OT Bio

Developed by The George Washington University

Technology Summary

- Obstructive sleep apnea (OSA)
  - highly prevalent sleep breathing disorder
  - occurring in about 24% of men and 9% of women in the US
- OSA increases the risk of
  - hypertension, cardiac arrhythmias, myocardial ischemia, and ventricular hypertrophy leading to a 3-fold increase in cardiovascular mortality
- No FDA approved pharmacological or other non-device based approaches to reduce the frequency or duration of obstructive events has been successful
- Untreated sleep apnea causes $3.4 billion in additional medical costs in the U.S
- Intranasal Oxytocin therapy
  - Natural neuropeptide
  - FDA approved for use in childbirth

Challenges with current therapies

- Few effective treatment options for sleep apnea other than positive airway pressure (CPAP or autoPAP) devices
- Despite the risks of OSA, CPAP is often discontinued because it is intrusive and poorly tolerated
- Approximately half of all patients with OSA **discontinue CPAP use** entirely or use it for less than 4 hours each night

OT Bio Solution

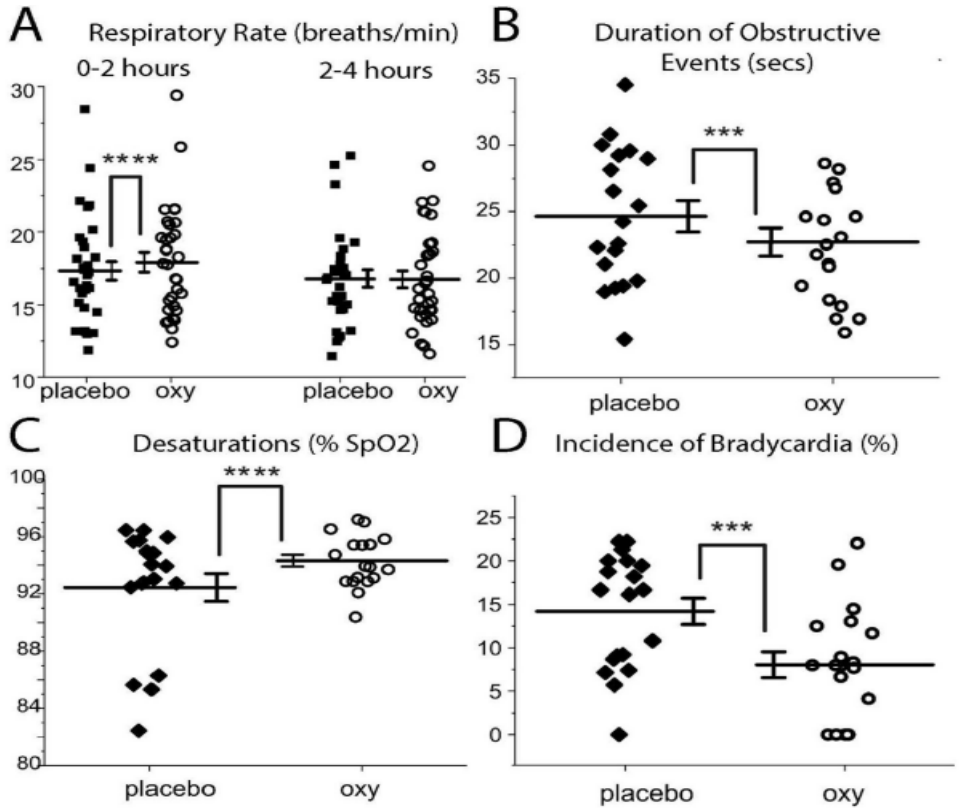
- Intranasal administration of oxytocin help patients with OSA

- Nasal administration of Oxytocin reduces:
  - Duration of obstructive events
  - Level of oxygen desaturation
  - Abnormal heart rate fluctuations

- May be used as a substitute for CPAP in patients with mild OSA and provide cardio protection

- In combination with CPAP for severe OSA to decrease severity of obstructions, increase sleep satisfaction and CPAP compliance

Randomized, Double-Blinded Cross-Over Study with 19 OSA Subjects (Identifier: NCT03148899)



These graphs compare the effects of oxytocin and placebo after 0-2 hours and 2-4 hours of polysomnogram (PSG) recordings.

Source: V. Jain et al.; Sleep Medicine 74 (2020); 242-247

Randomized, Double-Blinded Cross-Over Study with 19 OSA Subjects (Identifier: NCT03148899)

Outcome	Placebo	Oxytocin	Differences in Change (95%CI)	P Value
Duration	24.66 ± 5.12	22.72 ± 4.59	−1.94 (−3.31, −0.57)	0.004
O2 minimum	92.44 ± 4.24	94.31 ± 1.80	1.87 (−0.14, 3.87)	<0.001[a]
Bradycardia	0.14 ± 0.07	0.08 ± 0.07	−0.06 (−0.10, −0.02)	0.002
Respiratory Rate	16.69 ± 3.24	17.39 ± 3.50	0.70 (0.08, 1.32)	<0.001[a]

Plus-minus values are means ± SD.
[a] Normalized differences.

This study showed that intranasal oxytocin **significantly decreases**:

1. Duration of obstructive events.
2. Desaturations in obstructive events.
3. Chances of bradycardia accompanying obstructive events.

Source: V. Jain et al.; Sleep Medicine 74 (2020); 242-247

How big is the market?

- OSA prevalence of about 16% in US

- The **annual economic cost** of moderate - severe OSA in the United States is **$65 - $165B**, which is greater than asthma, heart failure, stroke and hypertensive disease ($20B to $80B)

<u>In addition to medical costs:</u>

- OSA-related traffic accident (*excluding medical costs):*

  $10 - $40 Billion

- OSA-associated workplace accidents *(excluding traffic accidents and medical costs):*

  $5 - $20 Billion

- OSAS-related lost productivity costs driven by absenteeism:

  $5 - $15 *Billion*

Competition

- CPAP therapy (non-compliance a problem)
- Several meta-analyses showed that the overall impact of CPAP on BP is modest (~2 mmHg)
- Patients on CPAP may still be at risk of heart failure
- CPAP Insurance coverage is based on Apnea Hypopnea Index (AHI)
  - AHI must at least 15 events per hour
- Apnea Hypopnea Index
  - average number of combined apneas and hypopneas per hour

None/Normal	AHI is <5 per hour
Mild	AHI≥5 per hour, but <15 per hour
Moderate	AHI≥15 per hour, but <30 per hour
Severe	AHI≥30

The Team

- **David Mendelowitz, Ph.D.**
- Interim Chair, Department of Pharmacology and Physiology
- Professor, Pharmacology and Physiology
- Research Interest: autonomic and respiratory control of brainstem cardiovascular function

- **Vivek Jain, M.D.**
- Associate Professor of Medicine
- Director, GW Sleep Disorders Center
- Research Interest: sleep disorders

Patent Information

Oxytocin Improves Treatment of Obstructive Sleep Apnea

US Patent Number: US10842845B2 issued on 11/24/2020

US Patent Number: US10166268B2 issued on 01/01/2019

The ASK

- What we are looking for:
  - Serial entrepreneur with potential for CEO role
  - Investment / Financing
- Is there a market for the newly developed Oxytocin Therapy?
  - Yes, in sleep apnea and other respiratory disorders for which there are limited treatment options.
  - Oxytocin is safe and marketed; requiring only a small investment for new indication and long term studies
  - Additional IP for targeting heart failure separately from OSA.
- How far from evaluation of the technology in patients?
  - We have completed pilot acute human trials, including a double-blinded placebo controlled study.
  - We would like to perform a chronic human trial.

Closing

- Intranasal oxytocin therapy platform can treat Obstructive Sleep Apnea (OSA) and Heart Failure
- Safe treatment already FDA approved for childbirth and tested in humans for OSA
- Oxytocin therapy for sleep apnea and associated heart failure protected by an issued patent and patent application with allowed claims
- Oxytocin therapy for heart failure protected by a patent application
- *OT Bio* team of clinician and scientist with strong and unique expertise to make the Oxytocin therapy successful in the treatment of Sleep Apnea