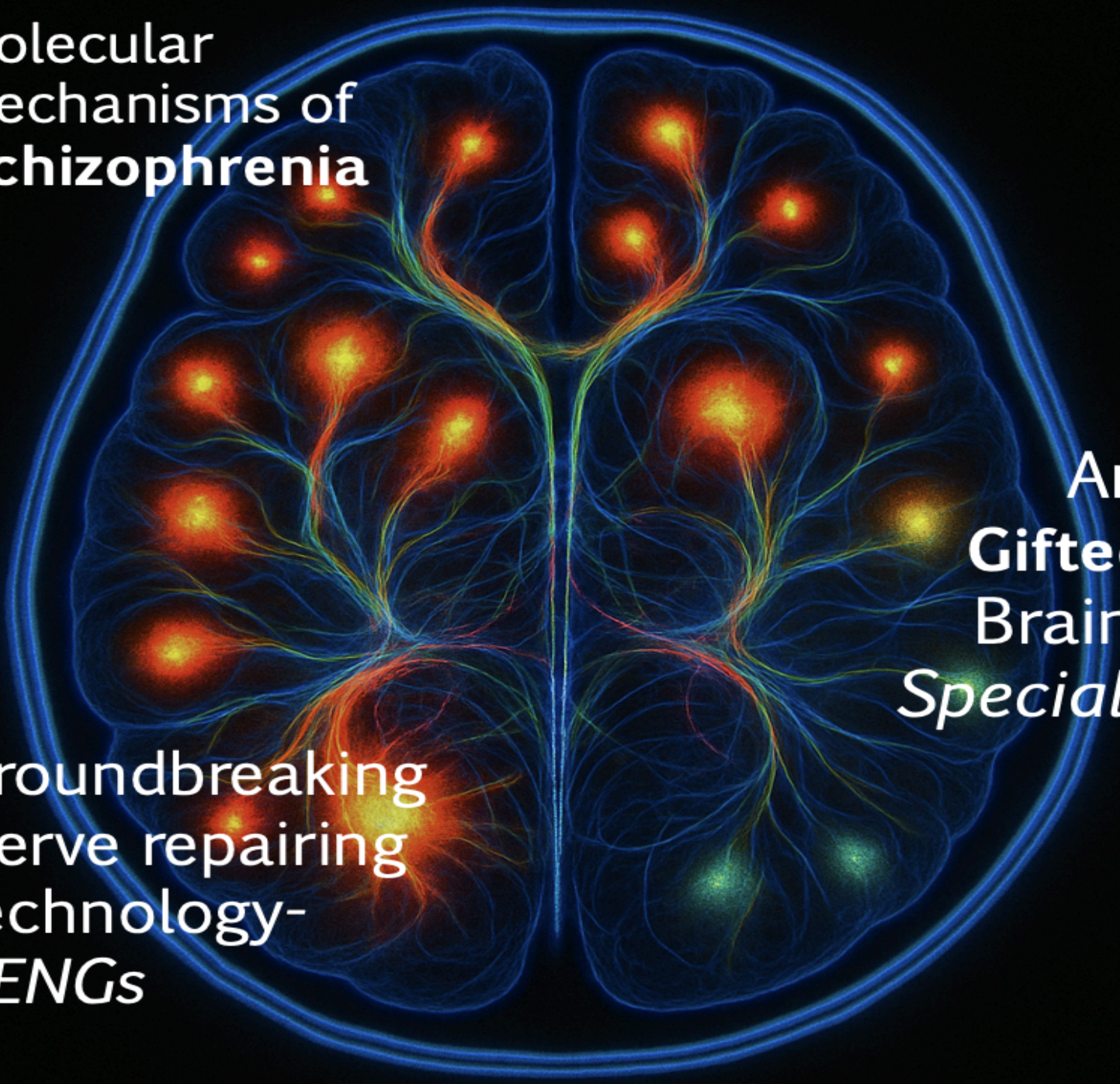
Grey Matters

Hopkins Chapter 1st Edition



Molecular Mechanisms of **Schizophrenia**

Are **Gifted** Brains *Special?*

Groundbreaking Nerve repairing technology- *TENGs*

Einstein's Brain

Inside the mind of a *Genius*

Spring 25'

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Identifying Structural MRI Patterns in Gifted Children using Machine Learning

By Rohan Venkatdas

Abstract

In today's world, test grades and other external quantities are used as measures of how gifted a child is. This study provides insight into the biometric characteristics of gifted children through a rigorous analysis of the differences in cortical thickness data between two groups. This study applies machine learning-based analysis, using a decision tree

(DT) model, to structural magnetic resonance imaging (sMRI) scans of gifted and normal juveniles. This research addresses the question of which volumes and cortical thickness changes are correlated with the gifted quality in children. The hypothesis was that the DT model would find altered gray matter volume in gifted children along with altered cortical thicknesses in the association cortex as well as other brain regions. The first step in extracting volumes, data preprocessing, involves standardizing raw sMRI scans across spacing, scaling, and other aspects for statistical analysis, specifically through bias field correction, skull-stripping, spatial registration, and segmentation using the program, functional magnetic resonance imaging of the brain software library (FSL), and Nipype registries/pipelines. Once the numerical volumes were extracted, the gray/white matter volumes and the cortical thicknesses were input into the DT model. The results from the DT model showed a testing classification accuracy of approximately 82.32 percent with strong correlations shown in the posterior cingulate cortex, paracentral cortex, superior temporal sulcus, superior parietal cortex, and superior temporal cortex, all specifically in the left hemisphere.

Clinical Relevance

This work investigates the relationship between giftedness in children and extractable sMRI features, in this case, cortical thicknesses and white/gray matter volumes.

Introduction

In our society, the quality of being "gifted" has been measured through various external methods such as intelligence quotient (IQ) tests, high school grade point averages (GPA), and more, but biometric measures of the gifted quality have not been explored extensively. sMRI is a neuroimaging modality that depicts the contrast between the gray matter and white matter of the human brain, further showing brain regions, regional integrity, shape, and size. The area of exploration for this study was the white/gray matter volumes as well as the regional thicknesses of the cerebral cortex, the outer layer of the brain composed of mainly gray matter. The cerebral cortex, amongst the neuroimaging community, has been divided into 308 standard subcortical regions from

which information is extracted, in this case cortical thickness. To identify the relationship between the variables being explored in the study, a DT model was used. A DT model is a form of machine learning in which a tree of binary decisions is created based on the training data set. Advantages of a DT approach include the interpretability of the model as well as the capability to easily work with categorical data [8]. Using the DT model, this study explored the correlations between juvenile gifted status and sMRI quantities, including white/gray matter volumes and regional cortical thicknesses. The hypothesis was that the DT model would find significantly altered cortical thickness in the associative areas and other regions as well as altered gray matter volume [11]. Research into sMRI allows for greater application in the clinical world as the modality is relatively commonly used for different purposes such as degenerative disorders. Potential consequences of this work would include the ability to clinically identify the sMRI features correlated with this quality in children.

Contributions

This work introduces a generative and interpretable approach for classification and exploration of giftedness in juveniles using sMRI and machine learning. The model is trained using gray matter volumes, white matter volumes, and regional cortical thicknesses of the juvenile brains in the training data set. The machine learning model is a decision tree model, which can be easily interpreted and can extract patterns between the different input variables. The model outputs weights corresponding to each of the variables in order to see the influence it has on the classification of the brains. Higher weights in the model typically correlated with altered amounts in gifted children compared to normal children.

Background

First of all, the research conducted by Sole-Casals et al. explores the brain structural network topographic differences in gifted versus normal children. Structurally, it was found that the neural topology of the brain was more “integrated” in gifted individuals when compared with normal individuals. Brain regional nodes, which were extensively explored

by the researchers, were relatively more integrated, connected, and versatile in gifted brains [11]. Secondly, the study conducted by Jin et al. explores the complex involvement of functional/electrical cortical efficiency, which is the idea that there is increased connection and function in the cortical regions, in gifted children. This idea of more efficient connection and functionality of cortical regions adds an extra variable into the equation of giftedness. This topic and its interplay with the size-related structural changes is a definite area of exploration for the future of research in this area [5].

Method

A. Data Collection

The raw sMRI scans, along with the cortical thickness values (308 cortical regions), were collected on the OpenNeuro data set, "Structural brain network of gifted children" [6]. The subjects used in this study, through stratified random sampling, were divided into training and testing data sets, which were used for the training of the model and the testing of the model respectively.

B. Data Preprocessing

Preprocessing of neuroimaging data consists of altering the data using graphical transformations and more in order to standardize the format of the images for better statistical analysis. As shown in Figure 1, this process consists of four main steps: bias correction, skull-stripping, spatial registration, and segmentation [7].

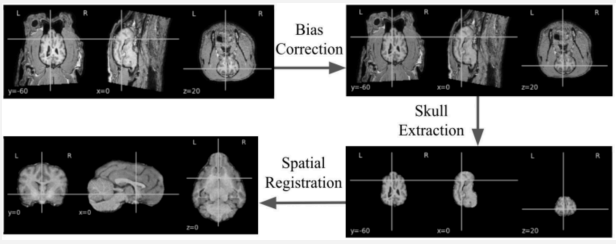


Fig. 1. The sMRI preprocessing steps include bias field correction, skull stripping/extraction, spatial normalization, and segmentation.

The first step in preprocessing is bias field correction. This is done in order to correct the partial "bias" throughout the MRI scan as a result of interruptions caused by the magnetic field during scanning. The nipype command, ANTs N4 Bias Field Correction, can be applied to the images via Python to correct the bias field in the raw sMRI scans [1]. Second, skull-stripping is an important step in

transforming the raw data into the standardized data. This step takes the unnecessary volumes out of the MRI scan to allow for easy brain analysis later on. The FSL program was utilized, specifically the FSL brain extraction tool (BET), to strip the images of the skulls and extracerebral spaces [10]. Following the skull extraction of the images, the brain scans need to be spatially uniform in order to compare and analyze the brains using standardized tools. To do so, a juvenile brain atlas template and the AAL template, which is widely used across the neuroimaging world as a basis for spatial registration and regional segmentation, were used to serve as a basis for the graphical translation in this study [2], [9]. The FSL linear image registration tool (FLIRT) is used to register the input images, in this case, the skull-stripped structural MRI scans, to the standardized space, established by the atlas template using linear graphical transformations [3], [4]. Before the numerical white/gray matter volumes could be extracted, the data had to be segmented. To do so, the registered brain scans undergo segmentation with the use of the command, FSL automated segmentation tool (FAST), which uses voxel intensities to determine the type of structure it serves as, whether white matter, gray matter, or cerebrospinal fluid, in the brain representation [13]. Finally, the numerical volumes of the white/gray matter volumes were extracted using the command, FSLstats, which displays the total volume of the white/gray matter based on the voxel characteristics and amount of voxels.

C. Decision Tree Model

After the white/gray matter volumes had been extracted, those values as well as the cortical thickness of the 308 cortical regions for each subject in the training data set were input into the DT model, which was then trained. The model then assigned weights to each of the variables, including the white/gray matter volumes and the regional cortical thicknesses, with high weights implying higher correlation between the respective brain region alterations and the gifted status (gifted or normal) of the children. In addition, the training data classification had an accuracy of 100 percent, suggesting that there are patterns present in the altered cortical thicknesses and/or white/gray

matter differences in gifted individuals when compared with normal individuals.

Results

The decision tree that the model generated included two variables, the left-hemisphere postcingulate cortex (part 2) cortical thickness and gray matter volume with binary decisions at each stage to help classify the subjects into either the “gifted” group or the “normal” group. The decision tree model is shown in Figure 2.

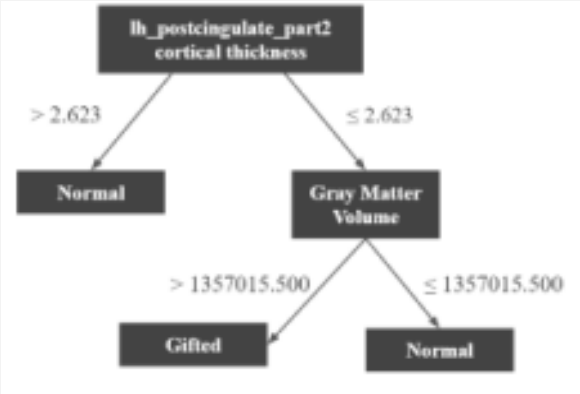


Fig. 2. The decision tree model following training using white/gray matter volumes and cortical thickness values of training data set.

As shown in Figure 3, the variables with the highest weights in the output DT model, implying high correlation:

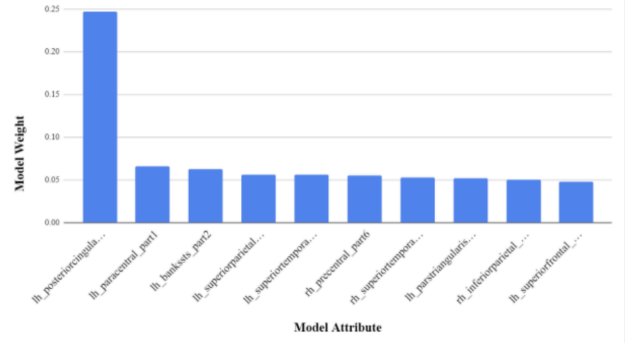


Fig. 3. The input variables with the top ten weights in the decision tree following training using white/gray matter volumes and cortical thickness values of training data set.

Include the cortical thicknesses of the left-hemisphere posterior cingulate cortex (part 2), left-hemisphere paracentral cortex (part 1), left-hemisphere superior temporal sulcus (part 2), left-hemisphere superior parietal cortex (part 7), and left-hemisphere superior temporal cortex (part 6), with a relatively large weight on the left-hemisphere posterior cingulate cortex (part 2). In previous literature, the cortex has been observed to experience changes in size and growth, but specific changes in regional sizes have not been extensively explored [5]. Rather, significant changes in certain cortical areas are expected. The trained model was then run on the testing data set which consists of eleven

juveniles (cortical thicknesses and white/gray matter volumes). When the model was used on the testing data set, it performed relatively well. The classification accuracy of the model was approximately 81.8182 percent. The testing data confusion matrix is shown in Table I with nine correct classifications and a false gifted classification and a false normal classification.

TABLE I

TESTING DATA CLASSIFICATION CONFUSION MATRIX

	Actual - Normal	Actual - Gifted
Predicted - Normal	36.4%	9.1%
Predicted - Gifted	9.1%	45.5%

The high classification accuracy of the model on the testing data set shows that there are significant regional differences between the two groups, specifically in the left hemisphere posterior cingulate cortex (part 2) and the gray matter volumes.

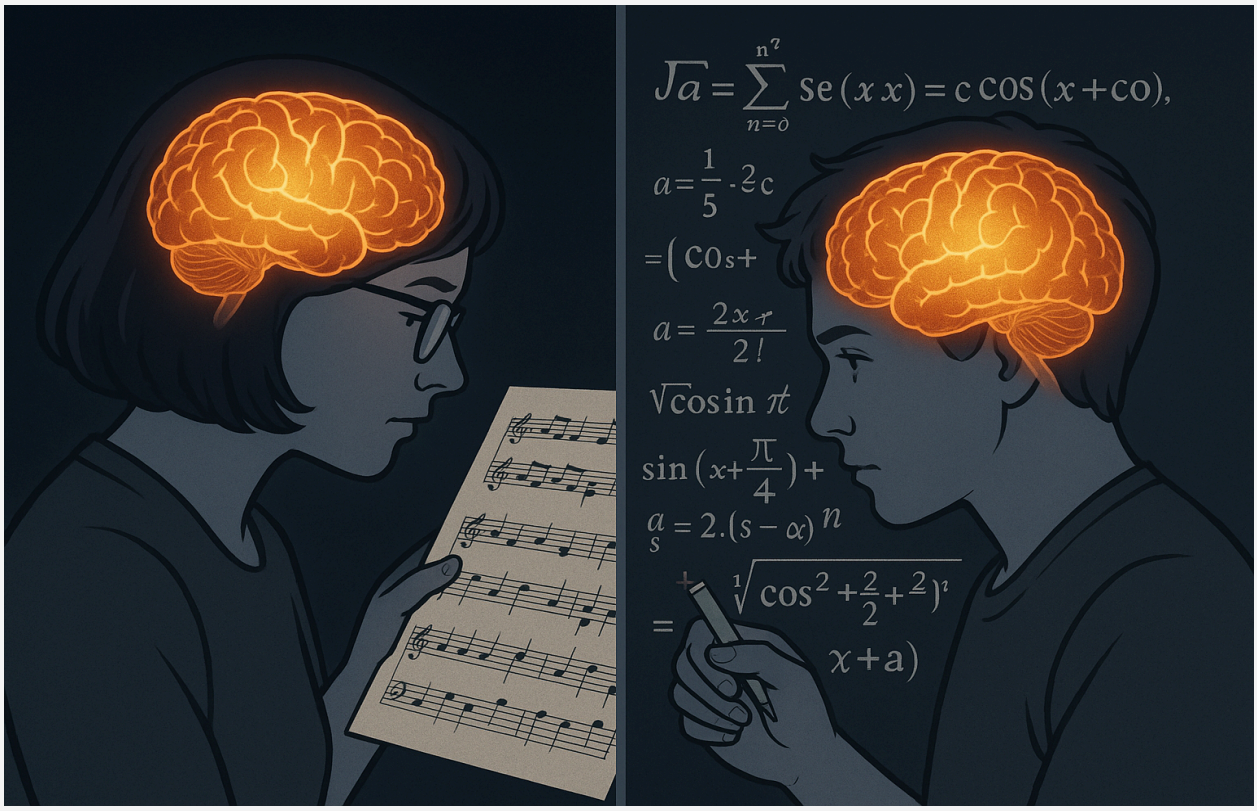
Conclusion

In the past, giftedness in children was measured using manually completed tests and records such as an IQ test or high school GPA, but in this study, a DT model is trained and executed in order to find an interpretable classification method that utilizes biometric measures, in this case, sMRI features. sMRI is a modality used when looking at structural aspects of the brain such as white/gray matter volumes while a DT model is a type of machine learning model that yields a complex yet interpretable decision tree for classification of the data into groups. The null hypothesis states that there is no significant correlation between the structural MRI changes (cortical thickness and gray/white matter volume difference) in gifted children and the child's gifted status (normal or gifted). Therefore, the null hypothesis is rejected. The alternate hypothesis of significant correlation between the structural MRI changes in gifted children and the children's gifted status (normal or gifted), specifically in the associative areas and other regions as well as the gray matter volume [11].

Through the OpenNeuro dataset, "Structural brain network of gifted children," the raw sMRI scans and regional cortical thickness values were collected [6]. Then, the raw sMRI scans were put through the various preprocessing steps: bias field correction, skull-stripping, spatial registration, and segmentation [7]. These processes were completed using primarily FSL as well as the nipype registries/pipelines [7]. The dataset was divided, using a stratified random sample. Then, the model was trained using the training data set. When implemented on the testing dataset, the model yielded a classification accuracy of around 81.8182 percent. The DT consisted of two binary decisions regarding the cortical thickness of the left-hemisphere posterior cingulate cortex (part 2) and the gray matter volume in order to classify a subject. The regions with the highest weights in the DT model, implying high correlation, are the cortical thicknesses of the left-hemisphere posterior cingulate cortex (part 2), left-hemisphere paracentral cortex (part 1), left-hemisphere superior temporal sulcus (part 2), left-hemisphere superior parietal cortex (part 7), and left-hemisphere superior temporal cortex (part 6) with a relatively large weight specifically on the left-hemisphere posterior cingulate cortex (part 2).

Future Work

In the past, it has been claimed that the brain, when categorized as gifted, not only has to do with certain volume differences but also with cortical efficiency [5], [12]. The next steps in the exploration of giftedness in the juvenile brain would be to investigate the complex interplay between regional size changes and cortical efficiency changes. In addition, the future of the research in this area includes the continued exploration of the biometric attributes associated with gifted children. Once researchers have identified the causes in the brain for the gifted quality in children, the next steps involve producing this cause in order to externally prompt giftedness.



The Brain’s Bridge Between Math and Music

By Mariam Husain

Introduction

Douglas Hofstadter's Gödel, Escher, Bach: An Eternal Golden Braid (1979) explores the interconnectedness of mathematical logic, artistic structure, and cognitive processes. The book highlights how self-referencing systems in mathematics, art, and music reflect recursive patterns. The unifying concept of recursion (Zhan, 2018) —patterns within patterns—is fundamental to understanding how abstract thinking manifests across different domains of human cognition. At the heart of music lie elements of rhythm, harmony, and frequency, all of which can be described mathematically. Rhythm, with its division of time into equal

segments, resembles the regularity of fractions; harmony, which is built on frequency ratios, entails relationships between music notes that follow precise mathematical rules; and frequency, which is inherently mathematical, refers to the number of vibrations per second of a sound wave. This concept of applying logical systems to creative artistic structures is particularly relevant to the bridge between math and music.

The Mozart Effect

The link between music and mathematical abilities has long fascinated researchers, with studies suggesting that specific aspects of musical training—such as rhythm, pitch, and sequential skill development—enhance mathematical performance, especially if cultivated at a young age. A study published in Nature demonstrated that first graders exposed to music instruction based on rhythm scored significantly higher in math than those who received a traditional music education. This improvement in math skills is related to two types of reasoning: spatial-temporal reasoning and language-analytical reasoning. Spatial-temporal patterns involve the brain's ability to form mental images, manipulate them, and sequence these patterns while solving problems that require an intuitive sense of movement through space and time, such as imagining shapes rotating or visualizing a chessboard. Innate spatial-temporal reasoning is essential for understanding geometric transformations and writing proofs, both of which require thinking ahead in logical steps. One phenomenon that was thought to highlight the connection between music and spatial-temporal reasoning is the Mozart effect. Researchers showed that listening to Mozart compositions, which are highly sequential, lead to short-term enhancements in spatial-temporal reasoning. Studies, including those by Dr. Gottfried Schlaug, revealed structural differences in the brains of musicians who began training at an early age. Musicians often have a larger corpus callosum and right motor cortex, suggesting that musical training physically alters the brain in ways that benefit reasoning skills. Further research by Xiaodeng Leng, and Gordon Shaw explored how music affects higher brain functions. They used the

Trion model, which maps specific neuronal firing patterns to musical elements. These patterns, when excited by music, are involved in memory, problem-solving, and spatial-temporal reasoning. Recent research at Stanford University, however, highlights a more nuanced relationship between musical training and cognitive function, suggesting that musicians' brains fire at faster speeds, aiding in both language processing and mathematical abilities. This study, led by John Gabrieli, involved fMRI scans of musicians and non-musicians while they were subjected to various auditory stimuli. Its findings diverge from the Mozart effect, which is largely debunked due to the effect being more inconsistent and smaller than initially reported. Stanford's findings focus more on the long-term cognitive benefits of active musical training rather than merely listening to Mozart. Keith Devlin, a Stanford mathematician, points out that while the strong connection between music and math seems intuitive—both disciplines involve pattern recognition and analysis—the evidence remains inconclusive. The cognitive benefits of music are real but may manifest in more subtle ways, particularly in improving the brain's ability to process patterns and sequences.

Cognitive Overlap And Shared Neural Pathways

Magnetoencephalography (MEG) studies have shown that the brain recruits both shared and distinct neural pathways during musical and mathematical tasks. Transposing is a musical task that involves shifting the pitch of a sequence of notes while maintaining its structure. It has been shown to engage similar brain regions as those activated during mathematical calculations. Using MEG and fMRI, researchers observed that tasks requiring musical transposition and mathematical calculations triggered multiple areas of neuronal activity, like the visual cortex and frontal lobe. One key finding was that both tasks demonstrated simultaneous activation of the frontal and occipital regions, but with distinct differences. For instance, transposing tasks showed slower frontal activation compared to mathematical tasks, a difference attributed to the higher visual working memory demands of processing musical notation. This suggests a

shared reliance on working memory. In music, the need for motor planning and visual interpretation engages broader neural networks, while mathematical tasks tend to focus more on memory retrieval and visual-spatial reasoning.

Music As A Tool To Enhance Mathematical Skills

The way the brain handles musical transposition offers insights into how music can influence mathematical skills. Musical transposition places a high load on working memory because it necessitates temporarily holding the original key in mind while adjusting notes to fit the new key. This task demands not only auditory and motor coordination but also cognitive flexibility and memory manipulation, like solving complex math problems. The findings of Holmes and Hallam (2017) from a study which involved young children in rhythmic music programs revealed that those participating in music activities displayed statistically significant improvements in spatial-temporal reasoning compared to control groups. This highlights the importance of incorporating music to foster skills that transcend artistic domains. The ability to mentally manipulate shapes and patterns in the absence of physical objects is integral not only to geometry but also to understanding quantities, solving multi-step problems in algebra, calculus, and number theory. Language-analytical reasoning is employed to solve equations and derive precise answers fundamental to arithmetic and algebra. The mental agility required for musical tasks can enhance mathematical capabilities. Other research by Bergee opens avenues to explore the nuances of the music-math relationship. While acknowledging the complexity of influences at individual, classroom, school, and district levels, Bergee cautions against interpreting the correlation as strictly causal, suggesting that music education is one of many contributing factors to cognitive development. The relationship between music and math remains multifaceted.

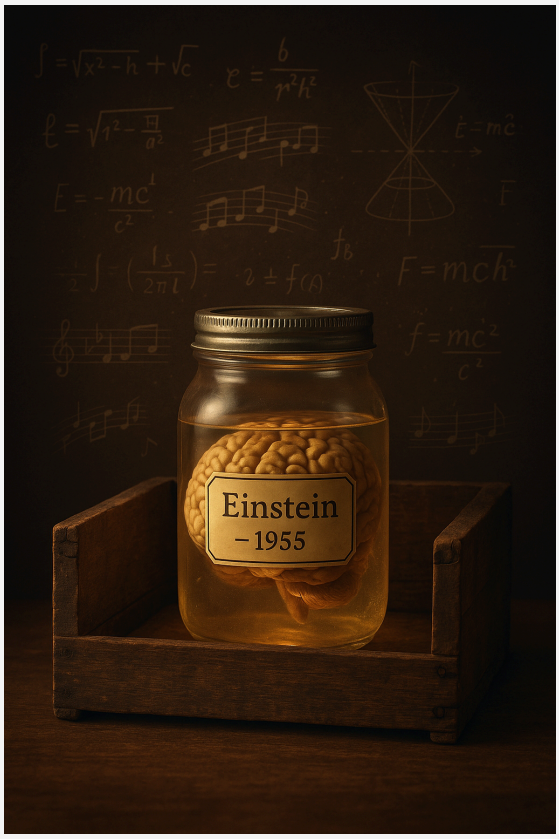
Brain Plasticity in Musicians and Mathematicians

Martin J. Bergee's research on the cognitive links between music and mathematics is reflected in professional fields such as

cryptanalysis at the National Security Agency (NSA.) Many NSA employees, including experts in mathematics and computer science, are also accomplished musicians. This intersection may not be coincidental; musicians often possess heightened abilities in mathematical comprehension, pattern recognition, and executive functioning. According to NSA employees, such as jazz saxophonist and Deputy Chief of Cryptanalysis and Signals Analysis Joseph C., the hiring pool for cryptanalysis exhibits a higher-than-average intersection with musical training. NSA employee Elise F., a development specialist with degrees in math and experience as a professional musician, notes that both music and mathematics involve dividing time and pitch concepts, which are deeply rooted in mathematical thinking. She emphasizes that her love of puzzles and ciphers grew naturally from a background in both music and math, illustrating how music and math overlap in real-world applications. It is suggested that while mathematical patterns outside of music are often challenging to grasp, the brain seems to handle musical complexity with relative ease in mathematicians who are also musicians.

Conclusion

The connection between math and music provides us insights into how the brain recognizes patterns and engages in abstract thinking. The transfer of skills from music to mathematics hinges on the complexity and specificity of the tasks involved. MEG studies show that the brain recruits both shared and distinct neural pathways during musical and mathematical tasks. The activation of frontal, occipital, and motor regions during transposing suggests deeper cognitive engagement in music than previously understood, paralleling mathematical problem-solving processes. Real-world examples from fields like cryptanalysis further support this connection. Recognition of these cognitive connections with their math and music programs initiates continued studies examining both musicians and non-musicians, promising to illuminate how music training influences broad cognitive skills, potentially offering new insights into how the brain bridges the gap between math and music.



The Bizarre Story of Einstein's Brain

By Rohan Venkatdas and Zewen Liu

On the morning of April 18, 1955, the world lost one of its brightest minds. Albert Einstein, the brilliant physicist who gave us the theory of relativity and the famous equation E = mc², died of a ruptured abdominal aortic aneurysm at the age of 76. He had been working on a speech to celebrate Israel's seventh anniversary when he collapsed from severe chest and belly pain. Though modern medicine might have saved him today, back then it was a fatal condition [3]. Before he died, Einstein mumbled something in German, but the nurse on duty at the time didn't speak German, so no one knew what he said before his unfortunate death [2].

Einstein had always said he didn't want to live artificially or be buried in a marked grave. He asked to be cremated and for his ashes to be scattered secretly. But as his body was being examined in the autopsy room at Princeton Hospital, something unexpected happened. The pathologist, Dr. Thomas Harvey, removed Einstein's brain—without asking anyone first [2]. This act marked the beginning of one of the most bizarre scientific journeys in modern history.

Dr. Harvey wasn't trying to steal Einstein's brain for personal gain. He believed that studying Einstein's brain might help unlock the secrets of genius. After removing it, he photographed it, preserved it in formaldehyde, and then cut it into 240 small blocks. From these blocks, he made 12 sets of over 200 slides. These slides were meant to be

shared with researchers around the world [2].

But instead of organizing a massive scientific study, Harvey took the brain with him. He stored it in a cider box, sometimes inside a beer cooler, and moved it around the country. For decades, hardly any research was done, and Einstein's brain was largely forgotten by the scientific community.

Then, in 1978, journalist Steven Levy tracked Harvey down in Wichita, Kansas. When Levy opened one of the jars, he found a fist-sized, wrinkly chunk of greyish tissue that looked like fired clay. In one of Levy's articles, he described the scene as "A conch shell-shaped mass of wrinkly material the color of clay after firing. A fist-sized chunk of greyish, lined substance, the apparent consistency of sponge. And in a separate pouch, a mass of pinkish-white strings resembling bloated dental floss." Another jar contained thin, clear rectangular blocks the size of candy bars. It was Einstein's brain—or at least what remained of it [2].

Harvey's obsession with the brain took a toll on his life. He lost his job, his medical license, and even his family. Yet he held on to the brain, believing its secrets were still worth discovering. Eventually, parts of Einstein's brain did reach researchers. The first major study came in 1985 when Marian Diamond at the University of California, Berkeley, examined slices of Einstein's brain under a microscope. She discovered something unusual: Einstein had significantly more glial cells per neuron than the average person. Glial cells support neurons and may play a role in learning by helping the brain maintain high levels of activity [2].

In 1996, Dr. Britt Anderson studied Einstein's prefrontal cortex, a region associated with decision-making and focused thinking. He found that the neurons there were more tightly packed, which might have allowed Einstein to process information more efficiently [2].

Three years later, neuroscientist Sandra Witelson made another major discovery. She found that Einstein's inferior parietal lobule was 15% larger than that of typical brains. This region is important for understanding math,

spatial relationships, and movement through space. She also noticed that Einstein's brain lacked a deep groove called the Sylvian fissure in this area, possibly allowing the lobes to communicate more easily [2]. These findings supported the idea that Einstein's brain was unique—but they weren't the end of the story.

In 2013, a groundbreaking study by Dean Falk and colleagues examined 14 newly discovered photographs of Einstein's entire brain. These high-quality black-and-white photos showed unusual views of Einstein's cerebral cortex, the outer layer of the brain responsible for high-level thinking [1]. They found:

- An extra ridge in the mid-frontal lobe, linked to planning, memory, and abstract thought.
- Four distinct gyri (brain folds) in the right frontal lobe, instead of the typical three. This may indicate expanded capacity for complex thought.
- A prominent "hand knob" on the right motor cortex—a fold often found in musicians, especially violinists. Einstein had played the violin since childhood.
- Unusual asymmetry in the parietal lobes, with one side appearing more expanded. This could support greater spatial reasoning or mathematical ability.
- Wider postcentral gyrus, suggesting enhanced sensory processing.
- Highly folded occipital lobes and a convoluted cuneus, regions tied to vision and visualization.

Together, these structural features provided more clues about how Einstein's brain might have supported his incredible mental abilities.

In 2014, a different team of researchers led by Weiwei Men studied another part of Einstein's brain: the corpus callosum. This thick bundle of nerve fibers connects the brain's left and right hemispheres, allowing them to share information quickly [4]. Using special software and comparing Einstein's brain to MRI scans of 67 typical male brains, the scientists made some exciting discoveries:

- Einstein’s corpus callosum was thicker than average in most areas, including the genu (front), midbody, isthmus, and splenium (back).
- These regions link parts of the brain responsible for planning, motor control spatial reasoning, and vision.
- Despite his age, Einstein’s brain showed minimal signs of aging or atrophy, suggesting it remained sharp and active to the end.

This "superhighway" of connectivity may have helped Einstein integrate left- and right-brain thinking better than most people. It might explain his ability to combine logic with imagination.

So, was Einstein a genius *because* of his brain structure? Or did his brain become unique *because* he used it so much? That’s a question science still can't fully answer. Some scientists warn that we should be careful not to draw big conclusions from a single brain. Dr. Terence Hines, a psychologist at Pace University, has said it's like looking at one person's foot and guessing their personality from the size of their shoe [2]. Even Einstein seemed to agree. On the blackboard in his office, someone once wrote a quote that summed it up perfectly: "Not everything that counts can be counted, and not everything that can be counted counts."

Perhaps the true secret to Einstein's brilliance was not hidden in a sulcus or a glial cell, but in his curiosity, his persistence, and his wonder about the universe. What remains of Einstein's brain has been returned to science and to history. Some slides are displayed in museums like the Mütter Museum in Philadelphia. An iPad app now lets people explore microscopic views of Einstein's brain from Harvey's original slides.

Despite its strange journey—from Princeton to Kansas to labs around the world—Einstein's brain continues to inspire scientists, students, and the curious minds of all ages. We may never fully understand what made Albert Einstein such a visionary thinker. But in studying his brain, we are reminded of

how vast, complex, and powerful the human mind can be. And maybe, just maybe, the next Einstein is out there—not because of a special brain, but because of a special spark.

Mind Over Spine

By Omkar Katkade, Jia Li Zhou, and Gabby Molina

Introduction

You never saw the truck coming. One second, you were cruising down the highway, thinking about what to grab for dinner. The next, you were weightless. Silence.

When you wake up in the hospital, something feels off. You try to sit up, but your legs don't respond. The doctor says you have a spinal cord injury. You are now paralyzed from the waist down.

As the days pass, you learn to work a wheelchair, relying on others for things you used to do without thinking. The questions echo in your mind: *Will people see me the same way? Am I a burden to my family? Will I ever feel normal again?*

Now, you find a statistic. Individuals with spinal cord injuries face a suicide rate nearly five times higher than the general population [1].

Each year in the U.S., about 18,000 people develop a spinal cord injury (SCI), most commonly due to car accidents, falls, violence, or sports-related injuries [2]. The spinal cord, a bundle of nerves that carries messages between the brain and body is extremely delicate.

Disruption of this messaging system can lead to paralysis, loss of sensation, and severe pain. While the physical effects of SCIs are well documented, the emotional effects often remain overlooked.

Emotional Aspect

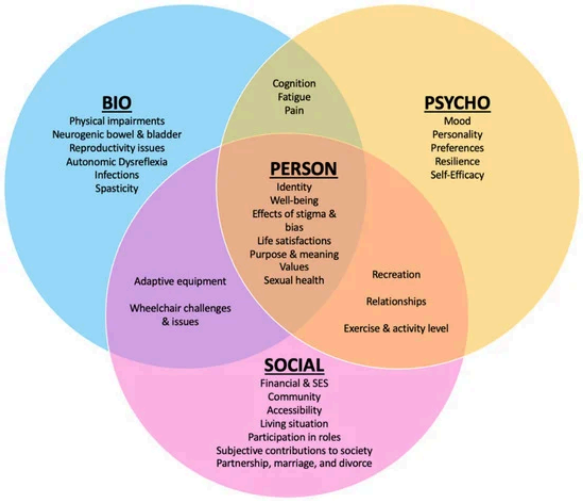
The implications of a spinal cord injury extend far beyond loss of mobility. The moment your body changes, so does the way you see

yourself—and the way the world sees you. The prevalence of ableist ideologies and prejudices are often overlooked due to the way they've been integrated into society. Lack of accessibility, both in physical spaces and social spaces, only perpetuates the psychosocial impacts that SCI has on an individual.

Studies show that individuals with SCI experience heightened anxiety and depression, yet only about 14% of these mental health struggles can be directly attributed to physical pain [3]. After experiencing a life-altering calamity, reintegration into past routines and environments can feel impossible. The confidence in one's ability to perform daily tasks they once did effortlessly, often crumbles after injury, replaced by a distressing dependence on others. The once-simple tasks of working, maintaining relationships, and being involved with their community becomes overwhelming.

People with SCI are often victims of degrading attitudes from the people around them, pity that feels suffocating, assumptions that their disability extends to their intelligence and competence, and a broader societal discomfort around the disability itself. Often these biases are internalized by individuals with SCI, leading to diminished self-worth.

To understand the full range of implications, the biopsychosocial model, developed by George Engel, attempts to provide a more holistic view of SCI [4].



There is significant overlap between the three facets that contribute to a person's well-being. Physical impairments can exacerbate psychological distress and intensify perceived pain. Which then in turn makes reintegration into daily life even more daunting. Some may turn to maladaptive coping mechanisms, such as substance abuse or isolation.

Individuals with SCI struggle with feelings of detachment from both their former

selves and the world around them. The inability to engage socially as they once did, the financial strains of medical care and unemployment, and the pressure to redefine their role in their family and community all contribute to how patients of SCI may battle with their new identity.

One of the most powerful determinants of psychological resilience in the face of all that's been discussed is support. The presence of strong, functional relationships significantly reduces grief and fosters a sense of purpose.

One Man's Story

In the Druze village in Golan, a 20-year-old man developed paralysis in all four limbs, a disabling condition called quadriplegia, after a blood blockage in his spine that occurred seemingly out of nowhere. The only potential cause was identified to be a minor motor accident that occurred eight months prior (Litwak, 2015).

While he was berating himself for being a burden to his family, his parents did everything they could to make his home more accessible, from renovating their house and learning how to take care of him to spending as much time as they could by his side. Although their family dynamic changed drastically, they were nothing but supportive of his condition which made his health outcomes excellent.

For this family, it was due to the overwhelming support from their village that they were able to integrate their social life with their new dynamic.

For patients with quadriplegia, relationships are a defining factor for their mental state and life satisfaction. With physical disabilities, the patients' social lives are stolen, and depending on their culture, they can face immense judgment as well. The study conducted in the Druze village also referenced how geographic and cultural differences can affect the life satisfaction of patients with spinal cord injuries. In particular, when comparing the life satisfaction of Swedish and Japanese patients, it was found that Japanese patients without life partners were unhappier than their Swedish counterparts. This is due to the difference in their views on relationships, as Japanese culture cares more about the group, rather than the individual, which is different from Swedish culture. Without them, patients' life satisfactions are lower. In a comparison between British and

Chinese patients, British patients were more positive compared to their Chinese counterparts due to the difference in cultures. In Chinese culture, disabilities are frowned upon and discrimination is still prevalent while British cultures do not share the same views.

On March 26, 2010, Drew Clayborn attempted a backflip which resulted in a broken neck and paralysis from the mid-neck down (Fromson, 2022). In situations such as these, it can be very easy to self-blame and fall into a chain of negativity, but Clayborn was different. Despite the severe injuries, he kept an incredibly positive mindset and refused to succumb to his paralysis. He asked one question: *How do I get back to doing life?* That single question motivated him to continue living, or rather, to flourish. His resilience, support from family, and assistive technology led to the creation of his nonprofit, aimed at empowering and mentoring those with similar disabilities and their families.

The most significant element in keeping a positive attitude with such disabilities stems from being psychologically flexible and having people to rely on. Hence, it is essential to reiterate the significance of social relationships and support through the life-long journey of adapting to a new, but debilitating lifestyle.

Future/Innovations

Beyond social support, technology offers promise for restored function for the SCI patients of the future. As of now, SCI has no permanent cure. Emergency treatment options after an accident include both surgical stabilization of the spine and medication to reduce inflammation, though complete function is often still lost ("Spinal Cord Injury," 2024). However, experimental transcutaneous spinal stimulation treatments which apply electrical currents through the skin have allowed some patients to regain motor function (Dantas, 2024). Scientists are also researching spinal cord implants that monitor and activate nerve activity to potentially restore movement function (Kaulitzki, 2024).

Neuralink is a neurotechnology company currently developing implantable brain-computer interfaces to enhance the quality of life for SCI individuals by helping them maintain independence. In January 2024, Noland

Arbaugh, paralyzed from the waist down, received a coin-sized "Telepathy" brain chip implant from Neuralink. Telepathy allowed Arbaugh to use his thoughts to play video games and communicate with friends online. Neuralink implanted the Telepathy brain chip in another patient in August 2024 (Hurley, 2024).

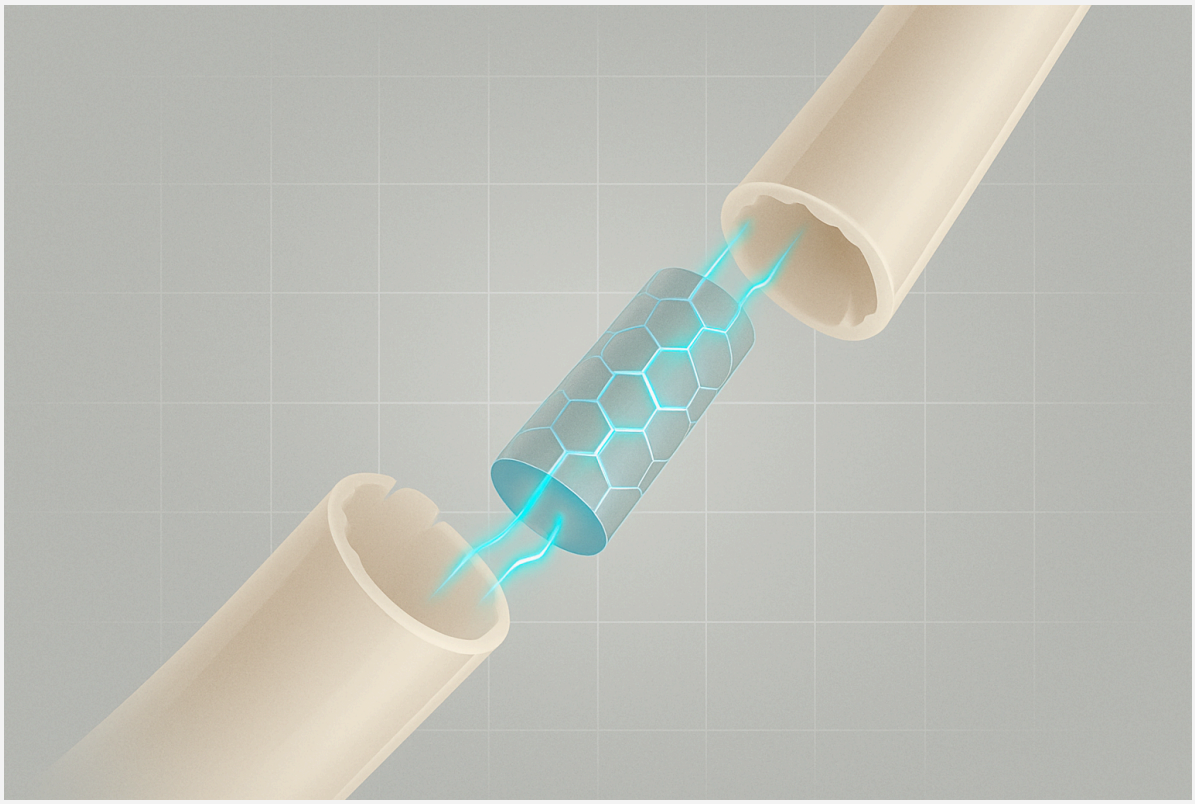
Researchers at Georgia Tech are developing tongue-controlled wheelchairs and wearable exoskeletons that provide independent mobility for spinal cord injury patients (Israel, 2024; He, 2024). Wearable exoskeletons are being developed to allow paralyzed patients to walk again. Mouth-based touchpads are enabling people living with paralysis to use computers (Winn, 2024). A cure for SCI might still be far away, but these innovative technologies are empowering SCI patients to regain more and more independence.

Conclusion

We offer this article not just to educate, but to inspire. Spinal cord injury is not the end. Drew Clayborn used his quadriplegia to propel him forward. He is now CEO of The Drew Crew, a nonprofit dedicated to supporting individuals affected by SCIs or other forms of paralysis, providing mentorship, guidance, and support for families to navigate life after a catastrophic injury. Teaching family and friends how to adapt is critical to maximizing the quality of life, as one of the most powerful psychological influencers is social support. Technological advances further support the quality of life in individuals with SCI, improving independence.

At the end of the day, our message is to not give up. Drew Clayborn said it best:

- “My life matters. It's better that I'm here now than if I had died that day. Now, I'm able to show that to others as well.”
- Drew Clayborn, 2022



Revolutionizing Nerve Repair: A Leap Toward Healing the Impossible

By Rebecca Crisp

The Problem with Nerve Injuries

The challenge of nerve regeneration has long loomed over medical research, particularly in addressing severe injuries. Unlike skin or muscle, nerves regenerate painfully slowly. When injuries span significant gaps, recovery becomes nearly impossible. Traditional methods like physical therapy or nerve grafting often fall short, leaving patients with chronic pain, limited function, or permanent disabilities.

What if nerves could heal faster, more effectively, and even bridge gaps once thought impossible to repair? Tissue-engineered nerve grafts (TENGs) are making that vision a reality. This exciting breakthrough is forever changing the field of nerve regeneration. TENGs can restore nerve function across 5-cm gaps in pigs, which no other traditional treatment has accomplished before. This is a significant milestone in science, opening up new

possibilities for treating nerve damage in the future.

A significant challenge in treating peripheral nerve injuries (PNIs) is the slow rate of axon growth and the eventual breakdown of the regenerative pathway in the absence of active axons. Traditional solutions, such as autografts—using the patient's own nerves to bridge gaps—come with significant limitations, including insufficient tissue for large-scale repairs and complications at the donor site. TENGs offer a groundbreaking alternative, serving as a structural bridge and a dynamic guide for healing, using living axonal support to steer host axons toward recovery.

How TENGs Work Their Magic

Imagine TENGs as advanced guides for repairing damaged nerves. Crafted from pig nerve cells that are stretched into long fibers, these grafts serve both as bridges and maps, directing nerves to their proper locations. They address two major challenges in nerve repair: the slow regrowth of nerves and the breakdown of healing pathways when axons aren’t active.

Even more remarkable, TENGs don't work alone—they team up with Schwann cells, the body's natural repair crew. Schwann cells are like the caretakers of nerve recovery, creating an environment that supports axon growth. By stabilizing this partnership, TENGs ensure the conditions for healing remain just right, even over extensive injuries. The result? Faster, more efficient nerve regrowth, even across gaps as big as 5 cm.

Why Use Pigs? The Perfect Partners for Nerve Research

Pigs might not be the first animals you think of for medical research, but their nervous systems share surprising similarities with ours. Their neurons and nerve structures are organized like ours, and they face the same challenges in healing large nerve gaps. Additionally, pigs and humans share key processes such as myelination, which influences nerve signal transmission and recovery. Even their immune responses to nerve damage—like inflammation—mirror those of humans. Because of these parallels, pigs are a valuable model for testing treatments like TENGs before moving on to human clinical trials.

A Big Win in Nerve Repair

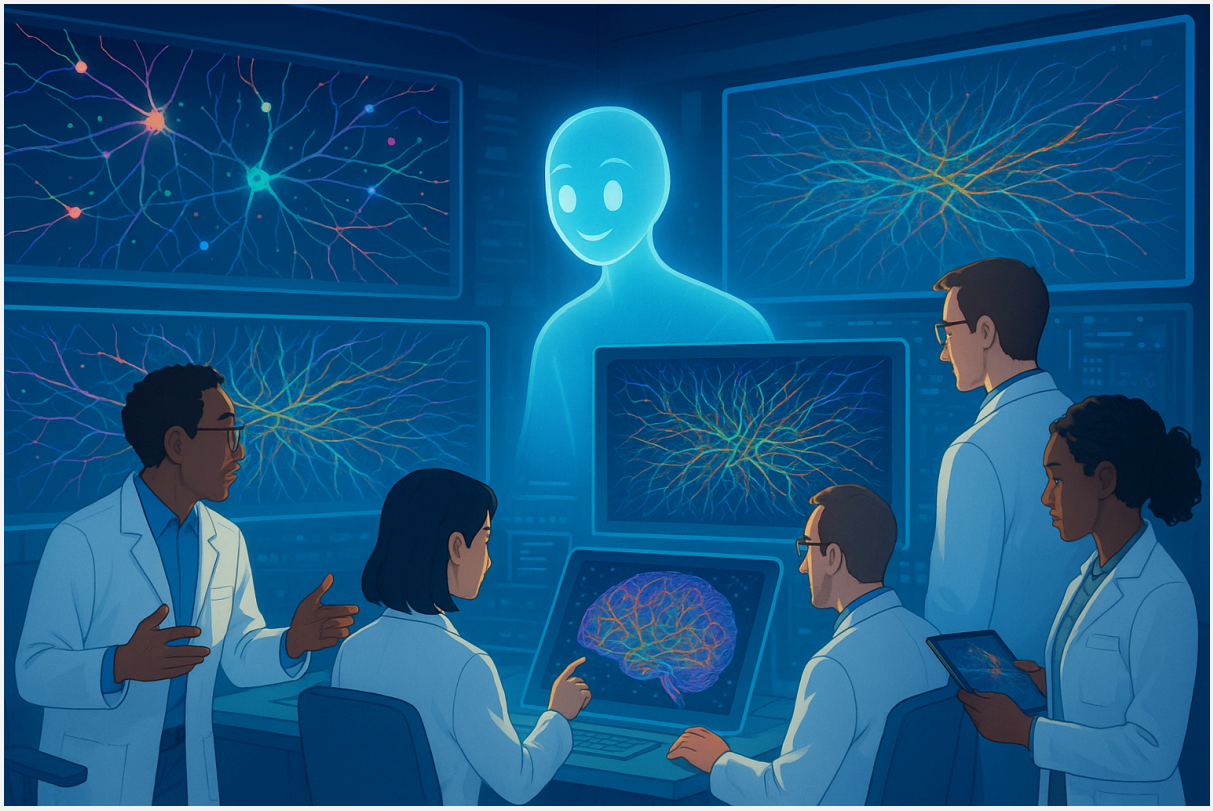
In recent experiments, TENGs produced astounding outcomes. They aided pigs' nerves in growing back over 5 cm gaps, a level of healing that is unfeasible with traditional methods. In addition to reestablishing connections, these grafts encouraged strong axonal regeneration and notable recovery in both motor and sensory neurons. The fact that the pigs could move and feel again demonstrated that TENGs are practical and effective.

Future Implications for Humans

Millions of people worldwide live with nerve damage caused by accidents, surgeries, or conditions like diabetes. Severe nerve injuries often come with grim prospects, as current treatments—like harvesting nerves from elsewhere in the body—introduce their own complications, such as pain and limited donor tissue.

By boosting regeneration and eliminating the requirement for donor nerves, tissue-engineered nerve grafts (TENGs) promise improved results and a quicker recovery than traditional methods of nerve restoration. Because of this breakthrough, even the most severe cases of nerve damage may become easier to treat.

Of course, we are not there yet. Much research is needed before TENGs can become a standard treatment in humans. However, the immense success of TENGs in pigs represents a major milestone in nerve regeneration, revealing significant potential for future medical applications. With continued advancements, fully repairing nerve damage could become a reality in healthcare in the future!



NeuroTrALE

Background: The Complexity of Brain Imaging

Analyzing brain imaging data has always been one of the toughest challenges in neuroscience. The sheer amount of data generated by modern brain scans, like fMRI, PET, and EEG, is overwhelming. Just imagine trying to make sense of gigabytes—or even terabytes of data, full of complex, ever-changing brain activity. It's like trying to read a novel by staring at the pages of a book that's constantly flipping itself open to new chapters, new stories, and new characters—all at once.

As recent research points out, "progress has been hindered by insufficient tools to visualize and process very large brain imaging datasets" (McGovern). Specifically, the ability to track axons—the long, thread-like extensions that neurons use to communicate with each other is something that we lack. By tracking axons, we can uncover how different regions of the brain are connected and how they work together to support cognitive functions, memory, emotions, and behavior. Mapping these pathways is critical for understanding how the brain works, but the

current methods remain inadequate, relying on humans to manually draw over axons and create maps of them. This tends to be rather labor-intensive and error prone.

The Solution: NeuroTrALE

Enter NeuroTrALE, a groundbreaking tool developed through a collaboration between Lincoln Laboratory and Kwanghun Chung's lab. Built on Google's Neuroglancer platform, NeuroTrALE takes brain imaging analysis to the next level by enabling more efficient and accurate annotations of complex brain images (Brady et al.) Using machine learning and active learning, it revolutionizes the way scientists annotate axons, making it possible to handle much larger datasets than ever before.

What is NeuroTrALE

NeuroTrALE uses advanced machine learning algorithms that continuously improve through a process called active learning which allows the algorithm to learn from the inputs made by human users to refine its predictions over time. In simpler terms, NeuroTrALE is like a smart assistant that gets better at recognizing patterns the more it's used which makes it possible to analyze large amounts of brain data.

With NeuroTrALE, scientists can now annotate large volumes of axon data and can help us create a deeper understanding of neural circuits and brain function.

Key Functionalities of NeuroTrALE

NeuroTrALE is designed with several powerful features to streamline brain imaging analysis:

- Data Ingestion: It can handle raw image volumes and outputs from algorithms detecting neurons, glia, axons, and other structures.
- Visualization: It enhances the visualization of detected structures by overlaying them on the original images, making it easier to interpret results.
- Editing Tools: Users can edit annotations as needed, refining the data before finalization.
- Data Scalability: NeuroTrALE can scale to handle very large datasets, ensuring that it remains efficient even as the volume of data increases.
- Multiple Data Formats: It supports a variety of data formats, including JSON, CSV, and HDF5, making it compatible

with a wide range of neuroscience research tools.

- Simultaneous Access: Multiple users can access and annotate different datasets simultaneously, improving collaboration and efficiency (Snyder et al.)

How Does Active Learning Work

In this process, the system identifies "uncertain" data points—those it's not entirely sure about—and asks the user for feedback (Hsu and Lin). This system improves the accuracy of the system with every input. The user plays an important role by guiding the algorithm and providing corrections. Over time, the system becomes more reliable.

The combination of human oversight and machine learning is what sets NeuroTrALE apart. While the system automates much of the process, it still relies on human expertise to fine tune the results. This partnership between man and machine is a core principle of many AI systems.

Efficiency and Speed

One of the standout features of NeuroTrALE is its impressive speed and efficiency. By using parallel computing, it can process large datasets quicker than traditional methods. For example, when processing a 32 GB dataset, users see a 90% reduction in computing time compared to older techniques. Furthermore, a 10,000% increase in dataset size results in only a 9% increase in processing time. (McGovern).

In simple terms, NeuroTrALE significantly speeds up data processing, and even as the dataset grows, the additional processing time remains minimal.

Possible Limitations of NeuroTrALE

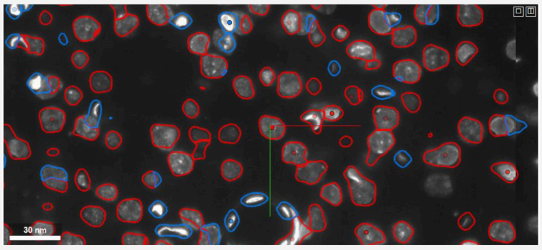
While NeuroTrALE has made remarkable strides in automating the annotation process, there are still some limitations to consider:

1. Dependence On Human Input:
   The system still needs lots of user involvement. In the early stages, the algorithm relies heavily on the user because it doesn't know much. If the user makes mistakes, it negatively impacts the system's performance (Ronneberger, Fischer, and Brox)
2. Specific to Certain Imaging Modalities:

NeuroTrALE is currently optimized for specific types of brain imaging like electron microscopy and light microscopy, where neurons are clearly identifiable. While it works great for these imaging techniques, it may not generalize well to other types of brain imaging like fMRI or EEG. (Cao et al.)

Visualizing NeuroTrALE in Action

NeuroTrALE's advanced visualization tools are another highlight. By providing detailed images of axon tracing and nuclei segmentation, the platform makes it easier for researchers to analyze and interpret their data. As shown in the visual from MIT Lincoln Laboratory, the algorithm does an excellent job of identifying neurons, including glial cells (highlighted in blue), with high precision.

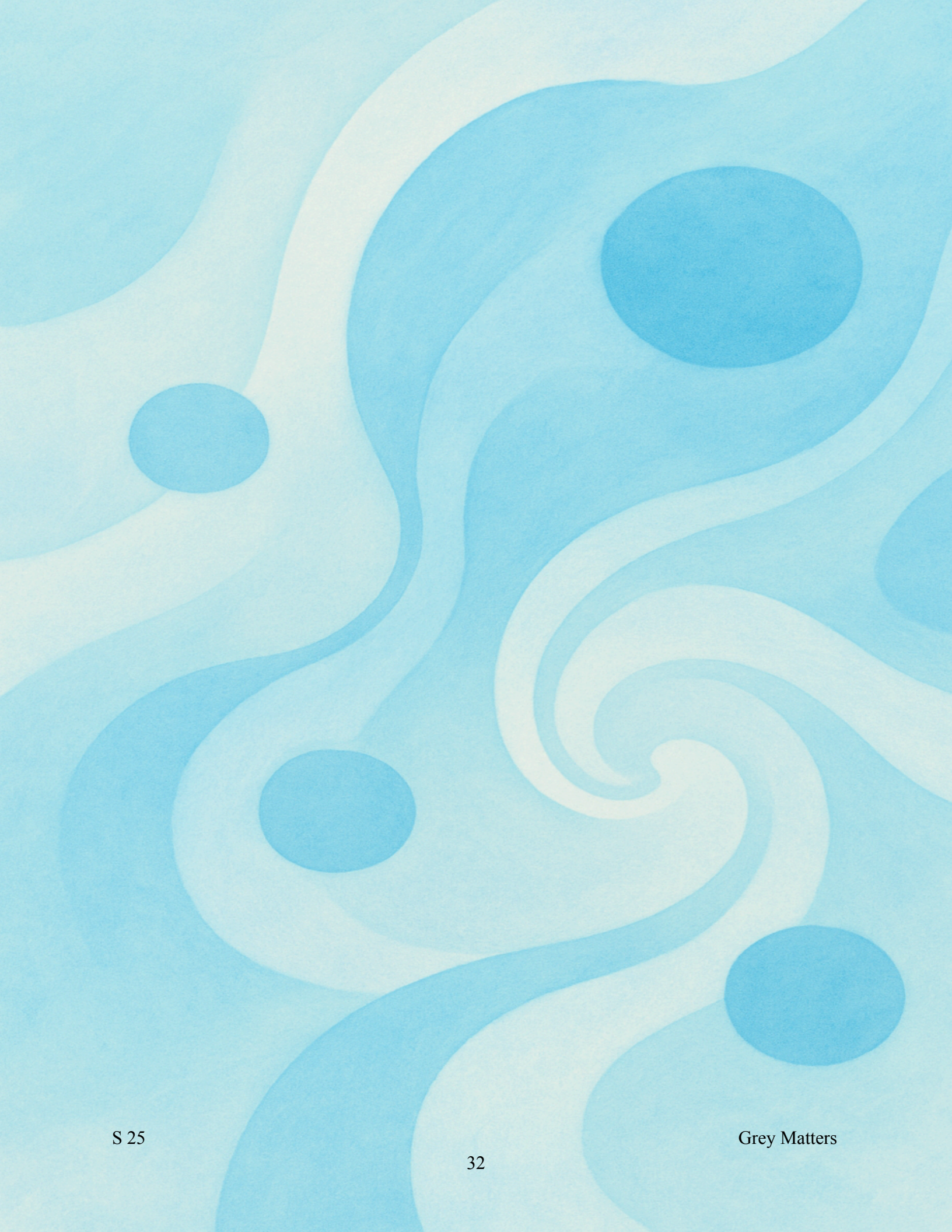


MIT Lincoln Laboratory

What Does this Mean For Science?

NeuroTrALE holds significant promise for advancing our understanding of critical brain diseases. By automating the creation of detailed brain maps, it opens up opportunities for studying brain diseases at a deeper level. This could lead to major breakthroughs in understanding and treating neurological disorders such as Alzheimer's disease, where mapping disrupted neural pathways could reveal information about disease progression and potential treatment targets.

Beyond basic research, NeuroTrALE also has the potential to accelerate the development of personalized medicine. By enabling researchers to analyze individual brain functions in greater detail, it allows for the identification of unique neural activity patterns tied



Why Understanding Neonatal Stroke Matters More than You Think

By Eva and Ben

Have you ever considered how a single moment, just a split-second disruption in blood flow, can change the entire course of a child's life? Neonatal Arterial Ischemic Stroke (NAIS) is exactly that kind of moment. Though it affects only about 1 in every 4,000 births, its impact can be lifelong. And yet, many people have never even heard of it. So, why should you care? Because this stroke happens in the most vulnerable population of all: newborns. Recognizing it early could mean the difference between a child struggling with basic tasks or thriving with support.

NAIS occurs when a blockage in the cerebral arteries cuts off oxygen and nutrients to a developing infant's brain. This can lead to serious neurological consequences, sometimes resulting in full recovery and sometimes in lasting cognitive and motor impairments. One of the most fascinating aspects of this condition is how some infants, thanks to the brain's neuroplasticity, can recover astonishingly well while others face lifelong challenges.
But what makes one infant recover and another not? And how do we give every child their best shot?

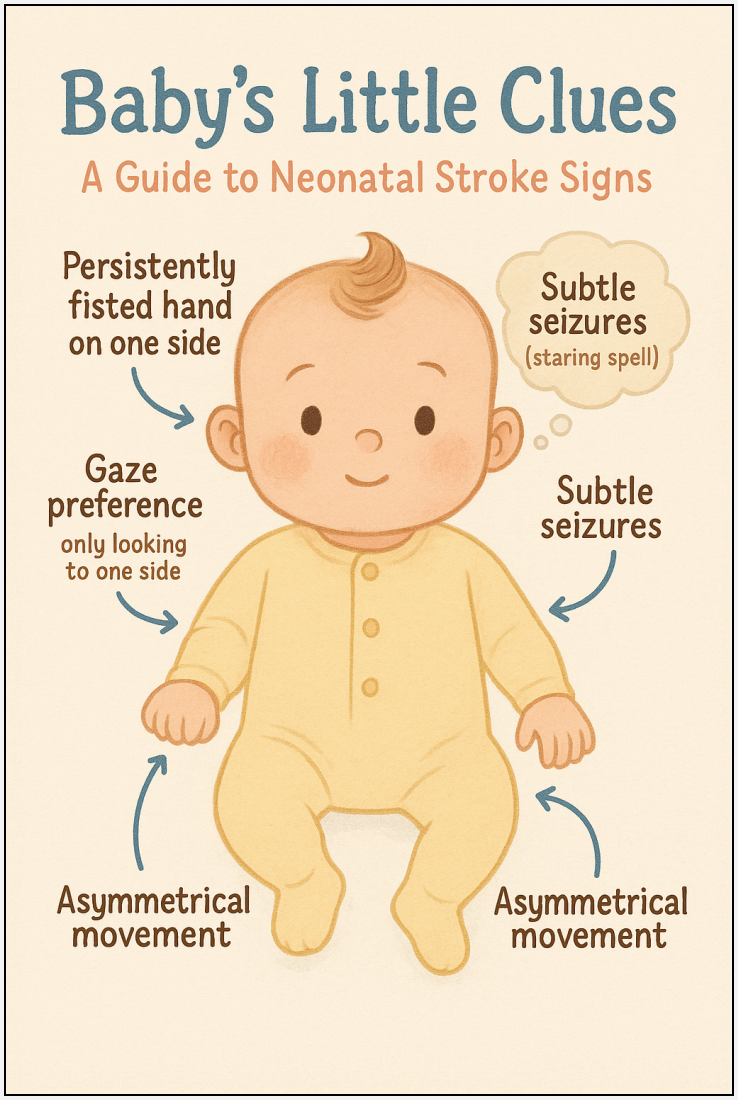
Let's break it down. NAIS is usually caused by clots or embolisms that disrupt blood flow in the brain. Risk factors range from maternal conditions like preeclampsia and infections to birth complications such as heart disease or perinatal asphyxia to even genetic predispositions. While rare, the stroke's potential effects are severe enough to demand early diagnosis and immediate intervention.

Unlike adult brains, infant brains are still forming and evolving. This gives them a better shot at rewiring and compensating for damaged areas. But neuroplasticity alone doesn't guarantee recovery. The extent of damage, which brain regions are involved, and how early treatment begins all matter tremendously. Some children can regain almost full function; others may struggle with memory, speech, or emotional regulation well into adulthood.

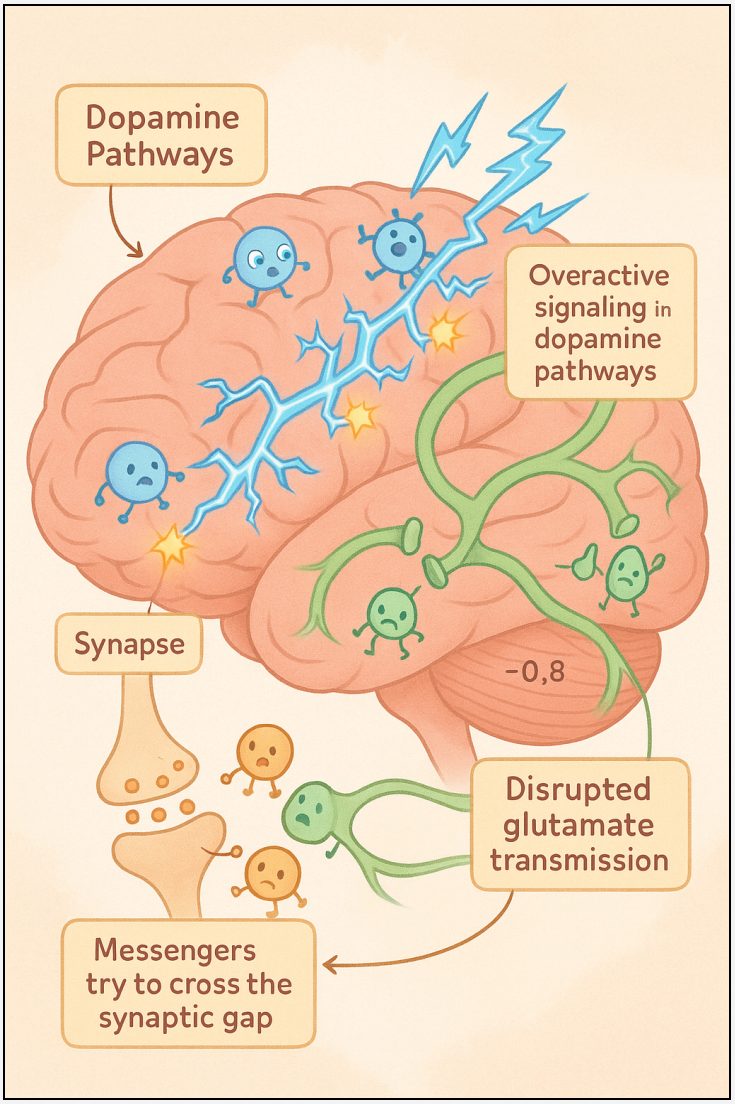
Imagine being a child who can't remember what happened yesterday. Or one who struggles to put sentences together while peers chatter effortlessly. The cognitive impacts of NAIS vary widely, but they often involve memory deficits (especially if the hippocampus is affected), delays in language development, and difficulties with executive function, which are all the skills that help with planning, focus, and impulse control. These challenges don't just affect school performance, but they shape how a child interacts with the world.

But early intervention works. Therapies like physical, occupational, and speech-language help target specific deficits. Cognitive training and tailored support in school environments help children with NAIS learn, grow, and connect. Just as importantly, families play a powerful role, providing emotional support, structure, and encouragement to keep children socially engaged and motivated.

NAIS isn't just a medical condition; it's a story of resilience, science, and the power of early action. So when we ask, "Why should we care?" The answer is clear: Every child deserves a chance to thrive, no matter how their life begins.



Neonatal Stroke: Diagram representing common signs to look out for if an infant is suspected of stroke.



Mechanisms of Schizophrenia: This image highlights the molecular changes typically seen from patients with schizophrenia.

Molecular Mechanisms Behind Schizophrenia

By Nyle Dar

Over a period of 9 years, symptoms of schizophrenia began to develop for Kurt Synder. He had a feeling that THEY were watching him, THEY were causing bad things to happen in his life, and THEY were everywhere. Kurt uses the term THEY to talk about a group of people that he believed took over his life. After years of struggle, Kurt was prescribed medication which greatly helped him in his battle with schizophrenia (Snyder, 2005). Yet, his story serves as a vivid recollection of how detrimental this disorder can be to someone's brain and their perception of reality. Established only in the 20th century, neuroscience is still a relatively new branch in the larger realm of scientific fields and discoveries (even at Johns Hopkins, the Department of Neuroscience was founded in 1980—over 100 years after the university was founded) (Brazier, 2018). In other words, there's still so much we don't know about our nervous of a person; however, it's not just restricted to this period (Torres, 2024). Furthermore, system, including the diseases and disorders that affect it. Thankfully, due to the advances in molecular biology, genetics, and AI, neuroscience research has evolved rapidly and continues to do so. Thus, paving a path for discovering treatments for disorders that destroy the nervous system and make day-to-day living greatly challenging.

Schizophrenia is a brain disorder that affects less than one percent of the US population and lasts for the entire lifetime of an individual with no cure. While most may associate schizophrenia with hallucinations and delusions, it is often much more complicated. Symptoms of schizophrenia fall under three categories: positive, negative, and disorganized/cognitive. Positive symptoms include hallucinations and delusions; negative symptoms include trouble with expressing emotions and speech as well as less desire for social interactions; and cognitive symptoms include trouble thinking logically and struggling with confusion. The symptoms of schizophrenia usually present themselves in the early adult life individuals with schizophrenia tend to have a span of 15 years shorter than the average

(Hjorthøj, 2017). Usually, finding the cause of the disease promotes finding treatment options. But schizophrenia isn't so simple. Researchers and scientists do not know the exact cause behind it. Schizophrenia can manifest from a combination of environmental, genetic, and molecular factors. Perhaps even a traumatic childhood or events in childhood can be a catalyst for the onset of the disorder ("Causes - Schizophrenia," 2023). Scientists have made many efforts trying to find genetic causes of schizophrenia. The idea behind there potentially being a genetic cause for schizophrenia came originally from studies with twins. If one identical twin has schizophrenia the other has a one in two chance of developing it - even if raised separately. However, for nonidentical twins the chance of the other twin developing schizophrenia if one has it is one in eight ("Causes - Schizophrenia," 2023).

An example of one gene called C4, which was discovered by Steve McCarrol of the Broad Institute, is upregulated in people with schizophrenia. McCarrol's study was quite comprehensive—his group analyzed the genomes of 65000 people, genetically engineered mice, and looked at 700 brains from deceased individuals. The protein that C4 encodes for plays a crucial role at synapses, which are functional points of contact between two neurons, allowing for communication. During the development of the brain, the C4 protein will mark a synapse to be eliminated, and in schizophrenia patients, the hyperactivity of this protein may cause excess synapse degradation (U.S. Department of Health and Human Services, 2016).

Besides the genetic component, there are also altered structural characteristics in the brain of patients with schizophrenia. In recent times there have been revolutions in medical imaging with MRI and PET scans developing—just to name a few. These imaging techniques allow us to view the brain's structure and changes in the structure. Individuals with schizophrenia have reduced volume in the cortex or gray matter of the brain. They are also characterized by increased lateral ventricle size, which does not contain any cell bodies and is just a cavity in the brain filled with fluid. These structural deficits may be due to a mishap in the development of the brain, yet it's not completely

understood why. Looking at a much smaller level, the cells of the cortex—called pyramidal neurons—give off fewer dendritic spines and have smaller dendrites. Dendrites are the processes given off by neurons that receive information from other neurons and the dendritic spines come off of dendrites and are points of excitatory synapses (Iritani, 2013).

Schizophrenia plays a major role in terms of neurotransmitters and their receptors. As mentioned previously, neurons give off many dendrites which are spiny-like processes that receive information from other neurons. Another neuron gives off an axon that transfers information to those dendrites by forming synapses with them. A synapse has two components: a presynaptic and a postsynaptic. The presynaptic is the end of the axon called the axon terminal and the postsynaptic is the dendrite (or dendritic spine). But how do the neurons *actually* transfer information at these synapses? This happens due to chemicals called neurotransmitters released from the axon terminal of one neuron onto the dendrites of the other neuron. Neurotransmitters get released from the axon terminal when that neuron generates an electrical pulse called an action potential, causing the vesicles that hold the neurotransmitters to be released into the space between the presynaptic and postsynaptic components. This space is specifically called the synaptic cleft. On the postsynaptic side of the synapse are receptors inserted into the membrane of the dendrite (or dendritic spine.)

But how do the neurons *actually* transfer information at these synapses? This happens due to chemicals called neurotransmitters released from the axon terminal of one neuron onto the dendrites of the other neuron. Neurotransmitters get released from the axon terminal when that neuron generates an electrical pulse called an action potential, causing the vesicles that hold the neurotransmitters to be released into the space between the presynaptic and postsynaptic components. This space is specifically called the synaptic cleft. On the postsynaptic side of the synapse are receptors inserted into the membrane of the dendrite or dendritic spine. The receptors bind the neurotransmitter and then produce a signal in the postsynaptic neuron. Much of the current knowledge of schizophrenia's role with neurotransmitters has

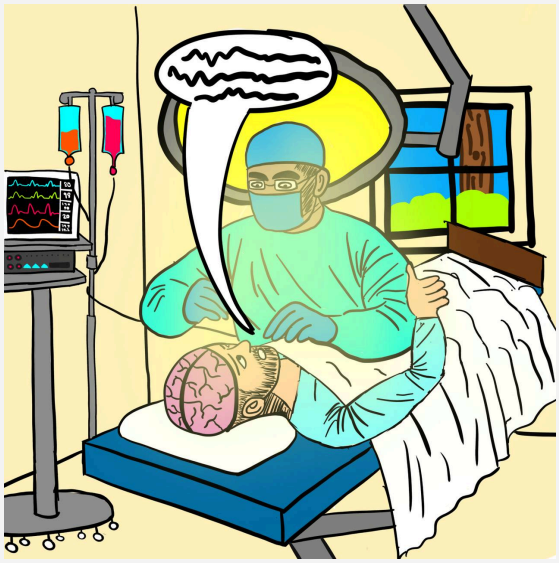
it targeting dopamine, serotonin, glutamate, and acetylcholine (all of which are neurotransmitters) (Iritani, 2013).

Looking at the dopaminergic system, scientists have observed that patients with schizophrenia have an increased amount of a type of dopamine receptor called a D2 receptor. In fact, many of the treatments for schizophrenia target this D2 receptor and attempt to block dopamine transmission. When people take amphetamines this causes a surge of dopamine and this high level of dopamine can cause schizophrenia-like symptoms and hallucinations. From this phenomenon, it was discovered that blocking dopamine receptors can prevent psychotic symptoms and can be potentially used as a treatment for patients with schizophrenia (McCutcheon 2020). Another neurotransmitter called serotonin also may play a role in schizophrenia. LSD binds to serotonin receptors and induces psychotic-like effects, displaying how the serotonergic system could be impacted in schizophrenia (Iritani, 2013). However, the hallucinations experienced by schizophrenia patients are positive symptoms and these dopamine-blocking drugs or antipsychotic medications only counter these positive symptoms. They don't tackle the negative or cognitive symptoms. However, new methods that target different neurotransmitter systems may have a treatment for these other symptoms. To look at the negative and cognitive symptoms we need to turn to a different neurotransmitter: glutamate. A major receptor for glutamate is the NMDA receptor and blocking these receptors can cause schizophrenia-like symptoms—not just the positive ones but also the negative and cognitive ones. Experiments testing this have been mainly run in non-human models for ethical reasons. Since blocking glutamate transmission causes these symptoms, perhaps schizophrenia alters some processes with glutamate neurotransmission (McCutcheon 2020).

In terms of treatments for schizophrenia, doctors often prescribe antipsychotic medicine which works to block dopamine and serotonin receptors (Mayo Clinic Staff, 2024). Yet, these only target the positive symptoms and can have troublesome side effects. In 2024, a new drug was released called Cobenfy. Cobenfy differs from the traditional antipsychotic medications

and instead of working at dopamine or serotonin receptors, it activates muscarinic receptors. Muscarinic receptors are for the neurotransmitter acetylcholine, so this targets a completely different neurotransmitter system. Cobenfy is made from xanomeline and trospium chloride. Originally used in patients with Alzheimer's, xanomeline later stood out for its effects on counteracting psychotic symptoms. Trospium chloride was added to it to reduce the side effects of xanomeline, producing Cobenfy (Katella 2025).

Schizophrenia proves to be a frightening disorder, completely changing the way an individual approaches their life. Yet, current therapies and treatments allow individuals to continue living a meaningful life and alleviate certain symptoms. As science advances, novel mechanisms at the root cause of schizophrenia can be discovered, and scientists can develop new treatments or even cures that will hopefully be better than ever.



Awake During Brain Surgery?

Here's How It Works…

By Nyle Dar

With extremely delicate and precise motions, the neurosurgeon weaves in and out of the brain, making sure to be as careful as possible. After all, the brain is composed of over 80 billion neurons and more than 100 trillion synapses (Caruso). Damage to any area would prove to be catastrophic for the patient and impede their day to day activities. The neurosurgeon is conducting a *different* surgery, though. Their patient—instead of being completely unconscious under anesthesia— is surprisingly awake. To top it off, the patient serenades the surgery team with a blissful melody as she plays her violin (Kennedy). Yet, how is this possible? How and why is the patient awake during one of the most intense surgeries someone could go through?

Awake brain surgery dates back to 1886, when Sir Victor Horsley operated on a patient with epilepsy and attempted to locate the part of the brain responsible for their seizures (Singh K). Awake brain surgery is also referred to as awake craniotomy; a craniotomy is when a part of the skull is removed so the neurosurgeon may access the patient's brain. After the surgery, that part of the skull is placed back into the same spot. Craniotomies are very common for brain injuries (such as a skull fracture) or when a brain tumor must be removed (Cleveland Clinic). Depending on the tumor's size, it can put pressure on surrounding areas of the brain, disrupting various functions (Calixtro). The main goal of a neurosurgeon is to remove as much tumor as possible while minimizing the damage to healthy brain tissue (NHS). If the entirety of the tumor isn't removed it has a chance of returning and thus continuing symptoms. However, removing the tumor may also result in damage to healthy areas.

This is where awake brain surgery comes in, especially when a tumor is near a critical area in the brain that controls motor, sensory, language, or other cognitive areas. If the patient can remain awake, the surgeon can know in real time the effects the patient will experience, thus greatly reducing complications. Before operating, it can be difficult to know exactly which brain area removal will produce what deficit (Mayo Clinic). In terms of general brain mapping, an fMRI (functional magnetic resonance imaging) can prove to be useful to get an idea of a patient's brain function. In an fMRI or MRI, a patient lies in a cylindrical machine where powerful magnets interact with the physical properties of the body to produce an image of the brain. Yet, an fMRI differs from an MRI because patients are asked to do tasks like thinking of different words or reading. As they participate, there's an increase in blood flow to that part of the brain, allowing doctors to see that area's role for that specific function (Yale Medicine). But once again, this is just a general map, and the accuracy of fMRIs isn't spatially perfect and may not align one hundred percent with neuronal activity (Uğurbil).

That's great, but let's address the elephant in the room… how could someone possibly be awake during a brain surgery – something that sounds incredibly uncomfortable and painful. Specifically, how could cutting and sawing into a patient's brain and skull not end in suffering? Well, the brain itself actually has no pain receptors, so hypothetically someone could poke your brain and you'd feel nothing. Then what about headaches— how can someone feel pain in their head if there aren't any receptors for pain in the brain? In reality, headaches are caused by nerves around the head and not by anything actually in the brain (OHSU Brain Institute).

The part that would cause pain, though, is drilling into the skull and removing a chunk of it in order to access the brain. So, for that part of the surgery an anesthesiologist provides the patient with medicine to put them to sleep. Furthermore, they provide numbing injections into the scalp. Once the skull is cut and the brain is exposed, the patient slowly gets awakened by having their sedation tapered off, and the removal of the tumor begins (UCSF Brain Tumor Center).

During the surgery, the patient is asked to do various tasks pertaining to the location of the tumor. The neurosurgeon provides electrical currents to stimulate the parts around the tumor, temporarily inactivating them. This allows the surgeon to see how removing or inactivating that specific part of the brain would affect the patient's ability to the corresponding function. For example, the patient may be tested by a neuropsychologist, who's also in the operating room (OR), on their language abilities since the tumor is near a language center of the brain, such as Broca's area. This part of the brain is found in the inferior frontal gyrus, and damage to it is called Broca's aphasia. Patients with Broca's aphasia have difficulty producing words and sentences, so it's important that the surgeon doesn't damage this area (Stinnett).

As the patient is asked to say different words or sentences, the surgeon will shock different parts of the brain and see if the patient stumbles over their words. If it produces a deficit, this tells the doctor that brain region is crucial for language ability and should not be removed. The surgeon will then work around that area (UCSF Brain Tumor Center). This surgery doesn't apply just to language—it can be applied to other areas of the brain that are responsible for sensory abilities, motor abilities, etc. If the tumor was near the motor cortex, the patient could be asked to move parts of their body. The surgeon would then shock areas of the brain and see if the patient struggled to move that body part.

Once the tumor has been removed, or as much of it as possible, the patient is heavily sedated again and put to sleep as the surgeon attaches the skull back. After the surgery, patients get monitored in the ICU, and there may be additional brain images taken to ensure that the surgeon removed as much tumor as possible (Cohen-Gadol).

Yet, awake craniotomies don't just apply to the removal of brain tumors—they can also be applied to helping people with epilepsy (as Sir Victor Horsely performed the first awake craniotomy to help someone with epilepsy). Epilepsy is a disorder of the brain where people have frequent seizures. Seizures occur when neurons begin to fire too many signals and overload the brain. The excessive activity impedes normal brain function (National

Institute of Neurological Disorders and Stroke*)*. Often, there's an "epileptogenic zone" which is the part of the brain responsible for the seizures, and therefore must be removed if possible (Jehi). If this epileptogenic zone is found near a location that controls a crucial function such as speech, awake brain surgery would potentially be useful in removing the epileptogenic zone while preserving speech function (Maesawa et al.).

Looking at the patient's experience throughout the surgery, they may be drowsy due to the anesthesia, but they will not feel anything actively being tampered with in their brain — they can have regular conversations with the surgeon and even play the violin. Even when a critical area is stimulated and they start stumbling over words or failing at a task, patients may not even notice or feel that they cannot physically perform a task (Weill Cornell Neurosurgery).

The immediate feedback and communication between patient and doctor during an awake craniotomy prove it to be a useful method in minimizing patient complications. The surgeon can be confident that the area they're working on won't leave the patient with a deficit that will stay with them for the rest of their lives. Afterall, the brain is quite delicate as the hub of our worldly perception. ding-headaches-and-migraines.

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Identifying Structural MRI Patterns in Gifted Children using Machine Learning

By Rohan Venkatdas

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THE BRAIN'S BRIDGE BETWEEN MATH AND MUSIC

By Mariam Husain

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The Bizarre Story of Einstein's Brain

By Rohan Venkatdas and Zewen Liu

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Awake During Brain Surgery? Here's How It Works…

By Nyle Dar

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Mind Over Spine

By Omkar Katkade, Jia Li Zhou, and Gabby Molina

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Why Understanding Neonatal Stroke Matters More Than You Think

By Eva and Ben S

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Revolutionizing Nerve Repair: A Leap Toward Healing the Impossible

By Rebecca Crisp

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