Obstructive Sleep Apnea in Down Syndrome Patients

Brooke Hobbs[1], Kathleen De Key[1], William Xander Patton[1], and Akhil Ganesan[1]

[1]Georgia Institute of Technology

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1 Case Description

Sleep apnea is a common medical condition in which the pharyngeal airway frequently collapses during sleep, preventing the body from getting enough oxygen and resulting in poorer sleep quality. Obstructive sleep apnea (OSA) is the most common type of sleep apnea; it is primarily caused by an anatomically small upper airway, but pharyngeal dilator muscles that are unable to function well during sleep, a low arousal threshold, and ventilatory control instability are likely contributors as well. OSA has been diagnosed in at least 4% of adult men and 2% of adult women (White, 2005).

OSA is more severe and prevalent in patients with Down syndrome (DS), presenting in 50-100% of children with DS and nearly 100% of adults (Simpson et al., 2018). This extremely high prevalence in DS patients is likely due to anatomical differences as well as higher risk factors for hypotonia and obesity. Some anatomical differences that lead to an increased risk of OSA in patients with DS include macroglossia, adenotonsillar hypertrophy, and midface hypoplasia. Macroglossia refers to an enlarged tongue (Sridharan, G. K. 2023). Adenotonsillar hypertrophy is an abnormal growth of the pharyngeal tonsils; it is the most common cause of OSA in children (Deshmukh et al., 2022). Midface hypoplasia occurs when the nasal, maxillary, and zygomatic bones grow more slowly than other facial structures (Marulanda et al., 2017). Other physical differences such as glossoptosis and mandibular hypoplasia can also worsen OSA. Glossoptosis is a condition where the patient's mouth is farther back in their throat and can affect the patient's ability to breathe (Cleveland Clinic Medical). Mandibular hypoplasia is the underdevelopment of the mandible or the jaw area (Zimmerer et al., 2023). Consequences of OSA include excessive daytime sleepiness, hypertension, and cognitive deficits, making it important to diagnose and treat this condition early (Simpson et al., 2018).

The most common treatment for OSA is Continuous Positive Airway Pressure (CPAP), which is a device that covers the nose and uses mild air pressure to keep the airway open and breathing consistent. However, some patients have trouble tolerating this treatment due to having face variations mentioned above or other sensory issues. Long-term adherence to this treatment plan is as low as 46 - 83% (Chang H-P et al., 2020). Therefore, it is important to consider patients with different needs when designing medical devices for disorders like OSA.

While it is patients with DS that have higher rates of developing OSA, they also experience the most complications with CPAP treatments, which is the most widely practiced solution. The main complications that occur in CPAP machine users with DS stem from sensory issues and variable facial structures. Patients with DS are more likely to have an aversion to objects touching them, especially for an extended period, which is exactly what the CPAP machines do. While there have been adjustments, such as the transition from a full face mask to a nose strap, people with sensory issues do not find it easier to process the constant pressure of the attachment from the CPAP machine (Will et al., 2019). During OSA studies on people with DS, a major limitation was poor mask fit, where even the smallest commercial masks proved to be oversized on the participants. This is due to the aforementioned anatomical differences, such as midface and mandibular hypoplasia and short philtrum, an abnormality in the distance between the nose and mouth. Such extreme differences should warrant alternative designs for people with DS, but there has been no such discussion. There have been recent advances in 3D printing technology, creating the possibility for personalized face masks. However, the industry has shown to not prioritize this issue and there is no documented progress toward the possibility of alternative mask designs (Hill et al., 2020).

These widespread complications with OSA and other sleep disorders across the DS community should warrant more attention from the research community. However, ethical approval boards tend to be skeptical of studies that involve participants with intellectual disabilities, making it harder to secure funding and large sample sizes (Hill et al., 2020). It is a widespread view that participants of studies should not be taken advantage of based on any sort of disability. However, in a study having to do with how people with intellectual disabilities view their participation in research, results align with the idea that they want to be involved in research to help researchers gain a better perspective of their experiences (McDonald et al., 2013). This highlights a bias in the broader category of research against people with intellectual disabilities. If they are willing to participate, but their voices are still not being heard, issues like ineffective OSA treatments in people with DS cannot be studied and subsequently resolved. It is this barrier to research, as well as a lack of passion within this industry, that limits action toward rectifying this common issue.

2 Quantitative Respiratory Model

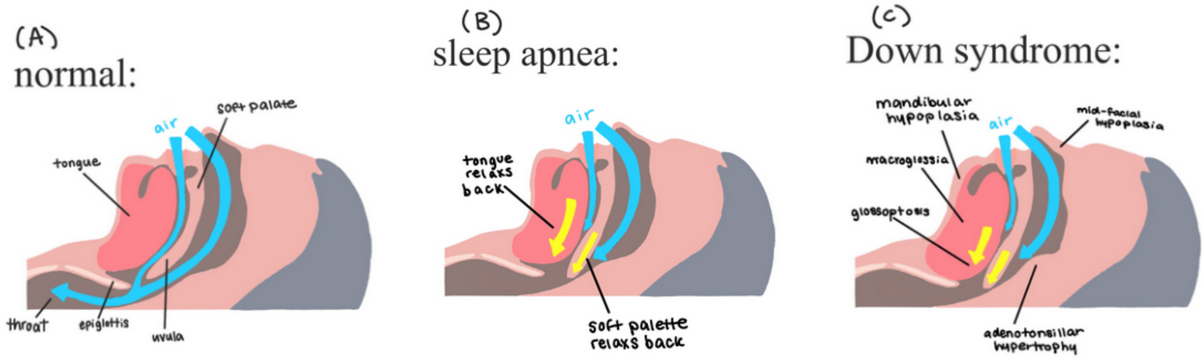

Figure 1: This figure shows the anatomical causes of sleep apnea. Diagram A represents the upper-respiratory anatomy of a typical patient without sleep apnea. While sleeping, there is a gap between the tongue and the soft palate as well as between the soft palate and the back of the throat, allowing air to easily pass into the lungs. As shown in Diagram B, an anatomically-typical patient with sleep apnea, the tongue and soft palate relax while the patient sleeps, closing off the airway so air cannot pass into the lungs. Diagram C represents a patient who presents with anatomical differences common to Down syndrome. These conditions further constrict the airway, making sleep apnea much more common and serious. Based on Sleep apnea. Respiratory tract diagram. Medical poster. Vector illustration [Photograph], by Ihor, Adobe Stock Images, https://stock.adobe.com/au/images/sleep-apnea-respiratory-tract-diagram-medical-poster-vector-illustration/536167883?prev_url=detail.

Our quantitative model aimed to determine the volumetric flow rate of air from the CPAP machine needed to keep patients with obstructive sleep apnea (OSA) asleep. The severity of OSA drastically varies, thus, the airflow rate likely varies drastically. We based our calculations on a range of OSA severities – from 5 obstructive events per hour (the baseline for OSA diagnosis) to 30 events per hour (a severe case of OSA) (Gottlieb & Punjabi, 2020).

In our model, the system (and thus the spatial scale) was the patient's respiratory system, with subunits for the mouth, lungs, and the rest of the body and bloodstream. The CPAP machine was classified as the surroundings. In our model, the in-stream was the air that flowed from the CPAP machine into the patient, and the out-stream was the air that the patient breathed out. We set our time basis to 1 minute as this is the typical breathing rate unit. Our basis was that the tidal volume of a normal patient while awake was 0.5 L, and that a normal patient has a respiratory rate of 12 breaths/min while awake.

For our quantitative model, we assumed the following:

1. Our system was open, reacting, and nonsteady state.
2. OSA patients require the same amount of air as patients without apnea.
3. The percent of air transferred from the lungs to the bloodstream was the same in OSA patients as in normal patients ($\tilde{5}\%$) (Pleil et al., 2021).

4. Air behaves as an ideal gas, and we distinctly differentiate between inhaled and exhaled air (treating them in the model as distinct components for simplicity).

5. During sleep, the average person has 73% of the tidal volume during their waking hours (Douglas et al., 1982).

6. The patient is sleeping at sea level.

7. The average pressure of the CPAP machine is 9.54 cm H_2O (Patz et al., 2010).

8. There is no leakage between the mask and the patient.

9. The patient has between 5 and 30 sleep apnea events per hour (Gottlieb & Punjabi, 2020); each event has an average of 10 seconds of full throat blockage (Wu et al., 2016).

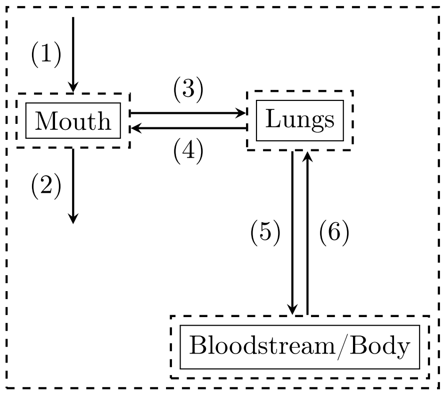

Figure 2: Engineering Diagram

Table 1: Stream Components

Stream	1	2	3	4	5	6
Air Type	In	Out	In	Out	In	Out

Given the engineering diagram and the table describing each stream, we developed the following calculations:

$$\dot{M}^3 \cdot 0.05 = \dot{M}^5 \tag{1}$$

This equation relates the airflow into the lungs (stream 3) to that entering the blood (stream 5) using the aforementioned 5% transference within the alveoli.

$$\dot{M}^3 = \gamma \dot{M}^1 \tag{2}$$

This relates the airflow into the lungs (stream 3) with the total inhaled air (stream 1) using a respiration factor γ

$$\gamma_{apnea} = \left(1 - \frac{\chi \cdot 10}{3600}\right) \gamma_{norm} \tag{3}$$

The ratio of the γ factor between apnea and normal patients is quantified here (χ is the rate of apnea (ranging from 5 to 30 events/hour), which completely block airflow for 10 seconds on average out of 3600 seconds in the entire hour of free flow)

$$\dot{M}^5 \propto \dot{M}^3 \propto \gamma \dot{M}^1 \tag{4}$$

This equation relates all 3 input air streams using equations 1 and 2

$$1 = \frac{\dot{M}^5_{apnea}}{\dot{M}^5_{norm}} = \frac{\gamma_{apnea}}{\gamma_{norm}} \frac{\dot{M}^1_{apnea}}{\dot{M}^1_{norm}} \tag{5}$$

This equation relates the ratio of the total inhaled air reaching the body in apnea and normal patients (which we assume has to be the same for metabolic functioning requirements) to the total air inhaled orally using the ratio of the γ factors

$$\frac{\dot{N}^1_{apnea}}{\dot{N}^1_{norm}} = \frac{\dot{M}^1_{apnea}}{\dot{M}^1_{norm}} = \frac{\gamma_{norm}}{\gamma_{apnea}} = \frac{1}{\left(1 - \frac{\chi}{360}\right)} \tag{6}$$

The ratio of the moles of inhaled air is quantified here by manipulating equation 5

$$\frac{P_{apnea}}{P_{norm}} \frac{\dot{V}^1_{apnea}}{\dot{V}^1_{norm}} = \frac{\dot{N}^1_{apnea}}{\dot{N}^1_{norm}} \frac{T_{apnea}}{T_{norm}} \tag{7}$$

This equation applies the ideal gas law to solve for the volume apnea patients need to reach the same metabolic needs as normal patients. This is done using the mole ratio from equation 6, assuming the external air temperature is the same across patients, and by using STP pressure for normal patients compared to CPAP pressure for apnea patients. This results in equation 8.

$$\frac{\dot{V}^1_{apnea}}{\dot{V}^1_{norm}} = \frac{1}{\left(1 - \frac{\chi}{360}\right)} \frac{P_{norm}}{P_{apnea}} \tag{8}$$

Equation 8 relates the ratio of inspired air volume between normal and apnea patients using solely the apnea rate (χ) and CPAP pressure. For our scenario, this results in the following conclusion (given tidal volume is 73% during sleep, and is typically 6 L/min):

$$\dot{V}^1_{norm} = 6 \frac{\text{L}}{\text{min}} \cdot 0.73 = 4.38 \frac{\text{L}}{\text{min}}$$

$$\dot{V}^1_{apnea} = \frac{1}{\left(1 - \frac{[5,30]}{360}\right)} \frac{34 \text{ ft } \text{H}_2\text{O} \cdot 30.48 \text{ cm/ft}}{34 \text{ ft } \text{H}_2\text{O} \cdot 30.48 \text{ cm/ft} + 9.45 \text{ cm } \text{H}_2\text{O}} \dot{V}^1_{norm} = \left[4.40 \frac{\text{L}}{\text{min}}, 4.73 \frac{\text{L}}{\text{min}}\right]$$

Thus, through quantitative analysis, we determined that the patient requires the CPAP machine to provide between 4.40 and 4.73 L of air per minute, depending on the severity of their OSA. Even with the CPAP in ideal conditions, apnea patients must inhale more air than normal patients at higher pressure. If the CPAP doesn't fit properly for patients with apnea such as those with Down syndrome (due to their altered skull structure), those patients would struggle significantly to meet their respiratory metabolic needs.

3 Bias

The fit of the CPAP mask on a patient's face is one of the determining factors for if CPAP treatment will be a success. An ill-fitting mask is not just uncomfortable, but it is ineffective, as it reduces the likelihood of the patient receiving the necessary air to prevent obstructive events. An ill-fitting mask will likely have gaps that allow air pumped by the machine to escape before entering the patient's mouth, resulting in them getting less air. Furthermore, openings defeat the purpose of the CPAP machine as it results in the system depressurizing. Air automatically moves from areas of higher pressure (within the mask system) to areas of lower pressure (outside of the mask). Thus, the mask must fit properly to ensure the machine can properly increase the system's pressure, preventing obstructive events and resulting in significantly better sleep.

The necessity of a properly fitting mask presents a serious problem in treating patients with Down syndrome (DS), who frequently have significant anatomical variations in their face and upper respiratory system. These variations, including midface hypoplasia, which is the underdevelopment of jawbones and other facial structures (Marulanda et al., 2017), result in patients struggling to find masks that fit them properly. This struggle has been documented in the literature, as a 2021 study found that DS patients experience significantly greater leakage rates compared to patients without DS (MacDonagh et al., 2021). In this study, they found that even when DS patients had higher rates of adherence to CPAP treatment, they still had worse clinical outcomes as a result of leakage.

We can quantify the consequences of this leakage. If there is a leak, the pressure inside the mask will be equivalent to the pressure outside the mask, which we assume to be 1 atm. This results in the patient breathing in the same amount of air as if they were not wearing the mask, and thus having the same number of obstructive events as before. Based on our calculations and assumptions above, this results in the patient getting between 0.02 (mild OSA) and 0.65 (severe OSA) L/min less air than patients without OSA.

As we have demonstrated through our quantitative model, CPAP treatment is often ineffective in delivering the necessary air for DS patients. There are few other options, leaving them to suffer with the consequences of OSA.

4 Recommendations

It has been established that generic face masks that are used in conjunction with CPAP machines are not made with people with different facial structures in mind. In order to create a better fit for individuals with DS who have to wear CPAP machine masks, we propose a solution involving personalized 3D-printed masks. With 3D-printing technology becoming increasingly more efficient and accessible, it is a realistic proposal to develop a system in which individuals can get fitted for personalized masks.

A recent study on individuals with abnormal facial structures identified three categories for assessing mask fit: comfort, extent of leakiness, and general satisfaction (Wu et al., 2018). While there are concerns about the comfort of these masks given that many 3D printing materials are rigid, it is possible and realistic to design comfortable silicon layers that fit around the rigid mask, as this is already present in existing CPAP masks. Masks tailored to an individual's face would inherently reduce leakiness, alleviating the main issue with existing CPAP masks. The improved seal would allow the pressurization necessary for the patient to receive the 4.40 L/min to 4.73 L/min of air needed.

In assessing general satisfaction, the majority of custom-fit masks have been rated higher than the generic masks (Wu et al., 2018). This piece of the literature motivates our recommended approach, leaving the remaining action to be the application to the specific user group of patients with DS. CPAP masks must be designed specifically for this population, as they develop OSA at rates of almost 100% (Simpson et al., 2018).

5 Bibliography

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