Working Productively

Every year, we mark a special day focused on improving how we work and live. World Productivity Day highlights ways to do tasks better and achieve more in less time! This day is not just about working harder but smarter. It encourages everyone to look at how they manage their tasks and find ways to enhance their efficiency. It also reminds us that by adopting smarter work strategies, we can improve our performance and overall well-being. It promotes innovation and sharing success stories that motivate others to aim higher in their daily activities. Ultimately, it asks us to reflect on our work habits and strive for continuous improvement.

#MEDICINE

Antabuse Can Cure Blindness Along With Alcoholism

Disulfiram can target that sensory noise and ultimately restore some vision.

Researchers may have found a way to revive some vision loss caused by age-related macular degeneration and the inherited disease retinitis pigmentosa.

Age-related macular degeneration is the leading cause of blindness. Retinitis pigmentosa (RP) is a rare genetic disorder that causes the breakdown and loss of cells in the retina.

The drug disulfiram, marketed under the brand name Antabuse, used to treat alcoholism, may hold the key to restoring this vision loss.

"We knew that the pathway drug disulfiram blocks, to treat alcoholism, was very similar to the pathway that's hyper-activated in degenerative blindness," says Michael Telias, assistant professor of Ophthalmology, of Neuroscience, and in the Center for Visual Science at the University of Rochester Medical Center. Telias is first author of the paper in *Science Advances*. "We expected some improvement, but our findings surpassed our expectations. We saw vision that had been lost over a long period of time, preserved in those who received the treatment."

In research involving mice, researchers found that disulfiram helped restore some vision by suppressing the sensory noise in the inner retina, caused by dying photoreceptors in the outer retina, that is brought on by the progression of outer retinal degeneration (such as age-related macular degeneration or retinitis pigmentosa), in which the light-sensing cells, called 'photoreceptors,' slowly die over years.

In past research as a postdoctoral fellow at the University of California, Berkeley, Telias found that as photoreceptors die off, it disrupts the function of the inner retina. This causes the sensory noise that ultimately becomes a barrier between the surviving photoreceptors and the brain.

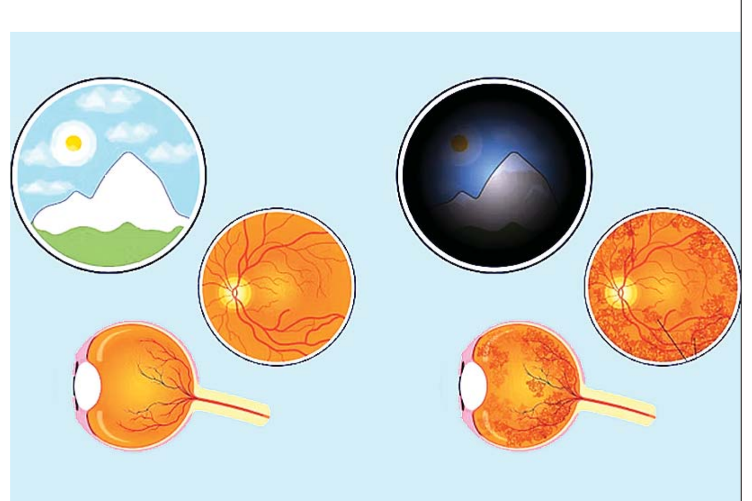
This latest research, led by Richard Kramer, professor at the University of California, Berkeley, and Michael Goard, assistant professor at University of California, Santa Barbara, found that disulfiram can target that sensory noise, allowing the surviving photoreceptors in the outer retina to complete the signal to the brain and ultimately restore some vision. They found that nearly blind mice, treated with disulfiram, were much better at detecting images on a computer screen. "Treated mice really see better than mice without the drugs. These particular mice could barely detect images at all, at this late stage of degeneration. I think that's quite dramatic," says Kramer.

"If a vision impaired human were given disulfiram and their vision got better, even a little bit, that would be a great outcome in itself. But it would also strongly implicate the retinoic acid pathway in vision loss. And that would be an important proof of concept that could drive new drug development and a whole new strategy for helping to improve vision."

The researchers are planning to partner with ophthalmologists to conduct a clinical trial of disulfiram on patients with RP. The trial would be carried out on a small set of people with advanced, but not yet complete, retinal degeneration. Disulfiram does have some severe side effects if alcohol is consumed while taking it, including headache, nausea, muscle cramps, and flushing. But if disulfiram can improve vision, more targeted therapies could be sought that don't interfere with alcohol breakdown or other metabolic functions.

The researchers have already tested an experimental drug named BMS 493 that inhibits the receptor for retinoic acid, and they have also used gene therapy to knock down the receptor. Both of these procedures also dramatically improved vision in mice with RP.

Additional coauthors are from the University of California, Santa Barbara and the University of California, Berkeley. The National Institutes of Health and the National Science Foundation funded the work.



Khus 'Thermantidote'

The colonial vision of containing or controlling the heat was fulfilled in 1833 when the first ship bearing 180 tons of New England ice arrived in Calcutta from Boston. The Boston businessman Frederic Tudor (1783-1864) began shipping ice from Boston to the southern United States, the Caribbean, Brazil, and then further abroad to South Asia in the early nineteenth century. Tudor and his partner Nathaniel Wyeth determined that regularly cut rectangles of ice suffered less melting loss, they covered the ice with sawdust, and they designed double-walled insulation aboard the ships to prevent melting. They also fashioned ice houses that preserved the ice upon arrival. The ice was carried as ballast for low freight rates on ships and, when it reached India, was exempt from import duties. The imports from New England were lauded in the British press for the solidity and clearness of the ice that was now available in the major cities of the British Empire. Given the price, the ice was limited to an elite of both British imperial officials and wealthy South Asian merchants in the cities, although the British tried to keep the best quality ice for themselves.

● Sylvia Houghteling

The paintings that depict the *khas weavings* are primarily those associated with the *ragamala*, or 'garland of raga' tradition. The paintings depict embodied enactments of the seasonal musical modes (ragas and raginis), corresponding to poetic verses that narrate the feelings of love, longing, discomfort, serenity, and pleasure, that the various seasons and moods will bring. Another ragamala painting that includes an image of 'khas' from later eighteenth century (ca. 1780) in Kota depicts the rainy season's *Savant Saranga Ragini*. This is one of the musical modes classified under the broader category of *Rag Megh* (also written as Megha), a raga that is sung during the season of the clouds (megh). Savant Saranga is a monsoon ragini, as indicated by the mineral blue sky above the scene, the densely hanging vegetation, and the peacocks peeking their crests out above. But in the main part of the scene, the reclining female figure cannot get cool. Her attendants serve her drinks in elegantly fluted rosewater bottles that have perhaps been chilled in saltpeter. The whole interior scene of the pavilion is one of burning orange hues and glowing turmeric colors. These colors end instantly when they collide with the flat, neutral brown of the khas pavilion, perhaps suggesting a change in heat and feeling. The *khas khana* is carefully described in this painting: the artist has rendered the structure made from bamboo stems with their characteristic protruding nodes and has shown how the deeper woven brown khas grass has been arranged in rows. Again, the bulging rounded lines, used to render the hut, suggest a thicker and more substantial screen of khas grass. We even see an attendant at the khas khana's window, pulling a cord to open or close the shade.

The depiction of these cooling khas screens within ragamala paintings suggests how another sense, that of sound, could bring relief in the midst of unbearable heat. The raga melodies themselves were understood to activate changes in the temperature. The best-known story related to this phenomenon is about Tansen, the famed musician at Emperor Akbar's court, who is attributed with having composed many lasting raga melodies. In the story, Emperor Akbar requests and then demands that Tansen perform one of the most intense, heat-inducing ragas, known as *Raga Dipak*. In one recounting of the story, Tansen requests two weeks to practice, during which time he teaches his daughter, Sarasvati, to sing *Raga Megh Mallar*, a cooling melody that he knows will work as an antidote and will bring the rains. Indeed upon his recital of Raga Dipak, Tansen's body is overtaken by a burning sensation, at which point his daughter sings the monsoon Raga Megh Mahlar and Tansen's fire is quenched and he is saved. The ragamala paintings depicting variants of Rag Megha bring together these sensory properties of cooling: the muted colors in the sky, the evocations of a calming rag, and the scent of khas, all working together to lower the temperature and bring on the rains.

Pankha Wala, India, in 1870s.

#BEYOND ICE

New England Ice and 'some relief we may enjoy'

A woman reading under a Pankah.

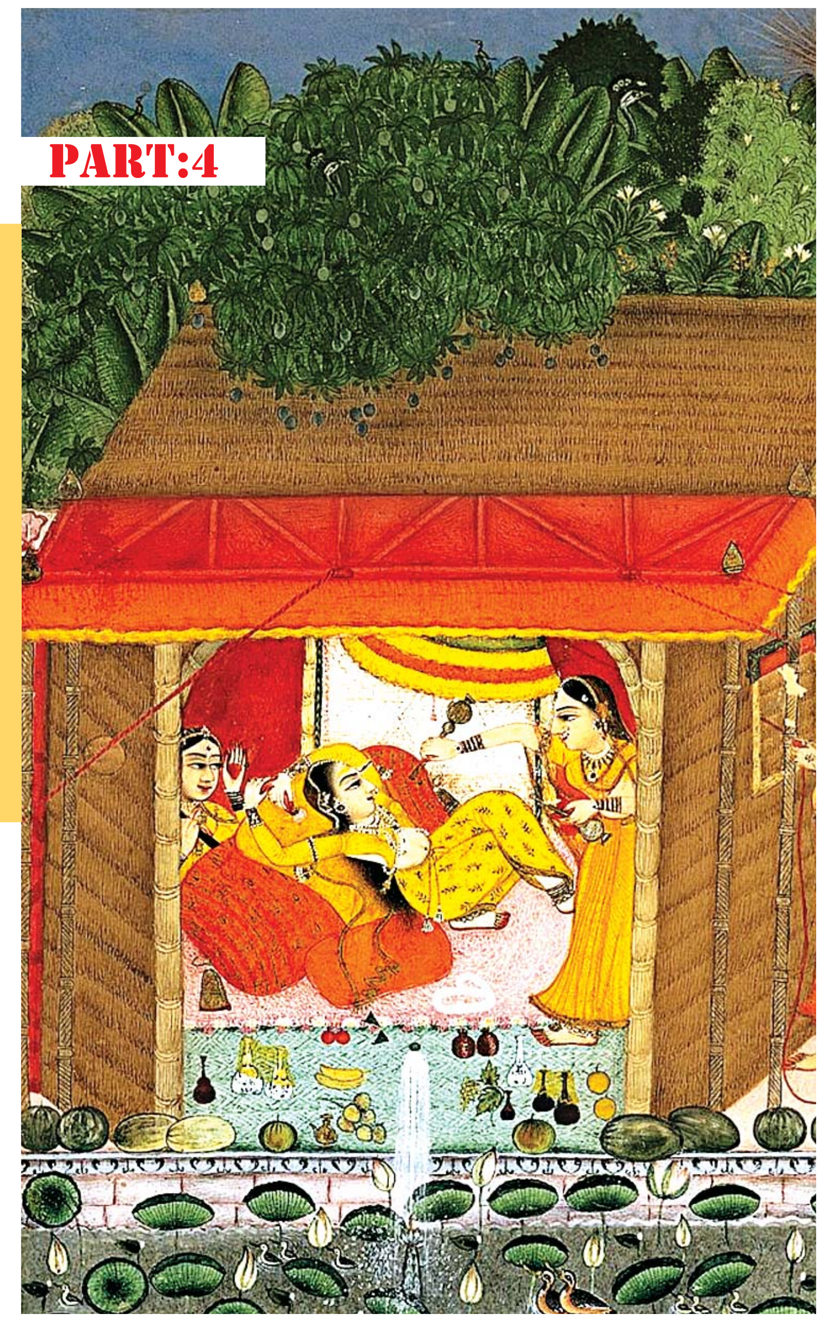
By the nineteenth century, when the British had established their main cities of the empire at Calcutta, Madras, and Bombay, the varied means of cooling gave way to imported ice. Since discomfort in the heat had long been a chief concern, Europeans in South Asia had previously appropriated many South Asian methods for relief from the heat in the summer. As early as the seventeenth century, there were ill-fated proposals at the English court to introduce methods of cooling using saltpeter to Emperor Jahangir (r. 1605-27), although Mughal documents suggest that this method was already well in use in Hindustan. By the eighteenth century, Europeans in South Asia employed an 'ab-dar' to cool their drinks, and had adopted the use of khas screens, even attaching the khas screens to a mechanical fanning system that had to be consistently turned and came to be known as the 'thermantidote.' Various pulley systems and large cloth fans, known as *pankahs*, were used to move the air throughout interior spaces.

Having determined that requisitioning ice from the mountains was too costly, the British at first looked to local, South Asian methods of cooling and ice creation. This involved leaving a few inches of water in numerous porous earthenware vessels overnight. In the cool of the evening, even when temperatures did not drop below freezing, very thin layers of ice would form on the surface and bottom of these vessels could then be pounded together to form a larger block of ice. At times, saltpeter was also used to further the cooling. Rajani Sudan argues that the quest for ice among European officials in South Asia related to an 'entire cultural imaginary of a contained or controlled landscape, untrammeled by climatic realities.' The colonial vision of containing or controlling the heat was fulfilled in 1833 when the first ship bearing 180 tons of New England ice arrived in Calcutta from Boston. The Boston businessman Frederic Tudor (1783-1864) began shipping ice from Boston to the southern United States, the Caribbean, Brazil, and then further abroad to South Asia in the early nineteenth century. Tudor and his partner Nathaniel Wyeth determined that regularly cut rectangles of ice suffered less melting loss, they covered the ice with sawdust, and they designed double-walled insulation aboard the ships to prevent melting. They also fashioned ice houses that preserved the ice upon arrival. The ice was carried as ballast for low freight rates on ships and, when it reached India, was exempt from import duties. The imports from New England were lauded in the British press for the solidity and clearness of the ice that was now available in the major cities of the British Empire. Given the price, the ice was limited to an elite of both British imperial officials and wealthy South Asian merchants in the cities, although the British tried to keep the best quality ice for themselves. On a hot day in June 1837, an anonymous writer (using the name 'Corn Cob') proclaimed appreciation for the ice while casting aside previous methods of cooling:

Now kus kus tatties fail to cool
And punkah breeze defying
The mercury marks 95
And we are almost frying.
....Still, some relief we may enjoy,
For with our 'dall' and rice, Sir,
Liquids become a luxury
From Yankee Tudor's Ice, Sir.

In this poem, the khas screens and the 'punkah' fans are supposedly failing to cool when the 'Yankee Tudor's' ice from the United States arrives. Though seemingly a frivolous change, the ice was used to cool cocktails and claret wine, the displacement and devaluing of indigenous methods of cooling upon the arrival of the imported ice connected to broader British colonialist discourses that sidelined local scientific knowledge in South Asia as 'primitive, obscure, ineffectual, and rudimentary.' Moreover, the decision to substitute locally sourced ice with an energy-intensive import paralleled much larger shifts in trade and manufacturing in the mid-nineteenth century, whereby the British displaced and disrupted the renowned cotton textile industry of South Asia, by flooding markets in India with British machine-made cloth. New England ice remained dominant in South Asia and throughout many colonial cities of the British Empire until the late 1870s and early 1880s, when the system started to flounder due to climate warming in Massachusetts (brought on by both cyclical atmospheric warming and fossil fuel pollution), which drove up prices for naturally occurring ice. By the late nineteenth century, natural ice from New England was being substituted with manufactured ice made through mechanical refrigeration.

PART:4



Raga Megha on Sarangi.

Conclusion

Just on the eve of the arrival of New England ice, Thomas Wise, a British official in India, wrote about the distinction between 'solid ice (pakka baraf); thinner ice that began to congeal later into the night (paperí); and the thinnest ice that froze only shortly before dawn (phúl baraf).' As Thomas Simpson notes, Wise was recording the different local Hindustani names for the substances that could come under the category of ice, each with its unique materiality. There was the solid, whole, and properly 'cooked' ice (pakka); the ice that was as thin as paper (paperi), and the blooming flower of the ice that came before dawn (phul baraf). These variants of ice had distinctive tactile properties, behaved differently as cooling substances, and brought to mind various associations of solidity and floral fragility. Writing a century after Anand Ram Mukhlis, Wise's observations conjure the image of Emperor Bahadur Shah peering out at the cracks in the thin morning ice, when 'his eyes sometimes would catch the cracks in sheets of ice. On this, he used to wait and learn a moral.' If there is a moral, it might be in the conclusion to the story of the colonizer's ice replacing pliable sheets of woven khas, or of energy-intensive travel that was valued over passive means of freezing. As mechanical cooling (and chemical coolants) has contributed catastrophically to the warming of the climate, the path forward may be found in these gentler materials and techniques that draw on all the senses to achieve a feeling of cold.

Concluded.

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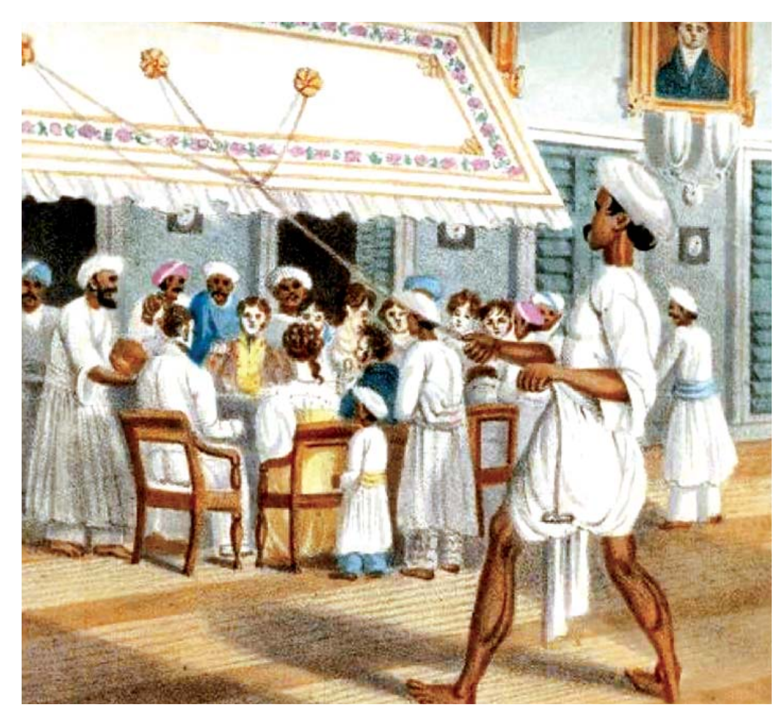


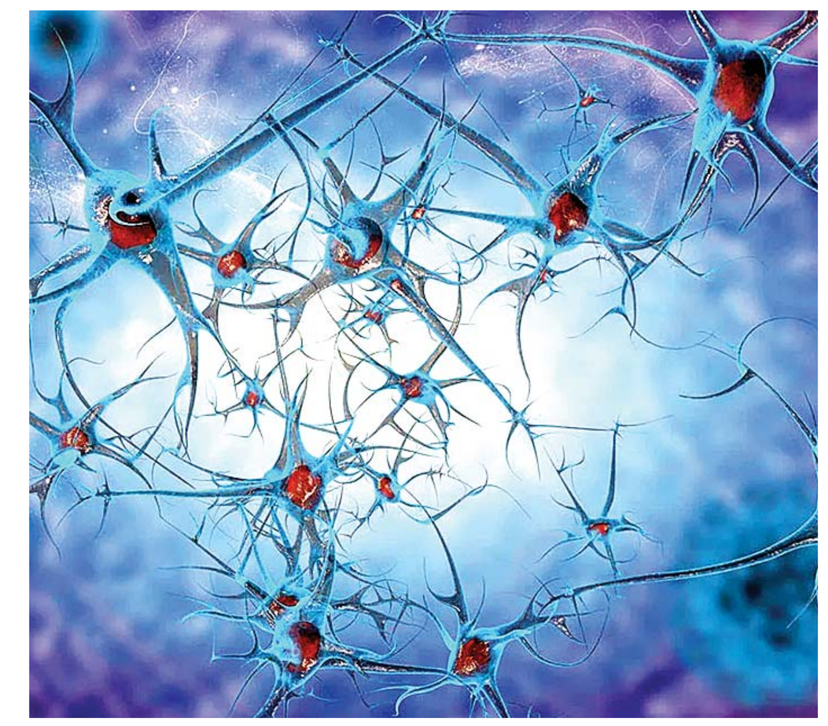
Cloth Pankha.

#BREAKING GROUNDS

Lab-Grown Brain Cells Will Treat Parkinson's

Japanese researchers have been successfully implanting lab-grown neurons into Parkinson's patients!

Parkinson's disease (PD) is a progressive neurodegenerative disorder that affects millions of individuals worldwide, leading to tremors, stiffness, and difficulties with movement. The condition occurs when brain cells that produce dopamine, a neurotransmitter essential for coordinating muscle movements, gradually die off. Although treatments have been developed to manage the symptoms, there is currently no cure for the disease. Recent breakthroughs, however, have brought new hope, particularly in the form of an innovative treatment using lab-grown brain cells. A groundbreaking clinical trial conducted by Japanese researchers has shown promising results by successfully implanting lab-grown neurons into Parkinson's patients. This study marks a significant step forward in the fight against Parkinson's and could have far-reaching implications for the treatment of other neurodegenerative diseases such as Huntington's, ALS, and Alzheimer's.



The Science Behind Parkinson's Disease

Parkinson's disease is characterized by the progressive loss of dopamine-producing neurons in the brain, specifically in an area called the substantia nigra. Dopamine is critical for controlling voluntary movements, and its depletion leads to the hallmark symptoms of Parkinson's: tremors, rigidity, and impaired coordination. As the disease progresses, patients may experience difficulty walking, speaking, and performing daily activities. Currently, there is no cure for Parkinson's, and available treatments, such as dopamine replacement therapy (levodopa) or deep brain stimulation, focus only on alleviating symptoms rather than halting or reversing the disease's progression.

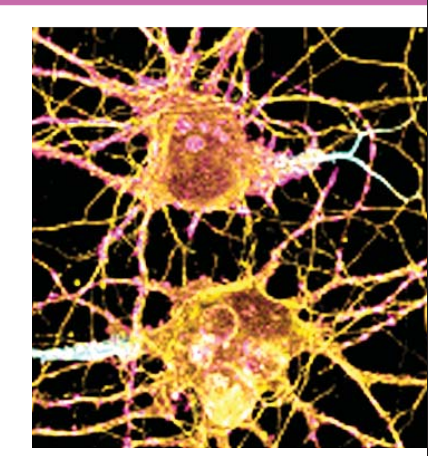
The Promise of Lab-Grown Neurons

The recent clinical trial represents a leap forward in the search for a cure. The Japanese research team employed an innovative method to generate dopamine-producing neurons by reprogramming adult cells into induced pluripotent stem cells (iPSCs). iPSCs are a form of stem cells that can be engineered to become virtually any cell type in the body. This reprogramming process involves reactivating certain genes that allow adult cells to return to an embryonic-like state, making them capable of differentiating into specific cell types such as neurons. Once these iPSCs were created, the researchers directed them to become dopamine-producing neurons, which were then transplanted into the brains of Parkinson's patients. By using iPSCs derived from the patient's own cells, the new method greatly reduces the risk of immune rejection, potentially allowing for more successful and safer transplants.

Clinical Trial Results

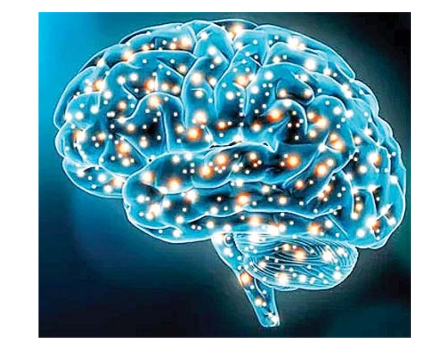
The clinical trial involved seven patients with advanced Parkinson's disease. These patients received transplants of lab-grown dopamine-producing neurons. The early results have been encouraging. Four of the seven patients showed a significant improvement in motor skills, with an approximate 20% increase in movement capabilities when off their usual medication. Brain scans revealed that the transplanted cells were successfully producing dopamine, which was a key indicator of the treatment's potential effectiveness.

Importantly, no major side effects were reported in the trial, which is particularly notable, given the risks involved in brain surgery and cell transplantation. While the study is still in its early stages and further trials



are necessary, these initial findings suggest that the approach could represent a viable and transformative treatment for Parkinson's disease.

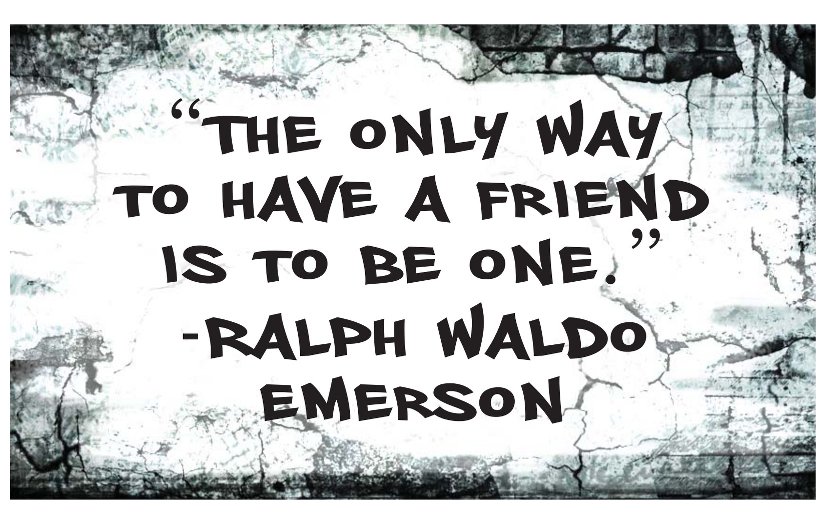
Broader Implications for Neurodegenerative Diseases



This research has far-reaching implications not only for Parkinson's but for other neurodegenerative diseases as well. Huntington's disease, ALS, and Alzheimer's also involve the progressive loss of specific types of neurons, and the ability to grow and implant healthy neurons into the brain could provide a pathway for treating these conditions as well. While the mechanism of cell loss varies among these diseases, the principle of replacing lost neurons with lab-grown cells remains applicable, offering the potential for groundbreaking therapies in the future.

The success of this clinical trial using lab-grown brain cells represents a major milestone in the treatment of Parkinson's disease. By overcoming some of the challenges associated with previous approaches, this new method of reprogramming adult cells into dopamine-producing neurons holds the promise of not only improving the lives of Parkinson's patients but also offering hope for those suffering from other neurodegenerative conditions. Although more research is needed to confirm long-term safety and efficacy, the early results suggest that regenerative medicine could play a crucial role in transforming the treatment of brain diseases in the future.

THE WALL



BABY BLUES

By Rick Kirkman & Jerry Scott

ZITS

By Jerry Scott & Jim Borgman