

## FESPARK NEWSLETTER



## CHANUKAH - TO SEE THE LIGHT WITHIN

Chanukah is the Yom Tov of light. Yavan represents darkness - חושך זו יון, while the miracle and light of the נרות חנוכה tell of the light that shines from within the darkness - אור מתוך החושך. What does this enlightenment mean to us, and how can it inspire and illuminate our lives?

תו"ל teach us that one of the manifestations of ,נס חנוכה, was the revelation of the wisdom of חורה שבעל פה As opposed to חורה שבכתב, this wisdom is not received directly from heaven, לא בשמים, rather it is only realized through the efforts of the חבמי החורה themselves. Via their exertion to penetrate the darkness, overcoming the challenges to master this discipline, they reach the radiant glow of חורה שבעל פה. In fact, the first time in חו"ל we find a statement credited to the name of a specific תנא is by שמעון הצדיק, the initial תנא of חורה שבעל פה (and the archenemy of 'וון') - as we learn in the beginning of Pirkei Avos: שמעון הצדיק... הוא היה אומר. The intense efforts of the חכמים

determine the truth, makes the Torah they discover 'their own', and therefore befitting to be ascribed to them directly.

The Ramban tells of another portal of access to the concealed light of חורה שבעל פה tells and .חורה שבעל פה us that after בואה) taken from us in the beginning of בית שניי, one of those to whom it was transferred were the חבמים. The Ramban explains that the vision of the חבמים is not a revelation from outside themselves, as was the case by the ביאים, rather, the חכמים are given the ability to tap into an inner truth that resides deep within their own souls: "יודעים את האמת ברוח הקודש שבקרבם"; they have access to an internal Holy Spirit, wherein the light of truth resides

Furthermore, the Vilna Gaon tells us that not only חבמים have access to the inner voice of רוח הקדוש , rather, every person can access it, as well. He writes that if one listens carefully, with an honest, open heart, he will also hear his voice of truth, steering him in the right direction, giving him sage, divine advice in all areas of life.

In our very difficult, dark times, we all search for clarity and light. It is our יום מוב of חנוכה that empowers us to navigate the labyrinths of darkness and discover our הקודש, our inner voice of eternal truth and enlightenment. The gift of אור מתוך החושך reflected in the ורות חנוכה, and the parallel illumination of חורה שבעל פה, lend us confidence along our journey, leading us to experience our own hidden light as well - until the light burns bright and the guiding whisper of our spirit becomes loud and crystal clear.

"Each and every person has their own personal path in life, for the minds of people are dissimilar from one another... when there were נביאים, individuals would go to the נביא for guidance, and the נביא would prophetically direct them upon their particular path, in accordance with their soul-root (שורש נשמה)...when נבואה ceased, there is always כלל ישראל, in accordance with their soul-root, בכלל ישראל, and a person's inner spirit will advise them of the path they should follow - for הקודש exists within each & every person" (גר"א, משלי טז.ד)

<sup>1</sup>ראה מגילה יא,א: 'ולא געלתים', בימי יוונים, שהעמדתי להם שמעון הצדיק וחשמונאי´ובניו וכו'. וע"ע יומא סט,ב.

 $^2$ אשר הוא גם שעת התחלת הגילוי של תורה שבע''פ.

. ממנו יחוזה', ר"ל, שרואה דבר שמחוץ ממנו $^3$ 

## Empowering Patients with Parkinson's: The Dual Role of Exercise & Physical/Occupational Therapy

Parkinson's Disease (PD) affects millions worldwide, posing challenges to movement and overall wellbeing. While a cure remains elusive, effective approaches to managing its impact have emerged. Exercise and physical therapy have gained prominence as essential tools in enhancing the quality of life for individuals with PD. It helps to enjoy the exercise so that it becomes a habit over time.

Therapy services covered through insurance typically need a prescription from the doctor and are limited in the number of sessions. A long-term goal should be to incorporate guidance from a therapist into a daily exercise program that can be done alone or with others in a group setting. Let's get into how and why this works.

## The Dopamine Boost from Exercise

Dopamine is a chemical in the brain that helps with smooth movements and mood regulation. In PD, dopamine is in short supply, causing movement issues. Exercise acts as a natural dopamine booster. When people with PD exercise, their brains release more dopamine, leading to improved movement and enhanced mood.

Research tells us that exercise is a game-changer for PD management:

- 1. Dopamine Connection: A study published in the Journal of Parkinson's Disease (2017) found that both aerobic exercise and high-intensity interval training increase dopamine release in the brain. This increase is linked to better motor function and overall quality of life.
- 2. Neuroplasticity Benefits: A review in the European Journal of Physical and Rehabilitation Medicine (2020) highlighted that exercise not only boosts dopamine but also encourages neuroplasticity, the brain's ability to adapt. This adaptation potentially slows down the progression of PD.

## The Role of Physical Therapy

Physical therapy customizes exercises to strengthen the body and improve flexibility, targeting issues like stiffness and balance problems. These exercises prompt the brain to release more dopamine, aiding in better movement.

Encouraging big movements along with boxing have been popular components of therapy sessions. The result of these interventions are typically seen immediately with better mobility, strength, and coordination afterwards.

## The Role of Occupational Therapy

Occupational therapy assists in daily tasks and cognitive challenges. It empowers individuals to handle activities like dressing, cooking, and memory tasks. These purposeful activities stimulate dopamine release while enhancing



independence. Many Occupational Therapist's will work on fine motor skills that involve hand movements affected by coordination and strength deficits. Intentional movements can also decrease the effect of tremors.

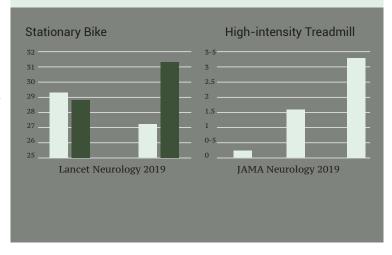
#### **Numbers that Matter**

Statistics underscore the impact of exercise and therapy:

- 1. Exercise Frequency: Studies suggest that people with PD benefit from exercising at least 150 minutes per week. This level of exercise has been linked to improved motor skills and mental well-being.
- 2. Therapy Efficacy: A study by the Parkinson's Foundation revealed that 88% of individuals with PD who participated in physical therapy reported improved mobility, and 74% reported enhanced balance.

PD might present challenges, but exercise and therapy are strong allies in the fight against its effects. The dopamine-boosting power of exercise is supported by research, while physical and occupational therapies provide tailored strategies to improve daily life. By embracing these approaches, individuals with PD can experience improved movement, independence, & an overall better quality of life.

## 1st Disease Modifying Therapy



# MEDICAL MOVEMENT.

By: Paulette Laniado, Patient Liaison, LifeSpark As mentioned previously on these pages [Issue #12 - Shevat edition], the Parkinson's medical community recently achieved a breakthrough in PD diagnosis. A PD biomarker has been discovered, i.e., a measurable bodily substance that indicates if one has, or is prone to, Parkinson's Disease. This material is the protein known as Alpha-synuclein, found throughout our bodies, and concentrated in our brain cells. Scientists have discovered that in individuals with PD, Lewy Body Dementia and Alzheimer's, the protein behaves differently than in other people. Through spinal tap, researchers can access the Alpha-synuclein, and thereby identify if it indicates a PD diagnosis.

However, although this is a major development, the spinal tap procedure is uncomfortable and even painful for the patient to endure.

Now, the Duke University School of Medicine has discovered a new test called Mito DNADX. This test is a simple blood test that can detect damage in the DNA from mitochondria; the inner part of cells that generates the energy to power the cells, that malfunction in those with Parkinson's. Research shows that an individual with Parkinson's will have a significant greater amount of mitochondria DNA damage than people without PD.

According to Mark Fraiser, PhD, The Michael J. Fox Foundation (MJFF) Chief Scientific Officer, the test can be used to diagnose an early detection of Parkinson's Disease.

Research suggests that while the new biomarker is similar to the Alpha-synuclein marker, however, they measure different aspects of the disease, and therefore they both will be used, depending on the particular case. It is important to note that while this is a stunning discovery, it is still in its early stages and does not yet take away the necessity of a clinical diagnosis and treatment from your neurologist.

## To the Extraordinary Community of PD Fighters:

It has been a painful start to this new year, and recent events in Israel have been, and will continue to be, the headline for our community. Nevertheless, I would like to draw attention to a valuable activity that can bring immense joy and positive change for those in the Parkinson's community.

Parkinson Disease was identified over 200 years ago. While we are making progress with different treatments and surgical interventions, we still do not have a cure. The only therapeutic modality that has been shown to slow progression of the disease is consistent exercise. There is abundant evidence that exercise improves brain health and vitality!

The greatest impact comes from doing a variety of routines to wake up as many muscles as possible, including aerobic activities, stretching, and strength training. But the most important component is deriving joy from any exercise that one may choose to participate in, because joy is the greatest motivator for repetition and consistency!

Happiness may be rooted in social engagement, intellectual stimulation, or pride in pushing oneself physically. I have personally gravitated toward the sport of table tennis because I have seen how it delivers on all three! There are pockets around the world where table tennis is more popular than it may be here locally, but we are eager to spread the word, because it is a wonderful activity that helps Parkinson's patients focus on balance, hand-eye coordination, and the challenge of reciprocal play. Most importantly, it is fun! It is a social activity by nature, and is a skill set that one can improve upon.

Table tennis may not be the cure, but gives us a fighting chance toward it, and helps us come closer together as a community.

Wishing you all health, happiness, and peace,

Flana Clar, MD



There once was a king who invested tremendously in his relationships with his neighboring rulers. He worked hard to cultivate a friendship with the kings who ruled over the two bordering countries. The three kings would meet every few months to discuss how to improve their economies and how to deter their mutual enemies.

In one of these kingdoms lived a wealthy, assimilated Jew, Emanuel. Although he was born into a frum home, he gradually left the Torah path in pursuit of wealth. He was a brilliant strategist and extremely wise. The king heard about him and made him a close advisor.

One day, the king sent out invitations to the neighboring monarchs, informing them that his wise Jewish advisor would be joining their meeting. One of the two kings was very upset that a Jew would be joining their private meeting. He could not picture himself sitting beside a lowly Jew as though the two were equals.

In his hatred, this king schemed to shame and degrade Emanuel as he arrived to the meeting. He arranged a group of wild young men should ambush and embarrass Emanuel as he traveled towards the meeting. As Emanuel's carriage slowly made it's way down the hill towards the palace, he aw a band of youths blocking the wagon, chanting "Jew, Jew, Jew!" refusing to move.

Emanuel let the teens continue chanting for a few more moments before handing his driver a heavy sack containing a thousand gold coins. "Scatter the coins," he instructed. "When they see the money, they'll move aside to gather it up, and we'll be able to move on." Sure enough, when the youths saw the coins, they began scrambling over each other to collect them. Emanuel watched in amusement as they filled their pockets, while his driver whipped the horses and traveled on with the carriage.

When Emanuel arrived in the palace all three monarchs were already seated. The hosting king greeted him with great honor and introduced him to the others. The anti-Semitic king

couldn't hold himself back and immediately brought up the embarrassing incident that he had orchestrated. He wanted to see the Jew's reaction when he brought up the event. "You know, Jew, we heard the report that there were about fifty young rascals waiting for you at the bottom of the hill, taunting you. I heard you gave them some money, too. I'm not sure I understand what happened there."

Emanuel realized immediately that this king had hired the youths to stand there and block his way. "Oh, those boys?" he said. "They didn't embarrass me. They gave me such a beautiful gift." The kings were surprised by this answer. "What do you mean?"

Emanuel smiled. "May I relate a brief story?" he asked respectfully. "Go ahead", they said.

"There was once a wealthy man who possessed the largest, most beautiful diamond in the world. When he died, he left over a tremendous inheritance for his only son, including the diamond.

"Unfortunately, however, his son was reckless and immature, and he had a terrible gambling habit. Within a matter of months, he succeeded in losing the entire inheritance on the gambling table. The only thing that remained was the diamond. He couldn't gamble with the diamond. It was much too big." "So, he took the diamond to the bank and asked to borrow \$50,000 against it. The bank agreed and took possession of the diamond as collateral for the loan. The reckless son, however, had not learned his lesson. Within a week, the entire sum he borrowed was gambled away.

"He returned to the bank and took out an addition \$50,000 against his diamond, but only ten days later, he was again out of funds. This happened over and over again. Like all gamblers, he was sure the next game would win him back all the money he lost, and so he went back to the bank to borrow more money against the value of his diamond.

"The bank manager, who had known his father, tried to talk him out of it. He pitied the young man and did not want to see him gamble away his entire fortune. The son, however, refused to listen and insisted on withdrawing an additional \$50,000. Predictably, he lost the money within a few days." When the son came around a fifth time to borrow money against the diamond's value, he categorically refused.

"The son begged and pleaded, sweet-talked and threatened, but the bank manager refused to relent. Despite the fact that he had only withdrawn forty percent of the diamond's value, the bank refused to lend him another cent. "Enraged, the son vented to a friend. 'I only borrowed \$200,000, and that diamond is worth at least \$500,000,' he complained. 'That stubborn bank manager! I've tried everything! How can I get him to lend me more money?' "The friend thought for a moment. 'Why don't you sell the

"The friend thought for a moment. 'Why don't you sell the diamond to the bank outright, instead of borrowing against it?' he suggested. 'You'll recoup the remaining \$300,000 and be able to spend it as you see fit.'

"The son whirled on his friend, a horrified expression on his face. 'Sell the diamond?' he asked, disbelief coloring his voice. 'Sell the diamond?! How could I sell my diamond?' "The friend didn't seem to understand what the problem was. 'Why not?' he countered. 'You'll get the money you need.'

"The son shook his head. 'You don't understand. My diamond is not just about money. It's my entire identity. Wherever I go, people point me out as the owner of the largest diamond in the country. That's worth much more than money!' "His friends stamped his foot in frustration. 'But you gambled away almost half the diamond's value anyway! What good do you have from a diamond that's sitting in the safe of the bank?'

"True,' the son responded. 'Right now, the bank is holding my diamond. But as long as I didn't sell my diamond, I know that one day I can pay back the bank and redeem it. The bank may be holding my diamond, but I am still pointed out as the owner of the diamond. And that is priceless." Emanuel stopped speaking and let his words settle for a

moment. "Your royal Majesties," he said in a trembling

voice. "I am a Jew, and my Jewishness is a diamond. It is the most precious treasure I own. Alas, I've traded my diamond for money, gambling away my

THIS WAS NOT AN EMBARRASSMENT; IT WAS A GIFT!

most precious asset for riches and fame.

"Still, I am a Jew! Despite the fact that I have given up Torah and Mitzvos, I will never sell my Jewishness. When someone points at me as a Jew, they are pointing me out as the owner of the diamond! What a priceless title!

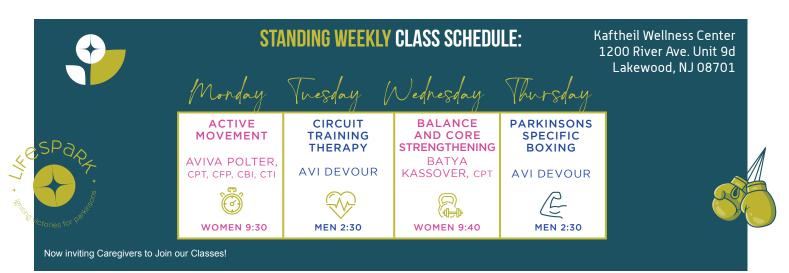
"Today, as I rode here to this meeting, I was accosted by not one, but fifty youths calling me the owner of the diamond. They were reminding one and all how lucky I am to have such a heritage. I am a Jew! This was not an embarrassment; it was a gift! That is why I gave them a thousand gold coins. In fact, had I had ten thousand coins with me, I would have given them that amount!"

The anti-Semitic king backed off, respecting the Jew who respected his origins.

"Emanuel was a Jew who strayed from the Torah path. But even a Jew like this, who abandoned all Mitzvos, understands that Yiddishkeit is the most precious thing he has.

"This was a man who understood that his greatest asset was not his assimilation among the nations, but that which keeps him separate from them. This is the extraordinary quality of a Jew."

In his sefer, the Ben Ish Chai concludes by explaining that this is what the posuk means by הן עם לבדד ישכון ובגוים לא יתחשב We are a nation apart from the gentiles. Even if we try to mingle, we are immediately separated. Either the gentiles prod us to separate through pain, or we come to the understanding on our own. Like oil to water, we are a nation that rises above, separate and holy.



## COULD CHANGES IN GUT BACTERIA CONTRIBUTE TO THE DEVELOPMENT OF PARKINSON'S DISEASE IN THOSE WITH GENETIC RISK?

Mutations in the GBA1 gene are one of the most common genetic risk factors associated with Parkinson's disease (PD). However, it's important to note that not all people with GBA1 mutations will necessarily develop PD. Furthermore, if they do, the onset may occur at different ages and with different clinical presentations. This variability highlights the critical need to identify additional factors, both environmental and genetic, that may influence the likelihood of developing PD in individuals with GBA1 mutations.

Individuals with GBA1-related PD often have a higher prevalence of non-motor symptoms, such as a reduced sense of smell and constipation, which typically precede the onset of motor symptoms. The characteristic tremors, rigidity, slowness of movement, and freezing in PD have been attributed to the loss of certain brain cells called dopaminergic neurons, along with the accumulation of a protein called  $\alpha$ -synuclein in the brain. Interestingly, a hypothesis emerged in 2003 that the initial pathology of  $\alpha$ -synuclein may originate in the gastrointestinal tract before progressing to the brain. Specifically, people with PD often have alterations in their gut microbiota, resulting in changes in the maintenance of the intestinal lining, inflammation, and the body's ability to defend itself against invading pathogens.

Of particular interest are short-chain fatty acids, which have potential anti-inflammatory and neuroprotective properties. These compounds are produced by certain types of gut bacteria through the fermentation of dietary fiber. They do not only provide energy to gut cells but also support the regeneration and maintenance of optimal intestinal barrier function. However, it remains unknown whether alterations in short-chain fatty acids and other microbial molecules influence the likelihood of GBA1 mutations leading to PD.

Supported by the US initiative Aligning Science Across Parkinson's (ASAP), our research laboratory is investigating how GBA1 mutations might interact with microbial molecules to promote inflammation and α-synuclein accumulation using various cell culture systems. So far, we've obtained skin biopsies from PD patients with the E326K or L444P mutations, two GBA1 variants commonly associated with PD. We reprogrammed the skin cells to create induced pluripotent stem cells (iPSCs), which have the potential to become any type of cell. We first differentiated iPSCs into two different types of immune cells peripheral macrophages and microglia found in the brain - to compare how GBA1 mutations affect immune cell function in the peripheral and central nervous systems.

Both types of immune cells exhibited reduced GBA1 activity. Interestingly, brain-dwelling microglia carrying the L444P GBA1 mutation showed an increase in cytokine secretion associated with the recruitment of peripheral immune cells. Building on this work, we analyzed intestinal organoids derived from GBA1-related PD patients. These organoids are three-dimensional structures that mimic the cellular composition and behaviour of the human gastrointestinal tract. We discovered that reduced GBA1 activity correlates with an increased presence of  $\alpha$ -synuclein, suggesting that our model system accurately reflects changes observed in PD patients.

In an effort to more accurately mimic the complexity of the human gastrointestinal tract and to study the spread of α-synuclein

from the gut to the brain, we are currently developing gut-brain chip models. The gut-on-chip model incorporates intestinal organoids and vascular cells with mechanical forces to mimic real physiological conditions. This system will allow us to study the role of GBA1 and short-chain fatty acids in maintaining the intestinal barrier, identify the molecular mechanisms involved in  $\alpha$ -synuclein accumulation, and assess the potential recruitment of immune cells from blood vessels into the tissue. We will then investigate whether manipulating the microbiome, balancing inflammation, or restoring GBA1 function could reduce the risk, delay the onset, or slow the progression of PD in individuals with GBA1 mutations. The results of this research have the potential to pave the way for personalized medicine tailored to this genetically distinct patient population.

Christin Weissleder, PhD, works at the Imagine Institute of Genetic Diseases (Paris, France). She was a Hot Topic presenter at the WPC 2023 in Barcelona on "Uncovering the interaction between gut microbial factors and GBA1 mutations in the pathogenesis of Parkinson's disease."

## WHO IS THIS?

He was built to resist, All that Greece stood for, Yet, he always prayed, They should win their wars

JOKE: Why did the dreidel go to the doctor?

### **WHAT WAS THIS?**

The Menorah of the Mikdash, A solid piece of Gold, While that of the השמונאים, Was different, we're told

**JOKE:** What did one candle on the Chanukkah menorah say to the candles?

## **WHAT IS THIS?**

The length of our Festival, Exactly for eight days, Is modeled after a Yom Tov, Observed in many joyous ways

JOKE: What gift do you get from your Bubby for Chanukkah?

#### **HOW MANY?**

Galus Edom seems endless, We've shed countless tears, Before them was Yavan, That lasted how many years?

JOKE: What did the faucet sing on Chanukkah?

## HOW MUCH?

'A few in the hands of many'
We fought them blow by blow,
Between us and the Greek soldiers,
What was the [minimum] ratio?

**JOKE:** What do you call a potato latke with an identity crisis?

#### WHO WAS THIS?

👝 The חשמונאים, they were holy,

Also, very brave,

In the end they were destroyed,

By a lowly slave.

**JOKE:** What did the older Chanukah Candle say to the younger one?

## WHO WERE THEY?

The חשמונאים dynasty, Eleven kings in all, Can you name (at least) six that reigned, Before their tragic fall

JOKE: Why did the Maccabee family refuse to eat donuts?

#### **WHO IS THIS?**

The first Greek king, In Egypt to rule, He transcribed the text, Of the Torah, our jewel

**JOKE:** Why did the Chanukkah candle refuse to light up the room?

1. His head was spinning 2. I'm feeling a bit burned out 3. A latke hugs and kisses 4. I have a little dribble! (Dreidel) 5. A latke-doodle-do 6. You're too young to smoke 7. They were trying to cut back on their oil intake! 8. It was too shy to shine!

SIDDLE ANSWERS:

airria :8# salaibles see Rel Fot raiblos nwarxr F.3# syeav (18 F.4# sox). See kooti room oo see suurii riri r nrar nark:8# annya, yara, yara, yara, yaranta'a, wraart, wraatre narca, anga השלישיו, ארשחובלום והשלישיו, ארשחובלום ארשב אנטינום. "7#



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On Oct 22nd, Dr. Rebbeca Gilbert, chief scientific officer, APDA, and Fayga Brisman, senior associate director Michael J. Fox Foundation, spoke about the trial process and how to become part of it.

Here are the links they shared with the attendees.

https://www.michaeljfox.org/trial-finder

https://drive.google.com/file/d/1NeSyFA37b9IbUzryRRP-EqrgScjCRL-3/view

https://clinicaltrials.gov/study/NCT05677633

https://foxinsight.michaeljfox.org



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