagnostic Technique	Prevalence of Obstructive Sleep Apnea Symptoms
Ali et al, 1993[4]	782 screened 132 monitored	United Kingdom	4–5	Pulse oximetry, video	0.7%
Gislason et al, 1995[5]	454	Iceland	0.5–6	PSG (AHI >3)	2.9%
Redline et al, 1999[6]	126	United States	2–18	PSG	1.6% (AHI >10) 10.3% (AHI >5)
Brunetti et al, 2001[7]	895 screened 12 monitored	Italy	3–11	PSG (AHI >3)	1.0%–1.8%
Anuntaseree et al, 2001[8]	1008 screened 8 monitored	Thailand	6–13	PSG (AHI >1)	0.69%
Sánchez-Armengol et al, 2001[9]	100	Spain	12–16	PSG (RDI >10)	2.0%
Ng et al, 2002[10]	200	Hong Kong	6.4 ± 4	PSG (AHI >1)	0.1%
Castronovo et al, 2003[11]	595 screened 265 monitored	Italy	3–6	Pulse oximetry	13%
Rosen CL, 2003[12]	243	United States	8–11	PSG (OAI >1)	1.9%
O'Brien et al, 2003[13]	5728	United States	5–7	PSG (AHI >5)	5.7%
Kaditis et al, 2004[14]	3680	Greece	1–18	PSG (AHI >5)	4.3%
Sogut et al, 2005[15]	1198	Turkey	3–11	PSG (AHI >3)	0.9%
Anuntaseree et al, 2005[16]	755	Thailand	9–10	PSG (AHI >1)	1.3%

Figure 1: Prevalence of Chilhood OSA

1.4 Etiology and Risk Factors

1.4.1 Anatomic Considerations

Like many common medical conditions, OSA has a multifactorial etiology which includes anatomy, growth cycles, genetics, and bodyweight. Broadly speaking, OSA etiologies can be classified into conditions which narrow the upper airway and those that result in increased upper airway collapsibility, usually due to decreased muscle tone. (Paediatric Obstructive Sleep Apneoa, 2010). In some subjects, the anatomy of the soft palate can contribute to the risk of OSA, as an increased dimension of the uvula and tongue, along with enlarged adenoids and tonsils can

predispose one to sleep-related breathing problems.. Tonsil and adenoid enlargement are very common in children. Removal is seen as first line treatment for childhood OSA (Vale, 2017).

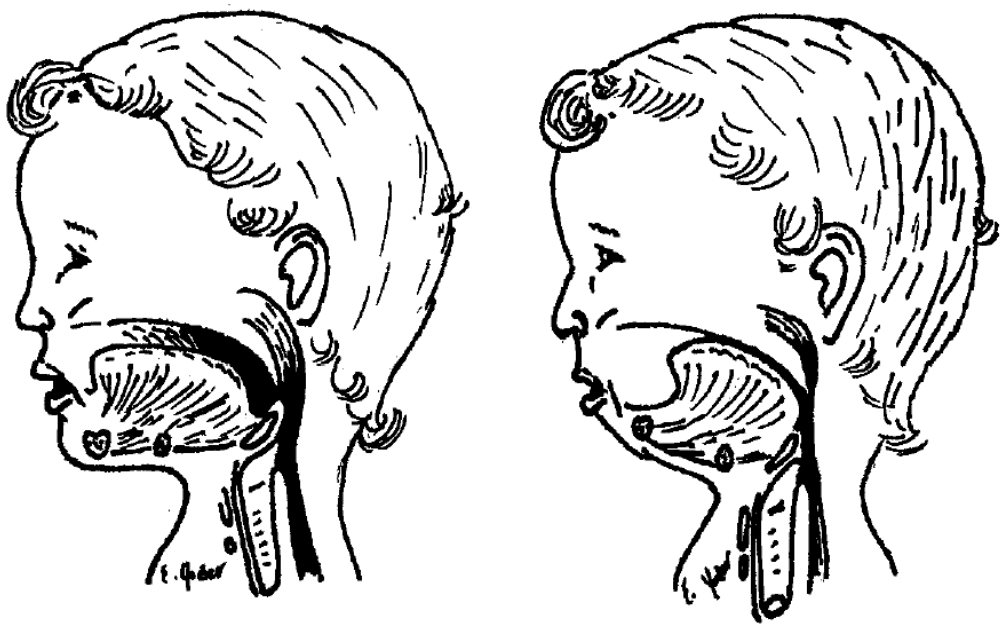

Figure 2: Effect of Micrognathia on the Airway

The pharynx is a collapsible tube with a genetically set diameter (Huang, 2017). This diameter, however, can be strongly affected by aberrant anatomical growth patterns or obstructions. Some patients are born with an airway that is simply too small to support the functional needs of the individual. Obstruction can occur easily when the airway is diminutive due to midface hypoplasia or micrognathia of the mandible. The posterior positioning of these boney structures can impinge on the pharynx and decrease the space available for the airway (Figure 2).

The most common anatomic cause of OSA in children is hypertrophy of the adenoids and tonsils. This tissue, collectively part of the lymphoid system, is largest between ages 2-8. The hypertrophy is coincident with the spike of the lymphoid growth curve and the spike in incidence of OSA (Jeans, 1981).

Nasal breathing can be affected by aberrant anatomy as well. A deviated septum can prevent adequate nasal breathing. The hard palate serves as both the roof of the oral cavity and the floor of the nasal cavity. It is hypothesized that constriction of the palate can have profound effects on the passage of oxygen through the nostrils and into the lungs. With constriction of the maxilla comes decreased total volume of the nasal passageways and a shift from nasal breathing to mouth breathing. Many studies involving lower levels of evidence have suggested a positive effect on sleep parameters after expansion of the maxillary bones with dental appliances. A systematic review and meta-analysis of 5 relevant publications evaluated the effect of rapid maxillary expansion on AHI. Results showed an overall reduction in AHI down to asymptomatic levels, and suggested use of RME on patients who do not respond well to adenotonsillectomy as well as the use of RME concurrently with adenotonsillectomy (Vale, 2017).

Alternatively, OSA can be caused by conditions that lead to upper airway collapsibility (Huang, 2017). During inspiration, the diaphragm contracts producing a reduced pressure in the chest. As the pressure drops, the lungs expand and the negative pressure is transferred to the upper airway. The respiratory effort of the diaphragm leads to a collapsing force on the pharyngeal tissues. The negative pressure which leads to the collapse is called the pharyngeal critical pressure (Pcrit). Pcrit differs from individual to individual but is largely determined by anatomy, body weight, body position, sleep stage and alcohol consumption (Sullivan, 2014). The pharyngeal muscles counteract this closing pressure by maintaining their tone throughout the inspiratory effort. During sleep, however, pharyngeal muscle tone rapidly decreases, increasing the collapsibility of the airway. REM sleep, in particular, is associated with the greatest drop in muscle tone (Huang, 2017).

1.4.2 Environmental Considerations

Inflammatory conditions such as allergic rhinitis or asthma can cause upper airway edema and decreased airway volume. Alcohol consumption, especially at dinner or during the evening, relaxes pharyngeal dilator muscles which increases upper airway resistance. Inflammatory conditions increase snoring and sleep apnea duration in susceptible individuals (Sullivan, 2014). Smokers are also at increased risk of OSA. Available evidence points to current smokers being 2.5 times more likely to have OSA than non-smokers (Kashyap, 2001). Medications which depress the respiratory drive can promote apneic episodes also. Muscle relaxants, sedative hypnotics, narcotics, and opioids all have a similar effect on OSA severity. The depression of the respiratory centers and reflexes decreases ventilator drive and increases apnea duration. The associated respiratory muscle hypotonia tends to further intensify the problem (Lee-Chiong, 2009).

1.4.3 Genetic Considerations

A study by the Cleveland Family Society showed an increased risk of OSA among first degree relatives. The heritability of OSA is estimated to be 30%. Factors such as obesity, craniofacial morphology, and soft tissue characteristics play an important role in the genetic transmission of OSA (Redline, 1995). In genome studies, a link has been found between AHI and chromosome 2p, 19p, and 8q (Palmer, 2004). Anatomic features that lead to a narrowing of the upper airway can have a profound effect on the risk for OSA. Genetically predetermined dental conditions like micrognathia, macroglossia, and midface hypoplasia can all contribute to obstruction. Some clinical syndromes that result in these dental abnormalities have been associated

with OSAS including; Prader-Willi, Bechwith-Wiedemann, Pierre Robin, and others (Follmar, 2011). A full list of medical conditions associated with OSA is listed below.

Table 1: Medical Conditions Associated with OSA

Craniofacial Syndromes	Crouzon Syndrome Aperts Syndrome Treacher Collins Syndrome Goldenhar Syndrome Pierre Robin Syndrome
Neurologic Diseases	Arnold-Chiari Malformation Meningomyelocele Cerebral Palsy Duchenne Muscular Dystrophy
Conditions with abnormal muscle tone	Down syndrome Prader-Willi Syndrome Hypothyroidism
Conditions with reduced airway patency	Adenotonsillar hypertrophy Obesity Allergic rhinitis Macroglossia

1.4.4 Obesity

Obesity is probably the most important risk factor for OSA , other than hypertrophy of the adenoids and tonsils. Obese individuals are more likely to have shorter sleep times and greater oxygen desaturation than non-obese ones. Each unit increase in BMI above the 50^{th} percentile is associated with a 12% increased risk for OSA (Hannon, 2012). Obesity can contribute to OSA through many different mechanisms. Fatty infiltrates dispersed throughout the soft tissue can narrow the diameter of the airway. Similarly, excess visceral fat attached to the chest wall can reduce the area the lungs can expand into during inspiration. This leads to a decrease in lung functional residual capacity and increases susceptibility to hypoxia during sleep (Tan, 2013). A summary of OSA etiologies is listed below.

Table 2: Summary of OSA Etiologies

Anatomic Obstruction	Adenotonsillar Hypertrophy Craniofacial Anomalies Hypertrophy of cervical lymphoid tissue Nasal Obstruction
Neuromuscular dysfunction	Congenital or acquired muscle hypertonia or hypotonia
Obesity	Upper airway fatty infiltrate Increased abdominal visceral fat Decreased lung functional capacity

Genetic Factors	Ethnicity Genetic polymorphism Airway irritants (smoking) Family history
Inflammation	Rhinosinusitis Asthma Nasal polyps Increased systemic inflammation

1.5 Symptoms of Obstructive Sleep Apnea

1.5.1 Clinical Presentation

The first clinical symptom of OSA in patients is likely to be snoring. The sound, often continuous and unbearable to a bed partner is the reason for the doctor's visit. Later, snoring can turn from a continuous noise to a pattern of interrupted silences and noises as the sufferer enters an apneic episode and is without air for some time (Paiva, 2014). Body position during sleep has a drastic effect on airway collapsibility and snoring. Sleeping on one’s back is associated with the highest risk of snoring, whereas sleeping on one’s side is associated with less incidence. While snoring is the main reason for consultation with a sleep physician, it is not the only symptom. Additional symptoms of OSA include hypersomnia manifested as easily falling asleep during

monotonous activities, dry mouth, nocturia, lack of concentration, hypertension and headaches. Table 3 includes many of the more commonly found symptoms in both adults and children (Au, 2009).

Table 3: Symptoms of OSA

Daytime Symptoms	Nighttime Symptoms
Daytime Sleepiness	Snoring
Difficulty awakening	Apneas
Headaches	Mouth breathing
Hyponasal speech	Snorting and gasping
Nasal congestion	Restless speech
Inattention	Diaphoresis
Hyperactivity	Unusual sleep position
Impulsivity	Sleep terrors
Mood instability	Sleep walking
Depression	Frequent awakenings
Aggression	Nocturnal enuresis

Excessive daytime sleepiness is a common complaint of OSA sufferers. This sleepiness can manifest in reduced performance during work or school, lack of the ability to concentrate, and even increased risk of automobile accidents. Most adult sufferers report excess daytime sleepiness. In children, daytime sleepiness is socially accepted and seen as normal. Because of this, OSA can remain undiagnosed for long periods of time. Whereas sleepiness is the symptom with the most logical biologic basis, in many children the opposite symptom can be seen more often: sleep-deprived children suffering from OSA commonly have hyperactivity (Paiva, 2014). Nocturia, or bedwetting, is also seen in children. An increase in negative thoracic pressure caused by OSA can compress the bladder and lead to symptoms (Jeyakumar, 2012).

The open mouth posture adopted by patients to compensate for poor breathing can have effects on the dentition. The dental literature refers to this open mouth posture associated with

lymphoid hyperplasia or nasal obstruction, as adenoid facies. Adenoid facies has been vaguely defined as a long, thin face with malar hypoplasia, high-arched palate, narrow maxillary arch, and angle class II malocclusion (Elluru, 2005). With the mouth open due to obstruction, the tongue places less pressure on the palate. With the mouth in a chronically open position, the forces on the mandible, temporal-mandibular joint, and dental arches are altered. These small force changes are thought to lead to aberrant growth such as maxillary constriction, forward head posture, and an increase in vertical height of the lower face (Elluru, 2005). This open mouth posture can directly affect the dentition. Dry mouth and diffuse gingival inflammation can alter the color and texture of the gums and make the patient more prone to periodontal conditions (Kaur, 2018).

1.5.2 Neurocognitive Abnormalities

Clinical trials have elucidated the prevalence of memory and concentration problems, mood disturbances and fatigue in those suffering from OSA. In adults, OSA can lead to lack of concentration and poor performance at work. Without sleep, the risk of automobile accidents is high. In 2000, there were 800,000 OSA related car accidents in the United States. The real economic cost of these accidents, attributable to OSA, are 15.9 billion US dollars and 1400 lives lost. (Sassani, 2004).

Neurocognitive abnormalities are most clearly seen in school-age children. Cognitive deficits associated with OSA include poor school performance, poor language skills, poor verbal skills, lower general intelligence, impaired ability to learn and ADHD-like symptoms. In a study of first grade children, OSA was shown to be disproportionally high in children ranked in the bottom 10% of the class (Gozal, 1998). A recent meta-analysis including 16 studies confirmed

clear links between OSA and poor academic performance for core academic domains related to language, arts, maths and science in school-aged children (Galland, 2015).

In adults, OSA disrupts sleep form architecture leading to symptoms of excessive daytime sleepiness, especially at work or during monotonous activities. Children differ in that their sleep architecture is commonly preserved. Instead of presenting with the excessive sleepiness seen in adults, the opposite symptom, hyperactivity, can be seen. This leads to abnormally high levels of ADHD diagnosis in this population. Commonly, children with ADHD or other hyperactivity related disorders, simply have OSA and are not sleeping as much as they need (Khalyfa, 2012).

Depression is much more common in OSA patients. 21-41% of those with OSA also have depression, compared to only 9% in non-apneic patients (Harris, 2009). This symptom of OSA is bidirectional. OSA is considered a risk factor for depression and depression is considered a risk factor for OSA. Clinically depressed patients commonly report symptoms of OSA which include sleepiness, fatigue, and lower quality of life. Treating OSA sometimes, but not always, cures depression (Harris, 2009).

Even after successful treatment of OSA, the neurocognitive effects may persist. A study by George et.al in 1997 showed that adults who underwent 12 months of positive airway pressure treatment for their OSA improved greatly in their performance on driving simulators, but still performed lower than those without OSA (George, 1997). In children, verbal and visual learning seem to normalize after only a few weeks of OSA treatment. Other areas, such as math and perceptual ability show an initial improvement but do not rebound fully. Even after curing of the OSA this leaves children with decreased cognitive functioning overall, compared to controls (Ferini-Strambi, 2003).

1.6 Diagnosis

1.6.1 Clinical Evaluation

Those suspected of having OSA should undergo a physical exam with accompanying diagnostic tests. The clinical exam should include examination of bodyweight along with facial asymmetry or aberrations which predispose one to OSA. Men with waist measurements over 102cm and women with waist measurements over 88cm are at increased risk for OSA (Fogelholm, 2007). The nose and nostrils are evaluated for asymmetry, obstructions, septal deviation, and nostril collapse upon inhalation. The upper airways are similarly evaluated for size and shape. Enlarged tonsils and adenoids, along with enlarged uvula, tongue, or narrow palate are noted. A low soft palate, diagnosed via the Mallampatti classification (Figure 3), predisposes one to a physical obstruction likely to cause OSA (AASM, 2005). Tonsils are classified based on their degree of hypertrophy. Grade I tonsils are inside the tonsillar fossa and the posterior pharyngeal pillars. Grade II tonsils occupy 25% of the oropharynx. Grade III tonsils occupy 50% of the oropharynx and Grade IV tonsils at least 75% of the oropharynx and usually meet at the midline, severely limiting airflow (Brennan, 2017).

1.6.2 Sleep Questionnaires

Sleep questionnaires are useful tools for identifying those suspected of having sleep-related breathing disorders . Questionnaires serve as simple, cost-effective screening methods that can be given to large quantities of patients. Available questionnaires include the Stanford Sleepiness

Scale, Epworth Sleepiness Scale (ESS) and Pediatric Sleep Questionnaire (PSQ). The Stanford sleepiness scale is a basic introspective measurement of sleepiness that can alert a physician to an abnormality (Figure 4) (Maclean, 1992). The Epworth Sleepiness Scale (Figure 5) is an 8 question self-diagnostic survey. Respondents are asked to rate, on a 4 point scale, their chances of falling asleep during different daily activities. The scale ranges from zero to 24 with higher numbers indicating an increased daytime sleepiness (Rosenthal, 2008). The Pediatric Sleep Questionnaire (Figure 6) is a 20 question series of yes/no answers that is filled out by the parent or guardian of a minor. Positive answers to 8 or more of the 20 questions indicates increased risk of OSA and warrants further diagnostic testing (Peña-Zarza, 2012).

1.6.3 Polysomnography

The clinical exam is but one small part of comprehensive diagnosis. The gold standard test of sleep diagnosis was, is, and is likely to be remain polysomnography (PSG). PSG is used to definitively diagnose the presence of sleep problems and their severity. This hospital based diagnostic test consists of an EEG, electro-oculogram (EOG), electromyogram (EMG) of the mentalis muscle, nasal and oral airflow cannulas, pulse oximetry, microphone (to measure snoring in decibels), ECG, blood pressure, and end tidal PCO2. In clinical terms, the PSG measures sleep stage, sleep quantity and sleep quality. Full PSGs are labor and resource intensive. They require a private room in a hospital with full time monitoring by a nurse or other health care practitioner. The results of the test must then be sent to a qualified sleep physician for interpretation.

1.6.4 Adjunctive Tests

Although PSG provides a comprehensive analysis of sleep parameters, the test has many drawbacks. Disadvantages include patient discomfort, high cost and the need for technical expertise to monitor and analyze the test. Watch Peripheral Arterial Tonometry (watchPAT) is a portable wrist- borne device that measures peripheral arterial blood volume changes, along with actigraphy to accurately record sleep parameters. The peripheral arterial volume changes in the fingertip have been shown to correlate well with sympathetic activation of the nervous system. Many research publications in the past decade have reported a strong relationship between sympathetic activation and rapid eye movement (REM) sleep and sleep stage (Yalamanchal, 2013). The watchPAT is capable of measuring with high accuracy, the presence and quantity of apneic episodes measured by AHI. Additionally, PAT can be easily coupled with technologies that measure total sleep time (TST), body position, blood oxygen saturation, RDI, ODI, and other parameters.

A systematic review and meta-analysis of available research comparing PSG and watchPAT showed a high correlation between the two tests. Comparison of AHI between the tests showed a correlation coefficient of $r = 0.889$. Comparison of the oxygen desaturation index (ODI) was shown to be $r = 0.942$. Overall, sensitivity was found to be 76.9% with specificity at 78.3% (Tanphaichitr, 2018). Another systematic review comparing at home sleep devices found a high specificity (96.05%) but a low sensitivity (67%) of PAT when measuring AHI score. Overall, they concluded that AHI can be underestimated in at-home sleep studies. The reasons for this include, (1) AHI is calculated using total recording time instead of total sleep time, (2) hypopneas resulting in an arousal but not a desaturation are not scored, and (3) information concerning sleep architecture cannot be measured (Tan, 2015). The high specificity allows PAT to be used as a very

practical and accurate means of screening potential OSA patients. Because of its low sensitivity, if OSA is suspected in patients without positive PAT results, a polysomnography is still warranted. At this time, watchPAT has been validated and FDA approved for use in adults and in children above age 12.

1.6.5 Diagnosis of Severity

The American Association of Sleep Medicine has clear diagnostic criteria for OSA. These criteria include:

1. At least one of the following:
    a. Patient complains of excessive daytime sleepiness, unintentional sleep episodes during daytime, fatigue, or insomnia.
    b. The patient wakes gasping for air or choking.
    c. The bed partner reports loud snoring or difficulty breathing at night.
2. Polysomnography displays one or more of the following:
    a. Five or more scored apneas per hour for adults
    b. One or more scored apneas per hour for children
    c. 15 or more total scored apneic events during the sleep cycle
3. The disorder is not better explained by another syndrome or condition (AASM, 2005)

To better understand diagnosis of sleep disorders, an understanding of types of respiratory events is necessary. As defined by the American Association of Sleep Medicine, an apnea is a complete cessation of airflow lasting 10 seconds or longer. In contrast, a hypopnea is a partial

cessation of airflow characterized by a 30% or greater reduction in airflow or a 3% reduction in oxygen saturation. A respiratory effort related arousal (RERA) is a breathing event which does not meet the threshold of a hypopnea or apnea; but causes a patient arousal from sleep (AASM, 2005).

The AHI or apnea hypopnea index is the most used sleep statistic for quantifying OSA severity. The AHI is a numerical measure of the number of apneas or hypopneas per hour of sleep (AASM, 2005). In adults, an AHI of less than 5 is thought to be harmless. An AHI of 5-15 per hour is consistent with mild OSA. An AHI of 15-30 is moderate OSA, and anything over 30 apneas per hour is considered severe OSA. Children differ slightly in that anything over 1 apnea per hour is considered abnormal (Mitchell, 2015).

The most important problem with AHI is that it does not give any information concerning how much the oxygen saturation drops during a particular episode (Temirbekov, 2018). The AHI provides an accounting for how many times a patient stops breathing throughout a night but it does not correlate this with the severity of the drop in arterial oxygen content. The oxygen desaturation index (ODI) solves this problem by describing all events in which the blood oxygen saturation drops by more than 4% for longer than 10 seconds (Temirbekov, 2018).

Another measure of apneic events is the respiratory disturbance index (RDI). This measure differs from the AHI in that it includes full apneas, hypopneas, and RERAs in its accounting (AASM, 2005). The RDI is a quantification of the total number of sleep events during the night.

1.7 Treatment

1.7.1 Weight Loss

As previously stated, obesity is probably the most significant risk factor for OSA. Every unit increase in BMI above the 50th percentile is associated with a 12% increased risk of OSA. First line treatment for many overweight patients is likely to be weight loss counseling. Data exists for the positive impact of weight loss treatment on OSA for adolescent and adult patients. In a study by Verhulst et.al., researchers showed a significant decrease in AHI after weight loss of at least 24 kg. All patients had at least a 30% decrease in AHI with some experiencing total resolution. Currently, there are no studies showing the effect of weight loss on younger children. (Verhulst, 2009).

1.7.2 Surgery

Adenoidectomy and tonsillectomy are the treatments of choice of adenotonsillar hypertrophy contributing to OSA. The Childhood Adenotonsillectomy Trial (CHAT study) found better outcomes concerning long-term resolution of OSA, with early AT surgery compared with watchful waiting (Mitchell, 2015). For this reason, AT is seen as the first line treatment of choice for children with diagnosed OSA and clinical symptoms. Withholding treatment, however, may be appropriate for those with only mild symptoms and low AHI numbers. Following the peak of lymphatic tissue growth between ages 2-8, the tissue atrophies back to a more normal size (Vale, 2017).

Uvulopalatopharyngoplasty, a surgical procedure where soft tissue of the pharynx is removed or reshaped, is not recommended at this time. Studies evaluating the effectiveness of these methods only shows at most, a 50% decrease in AHI, and in only 50% of those patients treated (Caples, 2010). In patients with dysmorphic jaws, maxillomandibular advancement (MMA) has been proven to provide resolution of OSA with few side-effects (Spinzia, 2017).

1.7.3 Positive Airway Pressure

Positive airway pressure (PAP) is the gold standard treatment for OSA in adults. This type of non-invasive ventilation overcomes the negative pressure built up by the diaphragm during inhalation and prevents the pharyngeal muscles from collapsing inward. Additionally, PAP can increase the pharyngeal volume; decreasing the propensity for airway collapse (Paiva, 2014). For children in whom adenotonsillectomy is contraindicated or insufficient for resolution, Continuous PAP or CPAP may be titrated and applied. These appliances remain uncomfortable for patients making cooperation less than ideal in most cases.

1.7.4 Oral Appliances

Dental protrusion devices are used to mechanically enlarge the pharyngeal cross-section during sleep. By advancing the mandible, the tongue and other soft tissue which would normally impinge on the airway are moved to a more anterior position, away from the airway. The appliance functions by attaching to the maxillary and mandibular jaws intraorally and forcing the lower jaw

to protrude in relation to the maxilla. These devices are recommended in patients with primary snoring, in patients with mild to moderate OSAS who prefer appliances, and in those who do not respond to or cannot tolerate CPAP.

In 1860, RME therapy was first published as an orthodontic correction of maxillary constriction. This dental device is placed into the patient's maxilla and turned via a jack screw to increase the size of the patient's maxilla. This therapy was first linked to SDB, when it was shown to decrease nocturnal enuresis in children (Huynh, 2015). A number of smaller studies have demonstrated a significant and clinically relevant decrease in AHI after rapid maxillary expansion. If RME is performed early enough, nasal breathing may resume which may render adenotonsillectomy unnecessary (Vale, 2017).

Purpose of the Present Study

The purpose of this study is to discover whether RME leads to an improvement in sleep quality and a reduction in the signs and symptoms of OSA. Previous low-level studies have identified a correlation between RME and AHI. This study aims to be the first high level randomized controlled clinical trial to provide a correlation between RME and measures of sleep quality as measured by a Home Sleep Test .

2.0 Materials and Methods

2.1 Assurances

An application for a full Board review was filed with the University of Pittsburgh Institutional Review Board. The research council approved the study design and methods for this randomized controlled crossover study and assigned the study to a category of minimal risk to the patient.

2.2 Sampling

A power analysis performed before sample allocation showed that 12 subjects would be needed to generalize the results of this study to the general population. A power of 80%, alpha of 0.05, and effect size were chosen. The effect size was taken from the existing literature concerning rapid maxillary expansion and was set at 10 units of AHI.

2.3 Inclusion / Exclusion Criteria

Inclusion criteria included patients between the ages of 12 and 16 who were at risk for clinically-significant SDB as revealed through the Pediatric Sleep Questionnaire (PSQ). These subjects presented with a noncontributory medical history other than the possibility of sleep

disordered breathing. Exclusion criteria included previous orthodontic therapy, previous rapid maxillary expansion therapy and any previously diagnosed medical syndrome.

2.4 Steps to Control Bias

Randomization was completed using a pre-determined, computer generated, separating algorithm (graphpad) which allocated patients into two equal groups for the control and treatment. The clinicians which placed the expanders were unable to be blinded as they could physically see the appliance. After the information from the sleep studies were gathered and de-identified it was given to a specialist statistician for interpretation and analysis. The statistician was blinded to which subjects were part of the control or treatment group.

2.5 Research Methodology

To gain interest in the study, an IRB-approved research poster was placed at two locations inside the private practice of GKG Orthodontics. This poster asks parents if they were "Concerned About Your Child's Sleep? Ask About Our Research Study!". All new patients at the private practice of GKG Orthodontics are given a Pediatric Sleep Questionnaire (PSQ) as part of their medical history forms. From previous research, a patient with eight or more "yes" answers on the PSQ is at risk for sleep disordered breathing (Peña-Zarza, 2012). All patients with positive PSQ

are counseled as to the possible meaning (SDB) of these results by the clinicians at GKG and asked if they would like to join a sleep study. When a parent or guardian shows interest in the study, a separate appointment is made with Dr. Peter Sulaiman. At the following appointment in a private office, the subject is screened for inclusion and exclusion criteria. All parts of the study are explained thoroughly and the parent is asked if they would consider taking part in the research. When parents agree to enrollment, all questions and concerns are answered and a consent form is signed by the parent and subject. Instructions for the WatchPAT home sleep test device are given. The subject is then randomly allocated into either the treatment or control group using a computer-generated separating algorithm. This algorithm replicates the separating process of placing six red cards (treatment group) and six blue cards (control group) into a hat and randomly drawing one for each subject who agrees to study inclusion. Patients in both groups will be analyzed via watchPAT and their pre-treatment (T1) data recorded. Guardians will place the device on the patient before bedtime and remove the device after the child wakes up. Parameters measured by the device include total sleep time (TST), % REM of sleep time, % light sleep time, % deep sleep time, respiratory disturbance index (RDI), apnea hypopnea index (AHI), oxygen desaturation index (ODI), % sleep time in supine position, % sleep time in non-supine position, supine RDI, supine AHI, supine ODI, oxygen saturation minimum, % time spent under 90% oxygen saturation, % time spent snoring louder than 45 decibels. The data collected by the WatchPAT device will be stored on a password protected/HIPPA compliant server of the PI and given to Dr. Ryan Soose upon completion of the study.

Soon after their T1 data collection, the patients allocated to the treatment group will be fitted with bonded type rapid maxillary expanders by Dr. John Grady and an orthodontic assistant. The expanders will be fabricated by taking an impression of the patient's maxillary arch using

alginate impression material. This impression will be sent to an orthodontic lab to have a custom fit expander produced. The RME will be cemented onto the patient's dentition using glass ionomer temporary cement. Maxillary expansion will be performed daily by the subjects parent or guardian, with one activation of the expansion screw five times each week for a three month period. Patients will return to the office of GKG Orthodontics for evaluation by Dr. John Grady. After completion of expansion, a post-treatment (T2) WatchPAT session will be undertaken and data stored in the data server. Analysis will be performed on the treatment group T1-T2 sample to evaluate the changes in the parameters previously discussed. Bonded expanders will be left in place 3 additional months to allow the bone to consolidate. At the 3-month stabilization benchmark, a third WatchPAT analysis will be performed again (T3) and the RMEs will be removed from the treatment group. The protocols for the control and treatment groups will now be reversed. Those subjects allocated to the control group for the purpose of "watchful waiting" will have a T1 WatchPAT study completed after consents have been signed. The results of this study will be stored with the other results, on the password protected server of the PI. Following the study, subjects in this group will wait three months without any treatment (expander) and have a T2 WatchPAT study performed at the completion of the three month waiting period. After the WatchPAT study has been logged, these subjects will be fitted with a rapid maxillary expander and asked to turn the appliance according to the previously described protocol. A final T3 WatchPAT study was performed at the completion of the turning regimen.

2.6 Outcome Measures

Change in sleep quality as measured by multiple variables of the WatchPAT sleep study. The data obtained from the WatchPAT will include total sleep time (TST), % REM of sleep time, % light sleep time, % deep sleep time, respiratory disturbance index (RDI), apnea hypopnea index (AHI), oxygen desaturation index (ODI), % sleep time in supine position, % sleep time in non-supine position, supine RDI, supine AHI, supine ODI, oxygen saturation minimum, % time spent under 90% oxygen saturation, % time spent snoring louder than 45 decibels.. The major outcome variable will be the change in AHI before and after rapid maxillary expansion treatment.

3.0 Results

Among the control group subjects, total sleep time increased from an average of 7.48 hours to 8.04 hours after a 3 month period (Figure 3). Percent REM sleep increased 9.53% from a baseline of 27.0% to 29.58% at T2. Percent light sleep stayed relatively unchanged at 50% of total sleep time. The percent of time spent in deep sleep decreased from 22.60% of the night to 19.95%. Respiratory disturbance index decreased from 12.24 to 9.95, AHI increased from 3.86 to 4.20, and ODI decreased from 1.50 episodes per hour of sleep to 0.90 episodes after 3 months. Oxygen saturation increased from an average of 90.40% to 93.00%. The percent of sleep time spent supine was 41.80 percent and 58.18 percent non supine. at baseline. At T2 these values were 49.15 and 50.80 respectively. Supine RDI decreased slightly from 11.72 to 11.50. Supine AHI increased from 4.08 episodes per hour on average to 5.65 episodes. Supine ODI decreased from 1.66 to 0.10; a

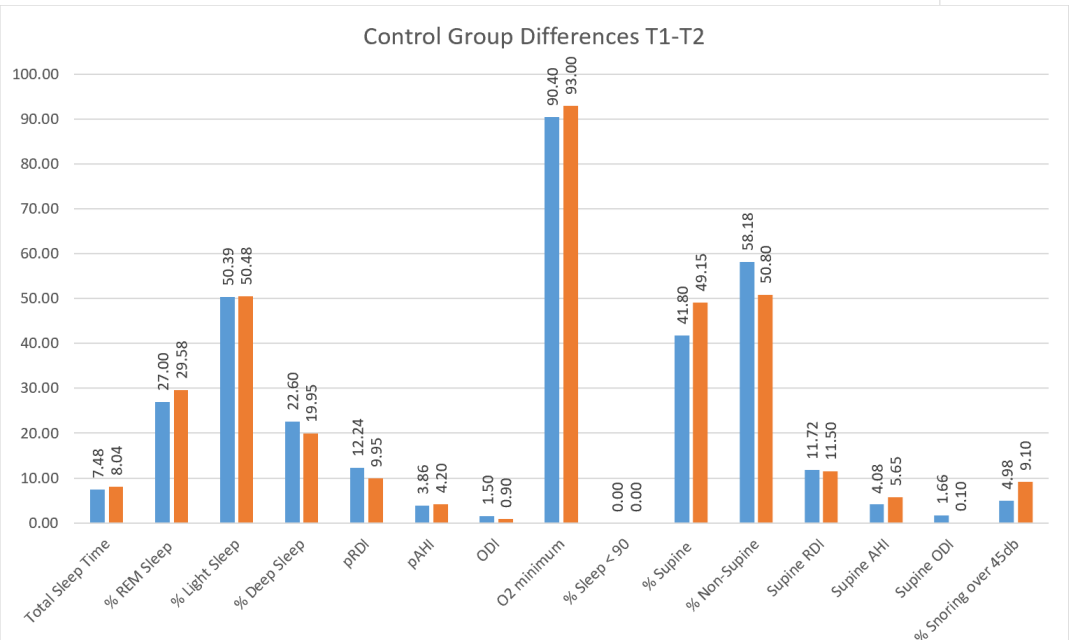

Figure 3: Control Group Differences

93.98% decrease. Snoring, measured as noise over 45 decibels, increased from 4.98 percent of the night on average to 9.10%.

The treatment group's average total sleep time increased from an average of 6.44 hours to 7.63 hours after treatment (Figure 4). Percent REM sleep decreased 7.72% from a baseline of 24.0% to 22.15% at T2. Percent light sleep fell 10.27% from 49.32 to 44.25. One of the larger increases in the data from T1 to T2 was the percent of time spent in deep sleep. At T1, the treatment group averaged 26.68% deep sleep and 33.60% after treatment. Respiratory disturbance index decreased from 9.53 to 6.30, AHI decreased from 2.47 to 2.10, and ODI decreased from 1.03

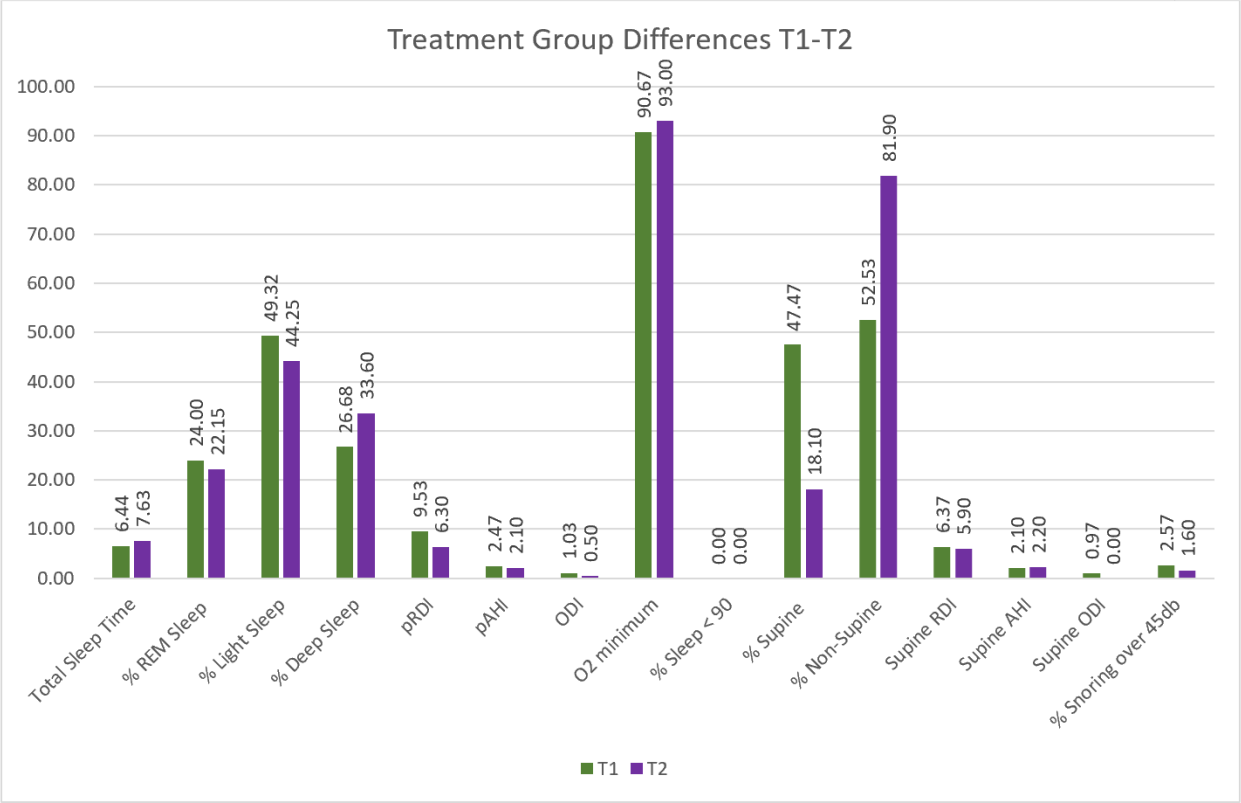

Figure 4: Treatment Group Differences

episodes per hour of sleep to 0.50 episodes after expansion therapy. Oxygen saturation minimum increased from an average of 90.67% to 93.00%. The percent of sleep time spent supine was 47.47 percent and 52.53 percent non supine. at baseline. At T2 these values were 18.10 and 81.90 respectively; a change of over 50%. Supine RDI decreased from 6.37 to 5.90. Supine AHI increased very slightly from 2.10 episodes per hour on average to 2.20 episodes. Supine ODI decreased 100% with our data set. Baseline ODI for the treatment group was 0.97. Average ODI at T2 was 0.00 episodes per hour of sleep. Snoring decreased from 2.57 percent of the night on average to 1.60%; a decline of 37.66%. Table 4 summarizes the data set.

Table 4: Study Data

Parameters	Control			Treatment		
	T1	T2	% Change	T1	T2	% Change
Total Sleep Time	7.48	8.04	7.52%	6.44	7.63	18.48%
% REM Sleep	27.00	29.58	9.53%	24.00	22.15	-7.72%
% Light Sleep	50.39	50.48	0.17%	49.32	44.25	-10.27%
% Deep Sleep	22.60	19.95	-11.76%	26.68	33.60	25.94%
pRDI	12.24	9.95	-18.71%	9.53	6.30	-33.92%
pAHI	3.86	4.20	8.81%	2.47	2.10	-14.86%
ODI	1.50	0.90	-40.00%	1.03	0.50	-51.61%
O2 minimum	90.40	93.00	2.88%	90.67	93.00	2.57%
% Sleep < 90	0.00	0.00		0.00	0.00	
% Supine	41.80	49.15	17.58%	47.47	18.10	-61.87%
% Non-Supine	58.18	50.80	-12.68%	52.53	81.90	55.90%
Supine RDI	11.72	11.50	-1.88%	6.37	5.90	-7.33%
Supine AHI	4.08	5.65	38.48%	2.10	2.20	4.76%
Supine ODI	1.66	0.10	-93.98%	0.97	0.00	-100.00%
% Snoring over 45db	4.98	9.10	82.73%	2.57	1.60	-37.66%

4.0 Discussion

Data was separated into two groups. Group 1 consists of only the numerical scores for the subjects in the control phase. As previously stated, subjects randomized to the control group had a baseline sleep study and a final study 3 months later. The purpose of this control group was twofold. First, to be used as a baseline to compare against the results of the treatment group; and two: to determine if sleep parameters remain consistent over time or change. Table 4 shows the percent change of various parameters from T1 to T2. The apnea hypopnea index was the main variable of comparison. Of interest is a slight increase in AHI for the control group from a baseline average of 3.86 to 4.20 after a 3 month waiting period. The treatment group, however, showed a 14.86% decrease in AHI. Impressions from limited data indicate a slight worsening of sleep quality over time for untreated controls and a modest increase in sleep quality for subjects treated with rapid maxillary expansion. This finding is consistent with anecdotal and low level studies published on the effect of RME on AHI.

Of further interest is an apparent shift from light to deep sleep. Over 3 months, controls showed a substantial decrease in time spent in deep sleep. Treated subjects showed a decrease in the percentage of time spent in light (transient) sleep stages with a large increase in the amount of time spent in deep sleep stages.

Snoring is never a normal finding in children. Snoring in children indicates a sleep problem of some kind that requires further testing and further evaluation by a trained sleep specialist. In the control group we found an increase in snoring from 4.98% of the night to 9.10% over three months of watchful waiting without treatment. Conversely, the group treated with expansion therapy had a 37.66% decrease in snoring. Further analysis shows an increased positive effect of the treatment

group compared to the control. The control group's average RDI scores decreased 18.71% compared to a 33.92% decrease for those treated with expanders. ODI decreased 40.00% for the control group and 51.61% for the treated subjects. For most sleep parameters, the treatment group outperformed the control group. This is positive news for those seeking to use RME to benefit those with sleep disordered breathing. The data in this thesis project shows a positive effect of RME on sleep quality compared to untreated controls.

May I suggest the following: hypertrophy of the adenoids and tonsils leads to a soft tissue tube (the pharynx) that is obstructed. Research done by Moss in the dental literature suggests that soft tissues and airways play an important role in the formation and shape of hard tissues. In essence, "spaces make faces." A normal functioning airway helps in the adaptation and creation of a properly formed and useful hard tissue structure. When children are deprived of this normal anatomy and diameter of their airways, the hard tissues grow abnormally, leading to a dolichocephalic facial form with a high narrow palate and open mouth breathing posture. In these children, there are actually 2 concurrent problems. One: the enlarged adenoids and tonsils are obstructing a portion of the airway diameter and are preventing normal flow of oxygen. Two: in response to this airway, the child's boney tissues have grown abnormally in adaptation to this airflow restriction. Recent studies by Lee et.al. actually show that despite T&A treatment, children may still present with mouth breathing and elevated AHI (Lee, 2015). Other studies report 20% of children still have OSA following T&A. (Tang, 2016) Treatment therefore, is actually twofold. First AT surgery should be performed to recreate the normal anatomy of the airway. Second, RME should be performed to reproduce normal boney proportions of the maxilla. If caught early enough, the idealized airway along with the idealized boney structure should allow the patient to grow in a manner so as to make the later diagnosis of sleep apnea unlikely.

Limitations of this study are based on the completeness of data collection. During the T2 and T3 collection timeframe, the coronavirus pandemic shut down most of the country. In line with state and local ordinances, all research data collection was put on hold. As a result, much of the T2 and T3 data was not obtained. Due to this limitation and to the status as a pilot study, conclusions are based on averages without further statistical analysis. All conclusions should be regarded as anecdotal until the completion of the data collection and publishing of the final paper.

This thesis seeks to be the first high level study to find an association between rapid maxillary expansion and sleep quality. Previous studies are anecdotal in nature without high level research methodology, control groups, or analysis of findings. Although the goals have not been met for this thesis, there is hope that this research will be taken to its completion. Further studies should focus on cementing the link between rapid maxillary expansion and sleep quality. If a positive link is found between the two, it would be helpful to determine if a positive treatment effect can be found for younger children, and if that effect maintains itself further into adolescence and even adulthood.

Appendix A : Figures

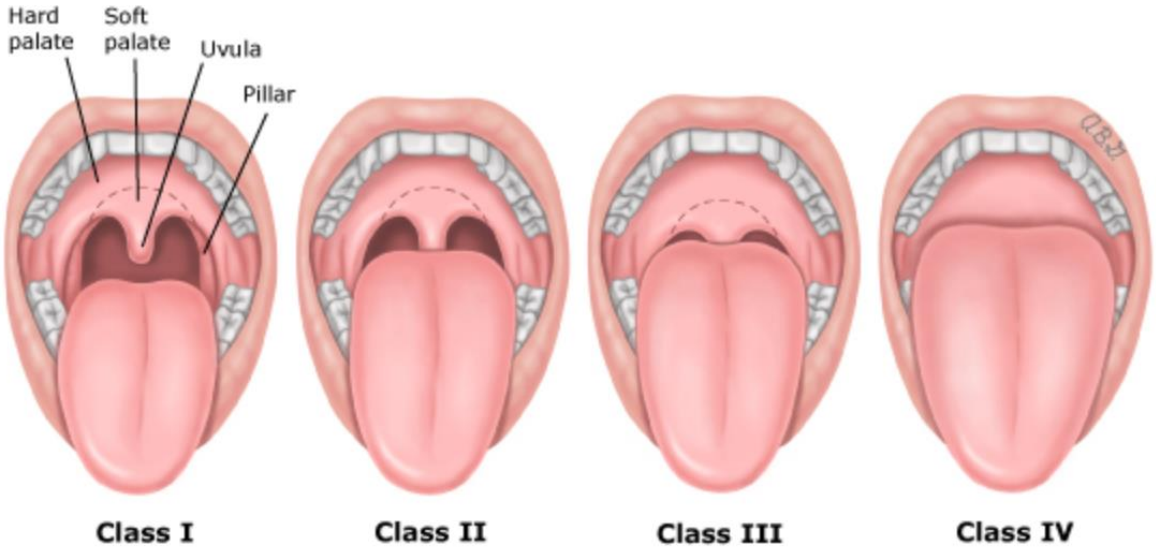

Figure 5: Mallampati Classification

Appendix B : Sleep Questionnaires

Degree of Sleepiness	Scale Rating
Feeling active, vital, alert, or wide awake	1
Functioning at high levels, but not at peak; able to concentrate	2
Awake, but relaxed; responsive but not fully alert	3
Somewhat foggy, let down	4
Foggy; losing interest in remaining awake; slowed down	5
Sleepy, woozy, fighting sleep; prefer to lie down	6
No longer fighting sleep, sleep onset soon; having dream-like thoughts	7
Asleep	X

Figure 6: Stanford Sleepiness Scale

Situation	Chance of dozing			
Sitting and reading	0	1	2	3
Watching TV	0	1	2	3
Sitting inactive in a public place (e.g. movie theatre or a meeting)	0	1	2	3
As a passenger in a car for an hour without a break	0	1	2	3
Lying down to rest in the afternoon when circumstances permit	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after lunch	0	1	2	3
Sitting quietly after lunch	0	1	2	3

Figure 7: Epworth Sleepiness Scale

IRB.

Airway History			
Patients Age:	**For internal use only:**	• Exp	• Non-exp
Sex:	Number:	• Initial	• Final
If this patient is under the age of 18 please answer the following questions:			
While sleeping, does your child…			
…snore more than half the time?		☐Yes ☐No ☐Don't Know	
…always snore?		☐Yes ☐No ☐Don't Know	
…snore loudly?		☐Yes ☐No ☐Don't Know	
…have "heavy" or loud breathing?		• Yes ☐No ☐Don't Know	
…have trouble breathing, or struggle to breathe?		☐Yes ☐No ☐Don't Know	
Have you ever seen your child stop breathing during the night?		☐Yes ☐No ☐Don't Know	
Does your child…			
…tend to breathe through the mouth during the day?		• Yes ☐No ☐Don't Know	
…have a dry mouth on waking up in the morning?		☐Yes ☐No ☐Don't Know	
…occasionally wet the bed?		☐Yes ☐No ☐Don't Know	
Does your child…			
…wake up feeling *un*-refreshed in the morning?		☐Yes ☐No ☐Don't Know	
…have problem with sleepiness during the day?		☐Yes ☐No ☐Don't Know	
Has a teacher or other supervisor commented that your child appears sleepy during the day?		☐Yes ☐No ☐Don't Know	
Is it hard to wake your child up in the morning?		☐Yes ☐No ☐Don't Know	
Does your child wake up with headaches in the morning		☐Yes ☐No ☐Don't Know	
Did your child stop growing at a normal rate at any time since birth?		☐Yes ☐No ☐Don't Know	
Is your child overweight?		☐Yes ☐No ☐Don't Know	
This child often does not seem to listen when spoken to directly.		☐Yes ☐No ☐Don't Know	
This child often has difficulty organizing tasks and activities.		☐Yes ☐No ☐Don't Know	
This child is often easily distracted by extraneous stimuli.		☐Yes ☐No ☐Don't Know	
This child often fidgets with hands or feet or squirms in seat.		☐Yes ☐No ☐Don't Know	
This child is often "on the go" or often acts as if "driven by a motor".		☐Yes ☐No ☐Don't Know	
This child often interrupts or intrudes on others (e.g. butts into conversations or games)		☐Yes ☐No ☐Don't Know	
Have your child's tonsils/adenoids been removed?		☐Yes ☐No ☐Don't Know	
And if so, when?			

Figure 8: Pediatric Sleep Questionnaire

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