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SHORTER SLEEP DURATION ASSOCIATED WITH LOWER GABA LEVELS

GABA: THE NEUROCHEMICAL BEHIND YOUR SLEEPLESS NIGHTS

NATURAL SHORT SLEEPERS' GENES

THE SLEEPLESS SECRETS HIDDEN IN OUR GENES

TIRZEPATIDE FOR OBSTRUCTIVE SLEEP APNEA TREATMENT

TIRZEPATIDE: THE DUAL THREAT AGAINST OBESITY AND SLEEP APNEA

NARCOLEPSY

THE SCIENCE BEHIND SUDDEN SLEEP

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Park, S., Kang, I., Edden, R. A. E., Namgung, E., Kim, J., & Kim, J. (2020). Shorter sleep duration is associated with lower GABA levels in the anterior cingulate cortex. Sleep Medicine, 71, 1–7. https://doi.org/10.1016/j.sleep.2020.02.018

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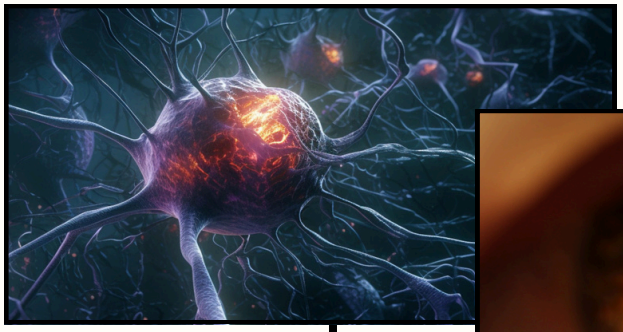
TABLE OF CONTENTS



STILL

SHORTER SLEEP DURATION IS ASSOCIATED WITH LOWER GABA LEVELS

Reference Article by: Park, S., Kang, I., Edden, R. A. E., Namgung, E., Kim, J., & Kim, J.

Digest by Daniella Ling

> ***"Short sleep duration is steadily on the rise, with more than 30% of adults in the US reported sleeping less than 6 hours a day"***
>
> ***–Park, S., Kang, I., Edden, R. A. E., Namgung, E., Kim, J., & Kim, J.***

In recent years, the importance of sleep for cognitive health has gained increasing attention in scientific research. While many associate sleep deprivation with feelings of fatigue or irritability, its effects on brain function–especially on tasks like memory, attention, and decision-making–are more profound than one may realize. A growing body of research highlights how disrupted sleep can lead to cognitive impairments, often through changes in neurotransmitter systems that regulate brain activity during rest.

One neurotransmitter of particular interest is **gamma-aminobutyric acid (GABA)**. GABA plays a key role in inhibiting brain activity, ensuring proper balance between excitatory and inhibitory signals, which are crucial in maintaining healthy cognitive function. Disruptions in GABAergic systems have been linked to various conditions, such as insomnia and may contribute to the cognitive difficulties seen in those with poor sleep. This is especially true for the **anterior cingulate cortex (ACC)** and **medial prefrontal cortex**

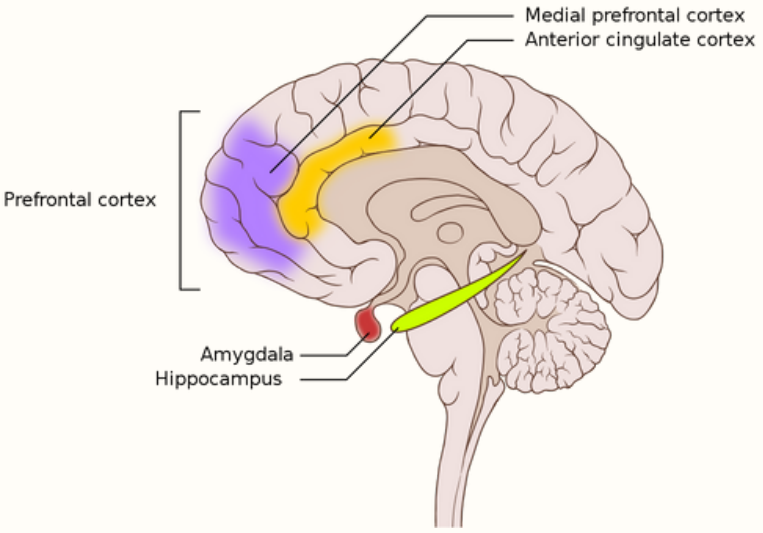


Figure 1: Diagram of the anterior cingulate cortex and medial prefrontal cortex regions in a human brain.

(mPFC), brain regions that regulate attention. Understanding how GABA levels in these areas respond to variations in sleep duration can offer valuable insights into the neurological mechanisms behind sleep-related cognitive impairments.

To understand GABA's roles in our bodies, it is crucial to understand how different parts of our body send messages to one another constantly. These messages are passed using chemicals called neurotransmitters. As said earlier, we will be focusing on the GABA neurotransmitter. This is an inhibitory neurotransmitter. This means its job is to slow down or calm brain activity. This is especially true for sleep because your brain needs to shift into a calmer state to fall and stay asleep. When GABA levels are low, the brain may stay too active, leading to difficulty sleeping or anxious feelings.

This study provides crucial findings that explore the connection between sleep duration, GABA levels, and cognitive performance. Not only investigating shorter sleep durations' linkage to reduced GABAergic activity in the ACC and mPFC, this paper will also examine how these changes in brain chemistry can affect working memory performance, a critical cognitive function.

The study involved 153 participants, categorized into two distinct groups based on their reported sleep duration: a short sleep duration (n=74) and a long sleep duration (n=79). Both groups were subject to Magnetic Resonance Spectroscopy (MRS), a neuroimaging technique that measures neurotransmitter levels, including GABA, in specific brain regions. The main goal of the study was to examine how differences in sleep duration are influenced by GABA levels in the ACC and mPFC.

Sleep duration was measured both through self-reports and objective methods with actigraphy, a wearable device that tracks sleep and wake patterns. Working memory performance was assessed through a spatial working memory (SWM) task, testing participants' abilities to recall and manipulate spatial information. MRS was used to measure GABA and Glx (glutamate-glutamine) levels in the ACC and mPFC, providing insights into the brain's neurochemical balance. By comparing these results, it was aimed to determine whether lower GABA levels in the ACC and mPFC could be associated with impaired working memory in individuals experiencing short sleep durations and whether such effects were unique to individuals with subjective sleep complaints.

The results of the study provide important insights into how sleep duration impacts brain function, particularly in areas related to memory and sleep quality. The research focused on two key factors: GABA levels and working memory. These factors were measured in two groups of participants: those who slept less (under six hours) and those who slept more (seven hours or more).

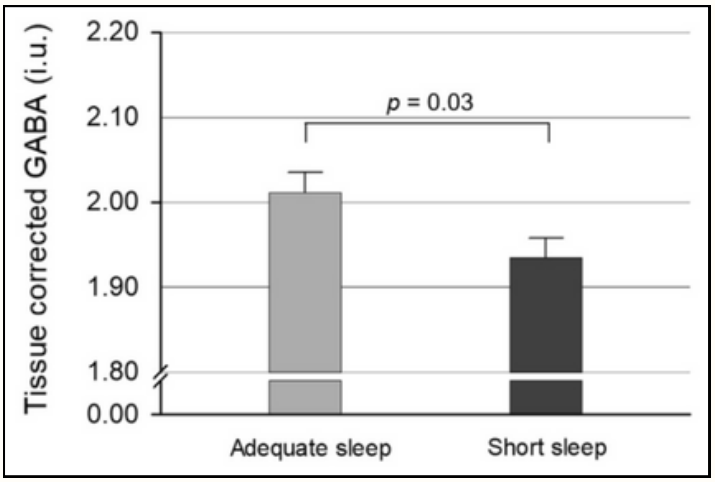


Figure 2: The results indicate that tissue-corrected GABA levels were lower in those with shorter sleep durations.

i) Sleeping Duration and GABA Levels:

One of the most significant findings of the study was that participants who reported shorter sleep durations had lower levels of GABA in the ACC and mPFC brain regions. These two regions are involved in important functions like decision-making, emotional regulation, and memory processing. Specifically, participants who slept fewer than six hours had lower GABA levels compared to those who slept more, suggesting that shorter sleep durations lead to reduced brain activity regulation. GABA is a crucial neurotransmitter because it helps to calm the brain and prevent it from being overstimulated.

This finding means that GABA plays a key role in calming the brain and preventing overstimulation. When GABA levels are lower, the brain may become more easily stimulated, leading to heightened emotional response or stress. For instance, students who do not get enough sleep may find themselves feeling more anxious or overwhelmed, affecting their ability to perform well in their daily lives.

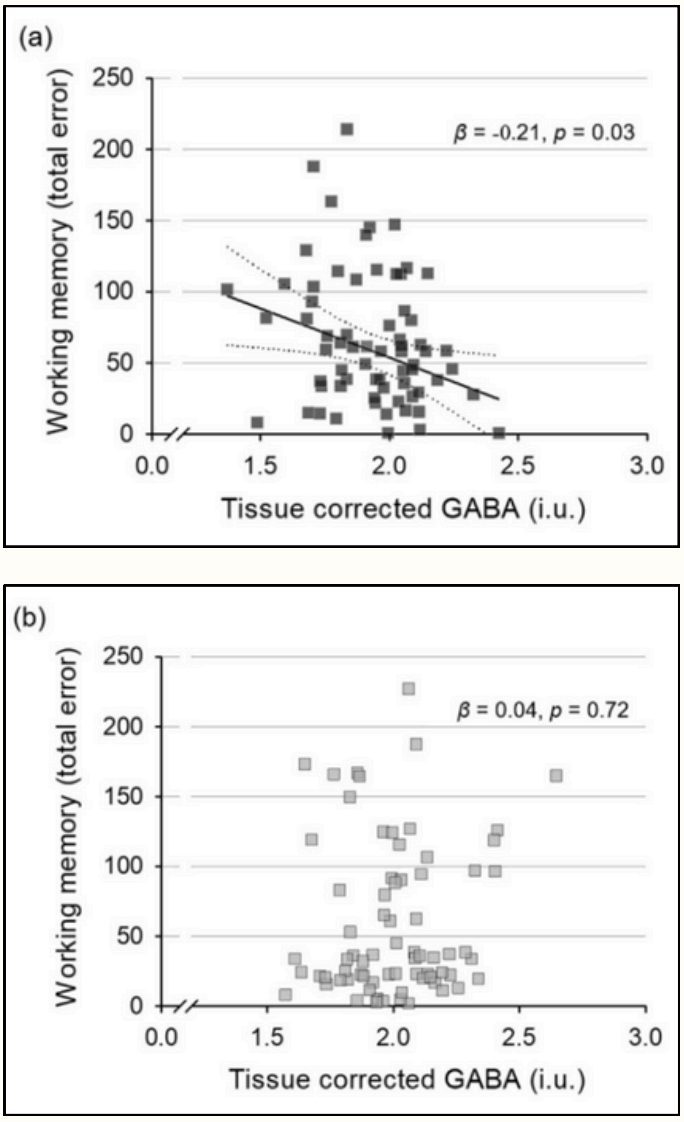


Figure 3: Negative correlation observed between tissue-corrected GABA and those with shorter sleep durations. No significant correlation observed between GABA and those with longer sleep durations.

ii) Working Memory and Sleep Duration

Another key aspect of the study was its focus on working memory, referring to the ability to temporarily store and process information. The study found that participants with shorter sleep durations performed worse on tasks that measured their working memory. These tasks required participants to remember and manipulate information, which is essential for various activities. This result is significant because it suggests that sleep deprivation can have a direct impact on our ability to perform tasks that require focus and memory. When a person doesn't get enough sleep, their brain's ability to process and retain information can be compromised. This study highlights how vital sleep is for cognitive function and memory retention, especially in academic settings.

Furthermore, the study proved a link between lower GABA levels and worse performance on said working memory tasks. Specifically, participants with lower GABA levels in the ACC and mPFC made more errors during these tasks, suggesting that GABA is not only important for regulating brain activity but also plays a critical role in supporting memory processes. These findings add to the understanding that neurotransmitters like GABA are crucial for maintaining cognitive abilities such as memory. When GABA levels are insufficient, the brain may struggle to perform tasks that require concentration and the manipulation of information. Overall, the study emphasized the crucial role of sleep in maintaining cognitive health, showing that deep deprivation can have a significant impact on brain function, particularly in areas related to memory and emotional regulation. These findings highlight the importance of getting enough sleep to ensure optimal brain function, especially for tasks that require focus, memory, and decision-making.

This study's findings suggest that even without formal sleep disorders like insomnia, shorter sleep durations can have measurable effects on brain chemistry. Specifically, individuals who slept fewer than six hours exhibited lower GABA levels in the ACC and mPFC brain regions. Therefore, we can take away that sleep doesn't just make you feel rested–it also helps with brain regulation. GABA plays an important role in keeping the brain balanced. When GABA levels are low, these regulatory systems become less effective, leading to hyperarousal even when you're trying to relax or sleep.

The study also found that lower GABA levels are associated with worse performance on memory tasks. These findings all support the idea that getting less sleep–even just for a night ot two–can subtly change how the brain functions. Although this study focused on adults, similar processes likely apply (and have greater impacts) with teens. Understanding how neurotransmitters such as GABA work can give us a better understanding of why sleep is not just a break but an essential action our brains need so they can rest and prepare for new information.

This study demonstrated that shorter sleep durations are associated with lower levels of GABA in the brain, and such lower levels are connected to poorer working memory performance. While the participants didn't have full-blown insomnia, their sleep complaints and reduced sleep time still affected their brain function. This can give us a clear picture of how important sleep is for mental performance, adding to research about the role of neurotransmitters like GABA in sleep regulation.

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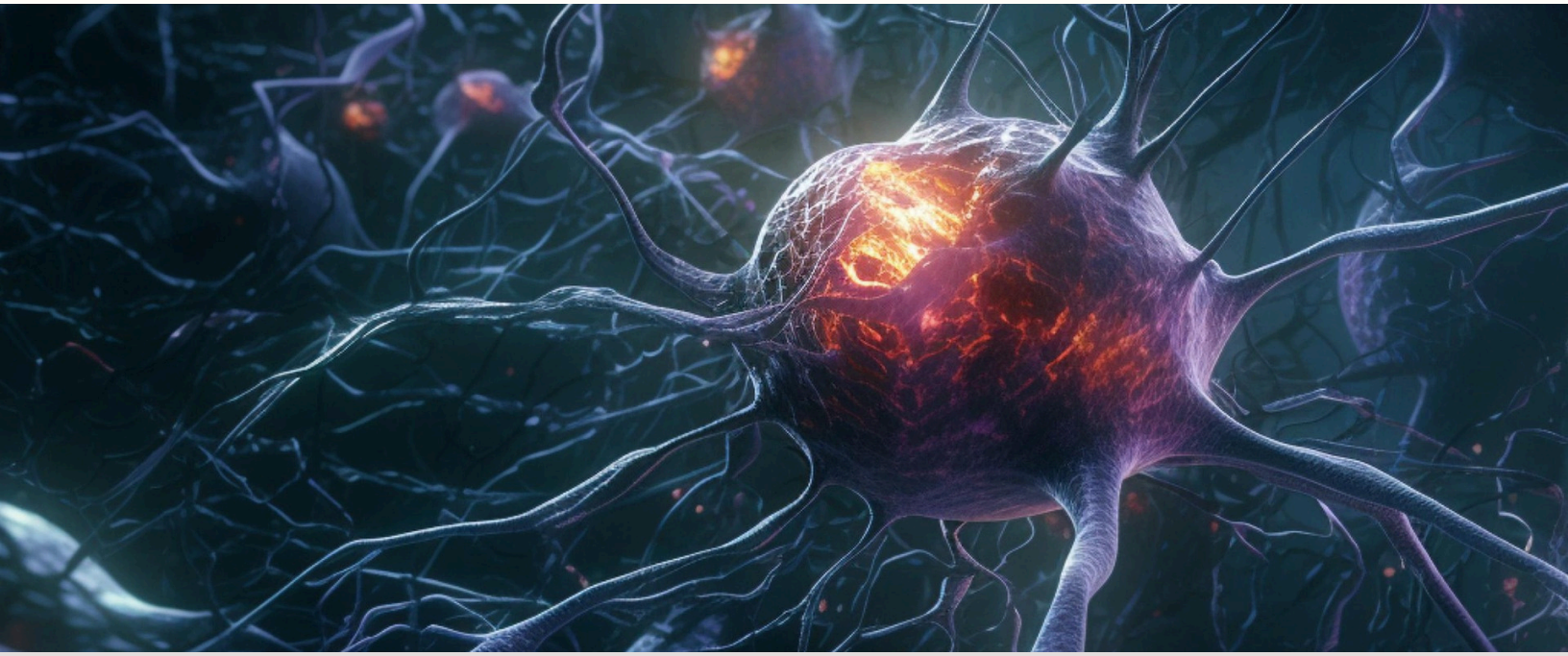


NATURAL SHORT SLEEPERS' GENES

Reference Article by: Yook, J. H., Rizwan, M., Shahid, N. U. A., Naguit, N., Jakkoju, R., Laeeq, S., Reghefaoui, T., Zahoor, H., & Mohammed, L.

Digest by Jessica Lu

For most individuals, insufficient sleep will adversely affect mood, health, memory, and performance, often causing daytime drowsiness and fatigue. Consistent short sleep duration has also been linked to depression, diabetes, hypertension, and cardiovascular disease. The National Sleep Foundation recommends that teenagers get 8-10 hours of sleep per day and adults get 7-9 hours per day. However, people with short sleeper syndrome (SSS), or natural short sleepers (NSS), can consistently sleep 4-6 hours daily without impacting their energy levels, function, or health.

Researchers have identified that certain variants in the *DEC2, NPSR1, mGluR1,* and *β1-AR* genes are responsible for this decreased need for sleep in humans and other mammals. He et al. identified a mutation in the *DEC2* gene in two natural short sleepers with a reported average sleep time of 6.25 hours. This mutation (DEC2-P385R) was replicated in fly and mouse models and then compared to a wild-type (WT) group without the mutation. The mutant-carrying group had shorter non-rapid eye movement (NREM) and rapid eye movement (REM) stages, and thus shorter sleep durations overall.

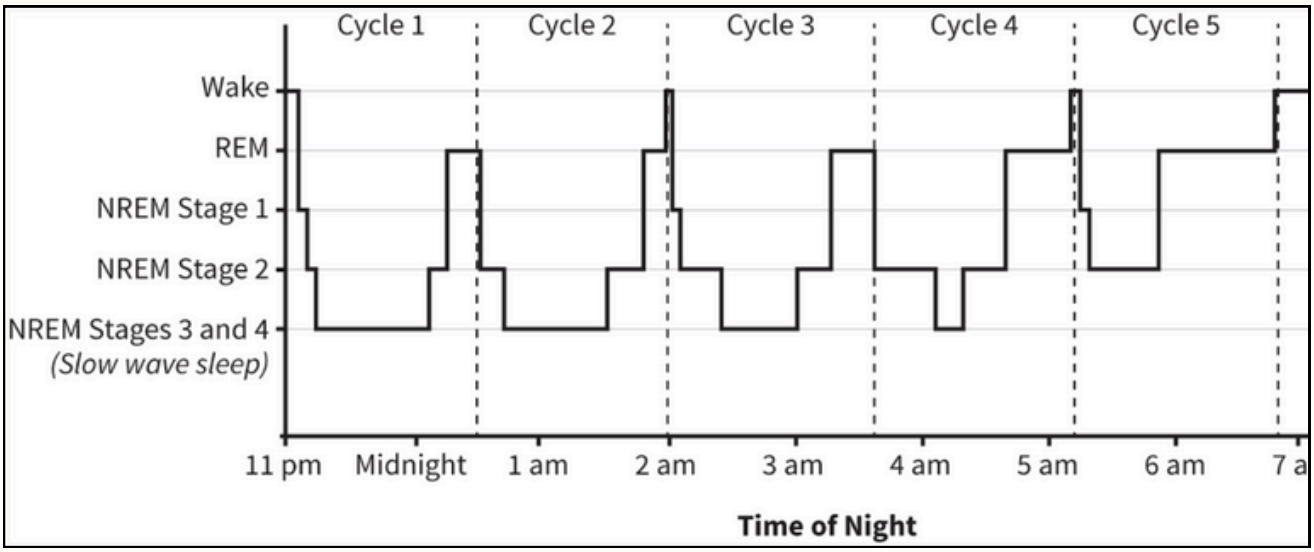


Figure 1: 90-minute REM and NREM Sleep Cycles in Regular Sleepers

Pellegrino et al. discovered that the variants of the DEC2 gene p.Tyr362His, p.Pro384Arg, and p.Ala380Ser inhibited the ability of DEC2 to suppress BMAL1 and CLOCK activators. BMAL1 and CLOCK activate PER and CRY proteins to regulate circadian rhythms (sleep-wake cycles). The researchers found that the altered activity of DEC2 shortened sleep duration and alleviated the impacts of sleep deprivation. Additionally, expression of the gene orexin was found to be increased in mice with a DEC2 mutation. Orexin is a neuropeptide (a signaling molecule in the brain) that controls sleep and arousal. Orexins promote alertness by stimulating neurons to release neurotransmitters such as dopamine and serotonin.

NPSR1 is a receptor in the brain that promotes wakefulness by switching on proteins in a signaling pathway through chemical modification. Xing et al. injected the neuropeptide S (NPS) into normal and genetically engineered mice to trigger NPRS1. They found that the mutation NPSR1-Y206H in the short sleeping mice was more easily triggered and, thus, more successful in switching on components of the signaling pathway. The researchers also found that the NPRS1 mutation limited memory problems that occur as a result of sleep deprivation. Normal mice were placed in a chamber and gently shocked; after sufficient sleep, they exhibited the expected fear-based behaviors when returned to the chamber.

The mice that were sleep-deprived did not remember the shocks and did not exhibit fear-based behaviors, while carriers of the NPRS1 mutation remembered the electrical shocks, even if they were sleep-deprived.

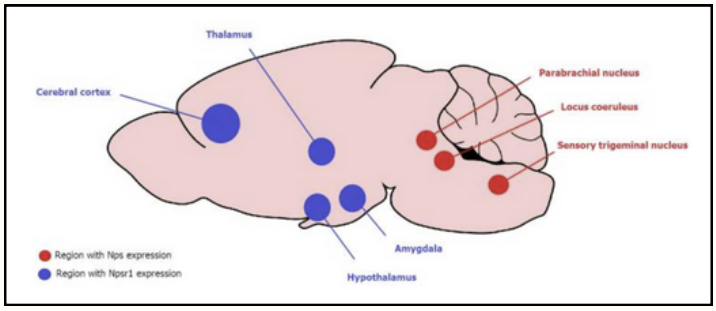
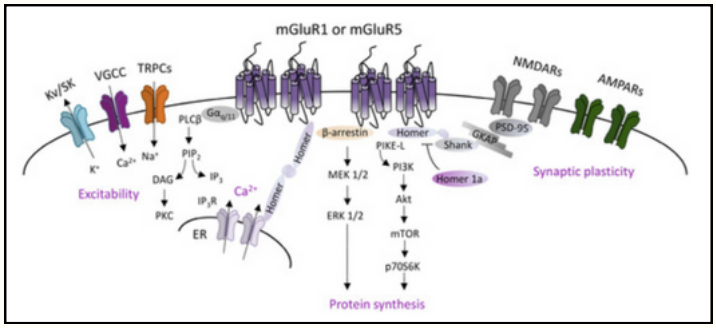


Figure 2: Major Regions where NPS and NPSR1 are Highly Expressed in the Mouse Brain

The mice that were sleep-deprived did not remember the shocks and did not exhibit fear-based behaviors, while carriers of the NPRS1 mutation remembered the electrical shocks, even if they were sleep-deprived.

Metabotropic glutamate receptors (mGluR1 and mGluR5) help regulate cellular activity, synaptic plasticity—the ability of synapses (junctions where neurons transmit signals) to change their strength in response to activity patterns—and sleep homeostasis (mGluR5). During sleep, these receptors decrease neural excitability and synaptic strength. The mutation in mGluR1 in short-sleeping mice showed decreased activation of extracellular-signal-regulated kinase, which lengthens sleep duration in mice. There was an approximately 25-minute reduction in sleep time due to this mutation.



The β1-AR (ADRB1) gene codes for B1-adrenergic receptors, which are found throughout the body and respond to hormones, including those that regulate the sleeping cycle. Genetically engineered mice with the mutation showed increased activity of brain cells with the B1-adrenergic receptor (primarily located in the dorsal pons) during REM sleep and slept about an hour less per day than regular mice.

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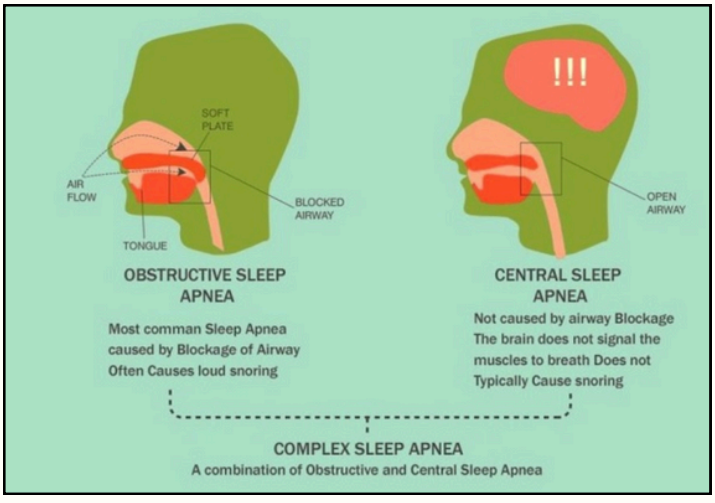
TIRZEPATIDE FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA

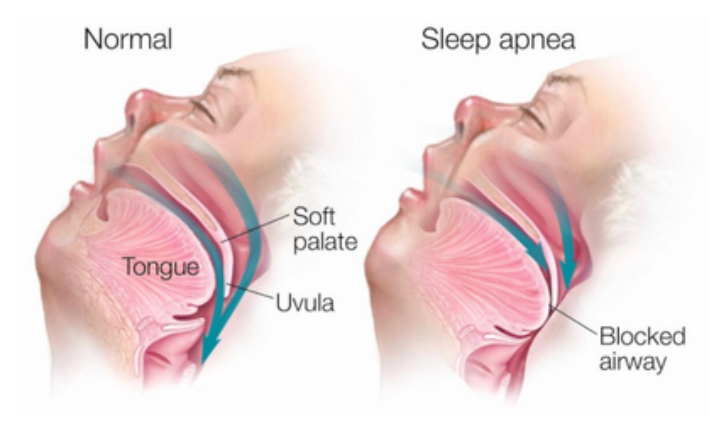
Reference Article by: Malhotra, A., Grunstein, R. R., Fietze, I., Weaver, T. E., Redline, S., Azarbarzin, A., Sands, S. A., Schwab, R. J., Dunn, J. P., Chakladar, S., Bunck, M. C., & Bednarik, J.

Digest by Nathan Zhuang

Sleep apnea is a sleeping disorder that affects a person's ability to breathe while sleeping. At times, during the night, a patient presented with sleep apnea may undergo long periods with no breaths or extremely shallow breaths. This lack of breathing leads to limited levels of oxygen reaching the body, causing potential high blood pressure, heart disease, stroke and type 2 diabetes.

Sleep apnea can present in patients in three different ways. Obstructive sleep apnea (OSA) happens when the throat muscles relax and block the flow of air to the lungs. The other type, central sleep apnea (CSA) happens when the brain doesn't send the proper signals that cause breathing. The last type of sleep apnea, Treatment-emergent sleep apnea, is when OSA becomes CSA due to treatment. The most common form of sleep apnea is OSA, thus the main target of treatment.

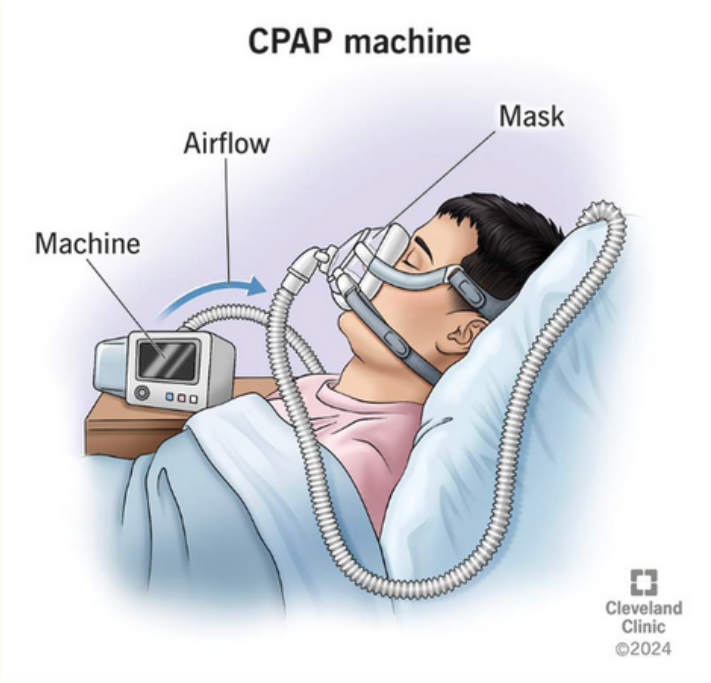




OSA affects a person's sleep, as when the throat muscles relax, the airways close as they breathe in. As a result, the brain sends a signal to wake the patient up, causing a lack of meaningful sleep.

The exact cause of sleep apnea has been attributed to many different health issues. The many different risk factors are but are not limited to excess weight, having a thick neck, having a narrowed airway, being a male, being older, family history, use of alcohol or smoke products, nasal congestion, and other medical issues.

Before testing with Tirzepatide, the only effective treatment for sleep apnea was mechanical breathing machines. These machines would forcefully ensure that the users did not collapse onto themselves during sleep. Below is an image of CPAP machine, or continuous positive airway pressure machine that is the current widespread method of treating OSA.



The study, conducted by Malhotra et al., in 2024 aimed to test the drug tirzepatide, a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist, a drug typically used to ounteract severe obesity by mimicking the GLP-1 and GIP hormones that are naturally secreted by the intestine after a meal, which prompts insulin secretion.

The main theory behind Tirzepatide working is to lower the BMI of the patient. In cases where OSA is caused by being obese, the theory of Tirzepatide working stands.

The experiment took place over 52 weeks and two trials in 60 sites across the world to determine the effects of Tirzepatide on obese patients with sleep apnea. The experiment was controlled by a placebo, and trial 1 included only patients refusing to use PAP (positive airway pressure), an artificial device used to open the airways of a patient with sleep apnea.

The second trial included patients who were under treatment with PAP for at least three months. The main unit of measurement tested was AHI or apnea–hypopnea index, a measure of how many sleep apnea incidents a person has in one night. The trial participants were either placed under a max dose of Tirzepatide (10-15mg) or the placebo.

Participants that were limited to this trial were people that met the requirements of being diagnosed with moderate to severe sleep apnea: having a AHI ≥ 15 events/hour, and being obese: have a BMI (body mass index), ≥ 30 in all countries other than Japan (which was ≥ 27). People with either type 1 or 2 diabetes were excluded from this trial. Other exclusion criteria included losing over 5kg in the last 3 months, planned surgery for sleep apnea or obesity, a diagnosis of central or mixed sleep apnea, and major craniofacial abnormalities. Male participants were limited to 70% to make sure there was enough female representation.

Participants were assigned to either trial 1 or 2, based on their current treatment status and then split 1:1 to receive either Tirzepatide or a placebo. Participants were also required to maintain a 500 kilocalories deficit and 150 minutes of activity weekly.

The trial measured the participants' AHI levels at weeks 20 and 52. Up to week 20, the dose of Tirzepatide was increasing weekly till the EMDCAI limit (10-15mg).

The results gathered showed promising changes in AHI values across the use of Tirzepatide. With a mean of 29.03 fewer events per hour across both trials under Tirzepatide (a 58.7 % change) compared to only 5.3 or 3.0% change within participants under the placebo.

Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.*

Characteristic	Trial 1			Trial 2		
	Tirzepatide (N=114)	Placebo (N=120)	Total (N=234)	Tirzepatide (N=120)	Placebo (N=115)	Total (N=235)
Age — yr	47.3±11.0	48.4±11.9	47.9±11.5	50.8±10.7	52.7±11.3	51.7±11.0
<50 yr	63 (55.3)	62 (51.7)	125 (53.4)	54 (45.0)	45 (39.1)	99 (42.1)
≥50 yr	51 (44.7)	58 (48.3)	109 (46.6)	66 (55.0)	70 (60.9)	136 (57.9)
Female sex — no. (%)	36 (31.6)	41 (34.2)	77 (32.9)	33 (27.5)	32 (27.8)	65 (27.7)
Race or ethnic group — no. (%)						
American Indian or Alaska Native	9 (7.9)	9 (7.5)	18 (7.7)	10 (8.3)	9 (7.9)	19 (8.1)
Asian	23 (20.2)	24 (20.0)	47 (20.1)	17 (14.2)	16 (14.0)	33 (14.1)
Black or African American	6 (5.3)	7 (5.8)	13 (5.6)	8 (6.7)	3 (2.6)	11 (4.7)
White	74 (64.9)	80 (66.7)	154 (65.8)	85 (70.8)	86 (75.4)	171 (73.1)
Multiple	2 (1.8)	0	2 (0.9)	—	—	—
Hispanic or Latino	51 (44.7)	47 (39.2)	98 (41.9)	38 (31.7)	38 (33.0)	76 (32.3)
Body weight — kg	116.7±24.6	112.8±22.6	114.7±23.7	115.8±21.5	115.1±22.7	115.5±22.0
Body-mass index						
Mean value	39.7±7.3	38.6±6.7	39.1±7.0	38.6±6.1	38.7±6.0	38.7±6.0
Distribution — no. (%)†						
<35	33 (28.9)	44 (36.7)	77 (32.9)	33 (27.7)	33 (28.9)	66 (28.3)
≥35 to <40	39 (34.2)	35 (29.2)	74 (31.6)	47 (39.5)	41 (36.0)	88 (37.8)
≥40	42 (36.8)	41 (34.2)	83 (35.5)	39 (32.8)	40 (35.1)	79 (33.9)
Waist circumference — cm	122.6±16.6	119.8±14.8	121.2±15.7	120.7±13.1	121.0±14.0	120.9±13.5
AHI — events/hr	52.9±30.5	50.1±31.5	51.5±31.0	46.1±22.4	53.1±30.2	49.5±26.7
Obstructive sleep apnea severity — no. (%)‡						
No apnea	0	1 (0.8)	1 (0.4)	—	—	—
Mild: AHI <15 events/hr	1 (0.9)	2 (1.7)	3 (1.3)	0	2 (1.8)	2 (0.9)
Moderate: AHI ≥15 events/hr	39 (34.2)	43 (36.1)	82 (35.2)	35 (29.4)	37 (32.5)	72 (30.9)
Severe: AHI ≥30 events/hr	74 (64.9)	73 (61.3)	147 (63.1)	84 (70.6)	75 (65.8)	159 (68.2)
Missing data	0	1 (0.8)	1 (0.4)	1 (0.8)	1 (0.9)	2 (0.9)
PROMIS Sleep-related Impairment T score§	53.2±7.5	54.3±8.5	53.8±8.1	55.3±8.4	55.0±9.5	55.2±8.9
PROMIS Sleep Disturbance T score¶	53.8±6.0	53.5±7.4	53.6±6.7	56.0±7.6	55.7±7.6	55.9±7.6
ESS score‖	10.3±5.3	10.8±5.2	10.6±5.3	10.8±4.6	9.5±4.4	10.2±4.5
Sleep apnea–specific hypoxic burden — % min/hr**	153.6 (102.7)	137.8 (104.1)	145.3 (103.4)	132.2 (83.4)	142.1 (112.5)	137.0 (97.5)
Systolic blood pressure — mm Hg	128.4±12.2	130.3±10.7	129.4±11.5	130.5±14.3	130.5±12.8	130.5±13.5
Diastolic blood pressure — mm Hg	83.7±8.9	84.0±8.6	83.8±8.7	83.2±8.2	80.5±8.6	81.8±8.5
Hypertension — no. (%)	84 (73.7)	93 (77.5)	177 (75.6)	91 (75.8)	91 (79.1)	182 (77.4)
hsCRP concentration — mg/liter††	3.5 (120.0)	3.6 (124.6)	3.5 (122.0)	3.0 (124.3)	2.7 (127.5)	2.8 (125.8)
Prediabetes — no. (%)	74 (64.9)	78 (65.0)	152 (65.0)	69 (57.5)	64 (55.7)	133 (56.6)
Glycated hemoglobin — %	5.69±0.37	5.64±0.35	5.67±0.36	5.62±0.37	5.65±0.44	5.63±0.41
Dyslipidemia — no. (%)	91 (79.8)	98 (81.7)	189 (80.8)	100 (83.3)	97 (84.3)	197 (83.8)

* Plus–minus values are mean ±SD. Categories include all participants who underwent randomization unless otherwise noted.
† Trial 2 had one missing participant value for body-mass index for each of the two trial groups.
‡ Participants with an apnea–hypopnea index (AHI, the number of apneas and hypopneas during an hour of sleep) of less than 15 events per hour were determined to have been enrolled in error and were withdrawn from the trial.
§ The PROMIS Short Form Sleep-related Impairment 8a consists of eight factors that the participant can recall in the past 7 days, with each factor rated on a 5-point scale from "not at all" to "very much." Scores for individual factors were totaled to obtain a raw score that was then converted to a T score (with the use of response-pattern scoring), with a mean score of 50 and a standard deviation of 10, with higher scores indicating more sleep-related impairment.[23]
¶ The PROMIS Short Form Sleep Disturbance 8b consists of eight factors that the participant can recall in the past 7 days, with each factor rated on a 5-point scale from "not at all" to "very much," "never" to "always," or "very poor" to "very good." Scores for individual factors were totaled to obtain a raw score that was then converted to a T score (with the use of response-pattern scoring), with a mean score of 50 and a standard deviation of 10, with higher scores indicating more sleep disturbance.[23]
‖ The Epworth Sleepiness Scale (ESS) is an eight-factor participant-reporting measure that asks the participant to rate, on a scale of 0 (would never doze) to 3 (high chance of dozing), their recent typical likelihood of dozing in eight different daytime situations. The ESS total score is the sum of the eight factor scores and ranges from 0 to 24, with higher scores indicating greater daytime sleepiness.
** Hypoxic burden is defined as the total respiratory-event–related area under the oxygen-desaturation curve from a pre-event baseline and is expressed as % min/hr — the time (in minutes) spent in oxygen desaturation (%) per hour of sleep. This measure is calculated from a polysomnographic study that encapsulated frequency, duration, and depth of respiratory event–related oxygen desaturation, and data are geometric means (coefficient of variation, %).
†† High-sensitivity C-reactive protein (hsCRP) data are geometric means (coefficient of variation, %).

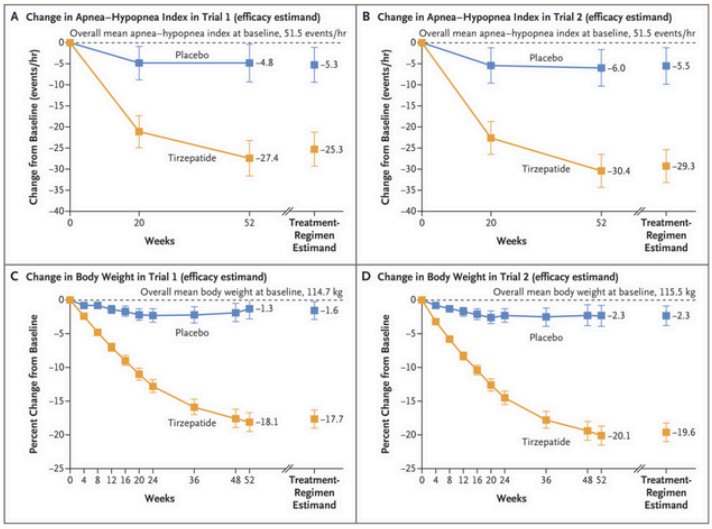
Above is a table taken from the study that outlines changes as a result of Tirzepatide treatment.

The safety of Tirzepatide was consistent with that observed in previous trials concerning the usefulness of this drug. As typically observed with Tirzepatide and GLP-1 receptor agonists, mild-to-moderate gastrointestinal events were the most frequently reported side events, occurring primarily during the dose-increasing periods. There were no differences observed between Tirzepatide recipients and placebo recipients concerning reported gallbladder-related events or hepatic and renal events. Showing that other than gastrointestinal problems, the side effects of Tirzepatide are not astounding.

However, it's important to note that the trial did not assess long-term cardiovascular outcomes and excluded individuals without obesity, limiting conclusions about the drug's effects in non-obese populations or over extended periods.

The results from these trials combine to show a potential solution to treat obese people suffering from sleep apnea in a non-intrusive way (as opposed to using a PAP or CPAP). The trials also tested people from different backgrounds around the world, aiding the potential effectiveness of the drug considering different ethnic backgrounds. Although the use of Tirzepatide has not been tested for full, long-term effects of treating sleep apnea, it will still be as effective 5 or 10 years after its first introduction. Additionally, Tirzepetide's effect on the heart has also not been studied to a meaningful level to determine its safety. As a whole, this clinical trial showed meaningful medical results regarding the effectiveness of Tirzepatide in treating sleep apnea.

Another key outcome related to sleep apnea itself is the weight loss effect of Tirzepatide shown through charts. The major findings of this trial also support the effects of Tirzepatide as a weight loss drug, similar to other drugs on the market, such as Ozempic. Due to these results, Tirzepatide treatment is currently only available to obese patients suffering from OSA. However, based on the weight loss trend along with the decreased OSA episode trendline, it can also be said that the patents were successful during this trial because of the weight loss that occurred over the 52 weeks.



These findings suggest that Tirzepatide may reduce OSA severity primarily through weight loss, though more studies are needed to determine whether it has direct effects on OSA beyond weight reduction.

Taken together, the findings from these trials suggest that Tirzepatide may offer a promising, non-invasive alternative for managing obstructive sleep apnea in obese individuals. The trials also tested people from different backgrounds around the world, aiding the potential effectiveness of the drug considering different ethnic backgrounds. However, while the results show a strong correlation between Tirzepatide use and reduced apnea–hypopnea index (AHI), it remains unclear whether the drug directly improves OSA or whether the improvements are primarily a result of weight loss. Since excess body weight is a major risk factor for OSA, the observed benefits may stem from Tirzepatide's weight-reducing effects rather than a direct impact on airway function or sleep regulation. This uncertainty underscores the need for further research to isolate Tirzepatide's specific role in treating OSA independent of its effect on body weight.

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NARCOLEPSY

Digest by Sky Phisuthikul

Narcolepsy is a chronic sleep disorder affecting the sleep-wake cycles of a person. It is a hypothalamic disorder. It specifically is related to the REM stage of sleep, with narcoleptics being unique in that the REM (rapid eye movement) stage of sleep occurs before NREM (non-rapid eye movement). In this way, they will start a sleep session with REM- 15 minutes after falling asleep- meaning that they are particularly prone to hallucinations in the moments before falling asleep. Not only are their sleep cycles different, but the total time spent in REM is greater than that of a person without the disorder.

They may sleep for a sufficient number of hours at night; however, they will not feel rested because their sleep quality is suboptimal. This can cause them to suddenly fall asleep during the day, even at undesired times. These short naps can be as momentary as a couple of seconds- short enough that the narcoleptic may not realize that they had fallen asleep and continue with whatever they are doing. Though they may feel rested after taking naps, they can quickly become sleepy again, causing the cycle to continue. Common symptoms are EDS, sleep-related hallucinations (hypnagogic hallucinations), sleep paralysis and cataplexy, the latter being unique to narcolepsy.

Cataplexy is where sudden weakness in muscles is experienced when an individual experiences heightened emotions such as excitement and laughter. Though severity varies among people, in the more extreme cases where the narcoleptic may collapse, they remain conscious throughout the experience. Because of these episodes, people may withdraw to prevent triggering cataplexy.

Only 20-25% of people experience all four of the symptoms, which have been crowned as the 'tetrad of narcolepsy'. Studies from various countries report figures anywhere from 0.2-600 cases appearing per 100,000 people, affecting both men and women equally. Fortunately, this disorder does not usually seem to worsen with age. Onset typically occurs during adolescence, but symptoms can take anywhere from weeks to years to be expressed, with excessive daytime sleepiness (EDS) often being the first symptom to appear. It can sometimes go undiagnosed or be mistaken for other conditions like sleep apnea or epilepsy.

Narcolepsy is mainly caused by a mutation in orexin receptors as well as the loss of orexin-producing neurons. Orexin, also known as hypocretin, is a neuropeptide that regulates wakefulness and appetite (it is named after the Greek word for appetite!) Sleep debt increases orexin levels, with a study finding that 24 hours of sleep deprivation causes a 70% increase of the neuropeptide. This increases food cravings, which explains why narcoleptics may experience excess weight gain, with some having a BMI which is 15% above the average.

There are 2 types of narcolepsy: type 1 and type 2. Type 1 is thought to be caused by an autoimmune disorder, with the risk being particularly high for people with 1st degree relatives with the condition. It is also associated with lower levels of orexin. In Type 2, orexin levels are normal, and cataplexy does not occur; the symptoms tend to be less severe.

Other causes can be injury to the brain, specifically the hypothalamus (secondary narcolepsy), which can come with additional extra long periods of sleep (10+ hours) and hormonal changes, such as during adolescence or menopause.

All in all, this disorder, though not life-threatening, can be disruptive to the daily life of an individual. It is with risks of injury, particularly with type 1, and unfortunately is without a direct cure. Despite that, measures can be taken to help ease the symptoms. Stimulating medication like Modafinil or armodafinil can be prescribed, aiding narcoleptics by promoting wakefulness. Improving sleep hygiene, making lifestyle changes as well and taking short naps throughout the day can help with easing tiredness. Most narcoleptics see improvements in their symptoms, having sought out treatment and adapted their lifestyle.

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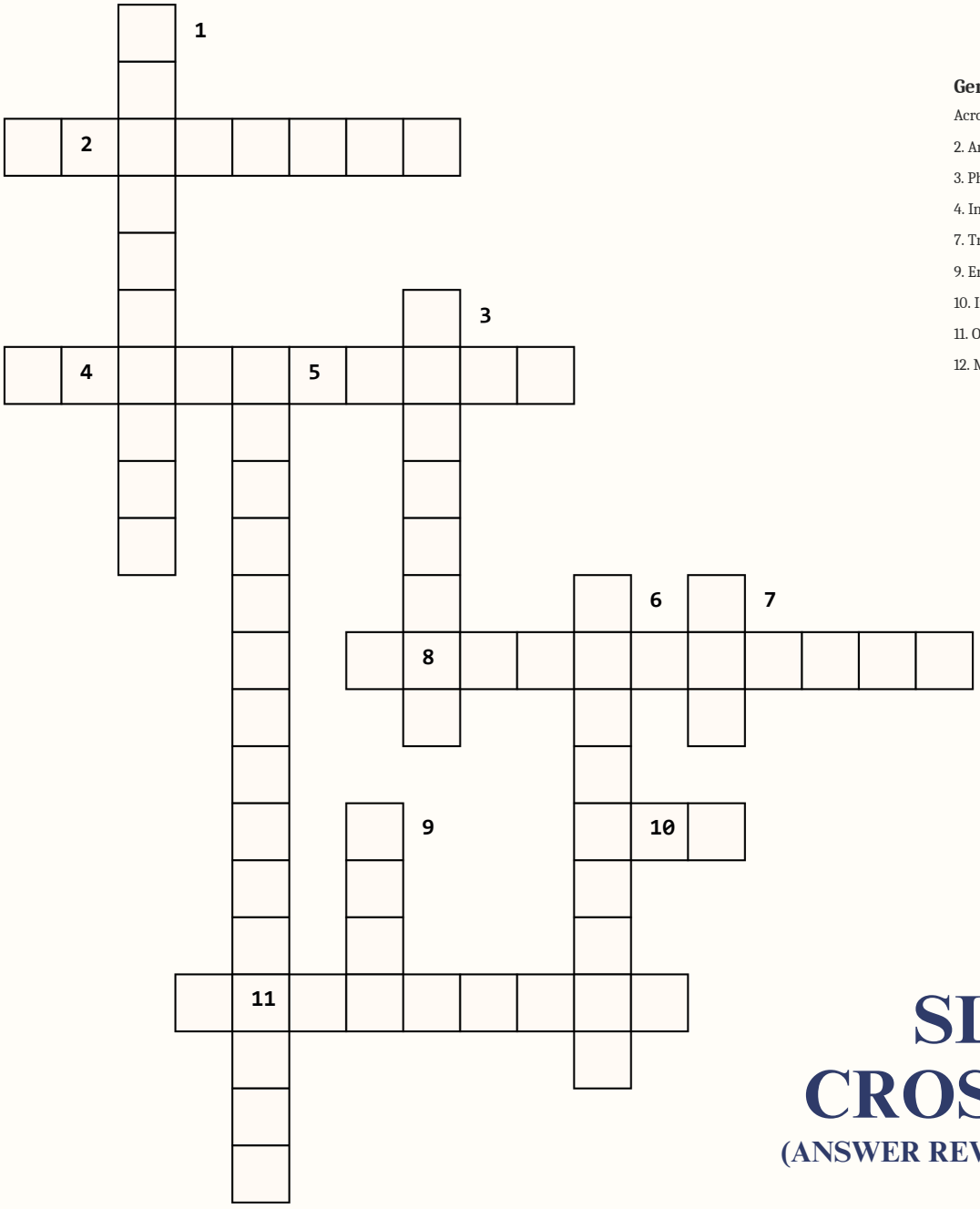


Genetics Crossword Answer Key

Across	Down
2. Aneuploidy	1. Receptor
3. Phenotype.	5. Transduction
4. Intron	6. Exocytosis
7. Transgenic	8. Recessive
9. Endocrine	
10. Integumentary	
11. Organ	
12. Mutation	

SLEEP CROSSWORD

(ANSWER REVEAL IN NEXT ISSUE)

Across

2. Hormone with peak secretion right before waking up

4. Disorder where breathing stops & starts in sleep

8. Used to treat 4 Across and Type 2 Diabetes

10. Abbreviation for the stage of sleep when you dream

11. Hormone regulating sleep-wake cycle

Down

1. The cause is orexin deficiency

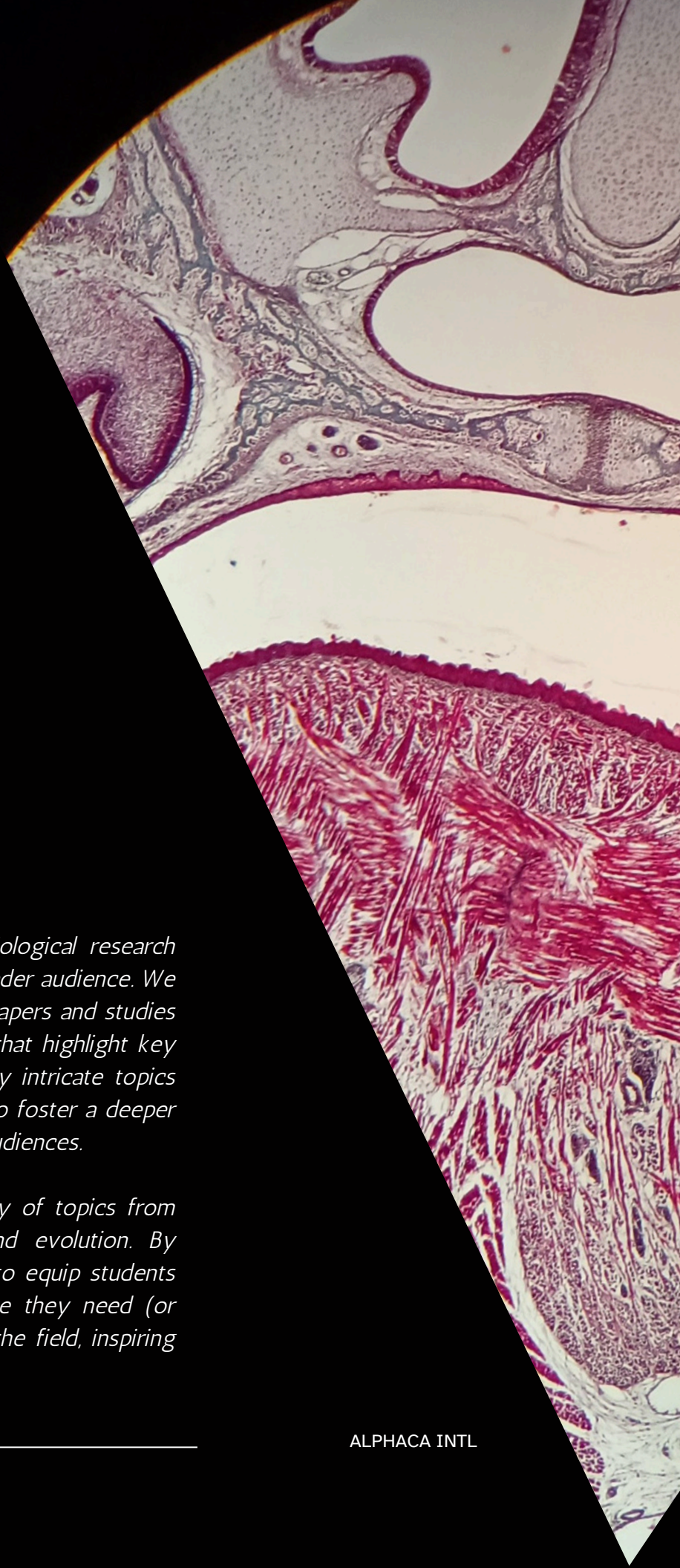
3. Sleep disorder where it is difficult to fall and stay asleep

5. System which controls body during sleep

6. Sea creature which does not sleep

7. You might do this during the day if you are tired

9. Abbreviation for a neurotransmitter which produces a calming effect



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