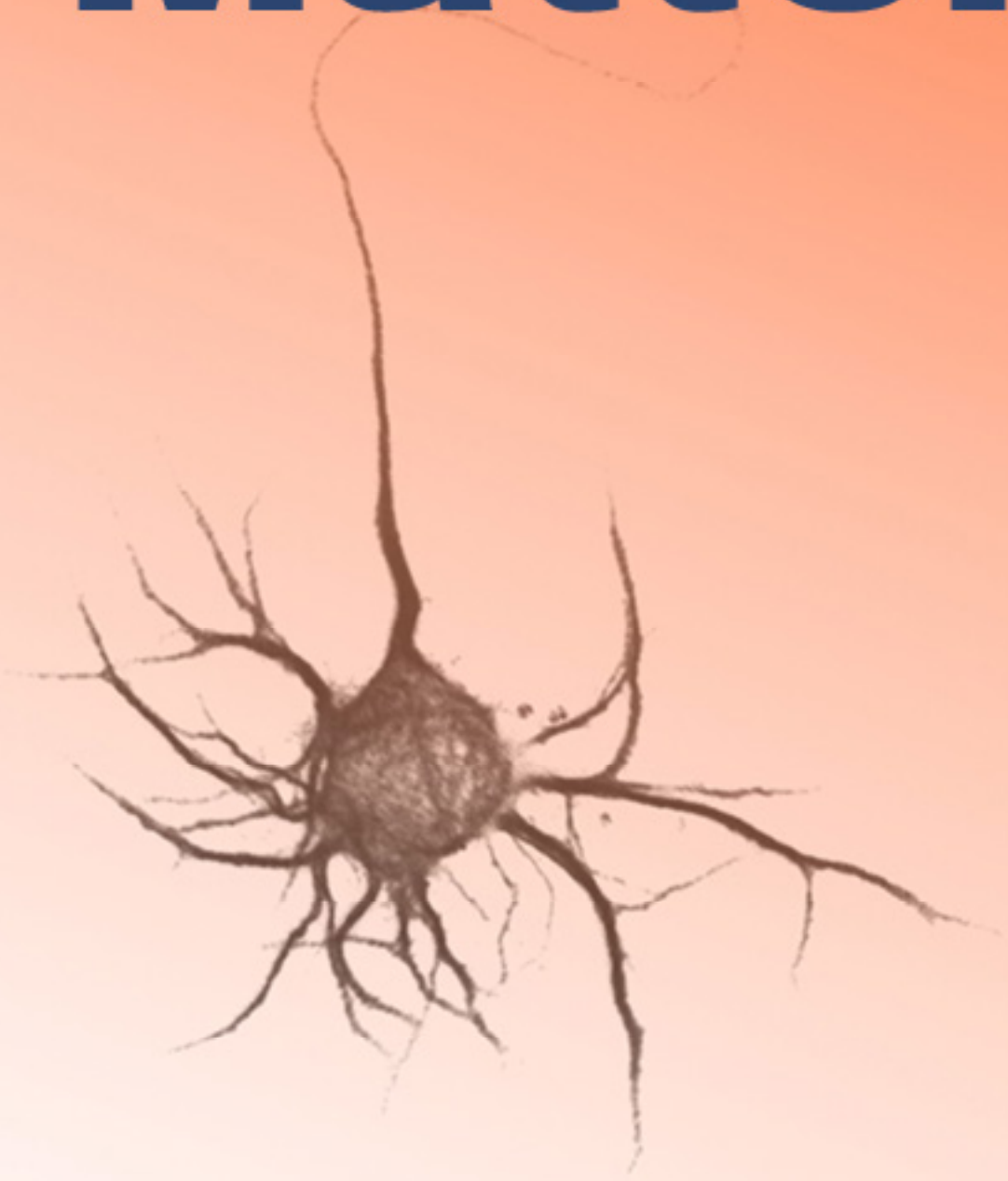
Brain Matters



Undergraduate Neuroscience Society
University of Illinois Urbana-Champaign
Volume 2

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Outcomes in Neuroscience Education: Modular Theory and Network Theory

Thomas Romanchek

A Prelude to Modular Theory

Few can contest the complicated and interdisciplinary origins of neuroscientific study, as its precise date of birth is obscure. However, it is important to place the first true and deliberate neuroscience studies in proper historical context so we can fully appreciate and understand why topics were studied through the lens of modular theory. Ancient Egyptians considered the brain and its organic projections to be little more than waste, instead believing that the true "seat of the soul" was the heart (Chudler, n.d.). This view was replicated in early Greek and biblical texts but represented the consolidation of personality and human character into physiological terms. Later, Hippocrates and his followers rebuked this dogma in early physiology, instead arguing that the brain was the major control center for the body and possessed three ventricles, each of which was responsible for a different mental faculty: imagination, reason, and memory (Chudler, n.d.). This view was supported by the Greek physician Galen who wrote extensively on the subject and had a profound influence on Enlightenment philosophers such as Rene Descartes (Chudler, n.d.).

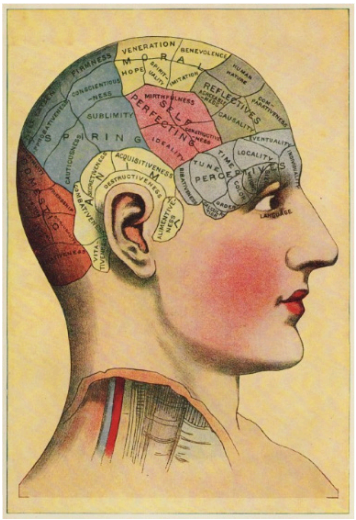

Figure 1: Phrenology chart [jpg]. (1920). Retrieved from https://www.sciencephoto.com/media/1002821/view/phrenology-chart

Hippocrates, Galen, and Descartes' collective writings emphasized an increasingly compartmentalized view of brain structure and function, a sentiment that came to a head in the early 19th century under the directorship of the German physiologist Franz Joseph Gall, the founder of the study of phrenology (Fodor, 1983). Phrenology borrowed major tenets of previous neurophysiological literature such as continuing to support the notion that the brain was the principal organ of the mind. Gall took those previous ideas to new maxims, claiming that the brain represented a collection of precisely localized cerebral organs with specific functions (Figure 1). The strength and proficiency of those particular functions, he argued, were proportional to the relative sizes and geometries of their respective skull regions.

Many would correctly conclude this understanding of neurophysiology to be akin to pseudoscience, but the dangerous influence phrenology has had on research in neuroscience must not be understated. The writings and lectures of Gall, his collaborators, and his students spread throughout the English-speaking world during the 19th century and fomented a number of debates about the methods employed to justify the major principles of phrenology (Yildirim & Sarikcioglu, 2004). Physiologist Jean Pierre Flourens performed experimental brain excisions on pigeons and observed their consequential behavior to demonstrate that the defined brain regions in phrenology had little experimental backing. These ablations, however, caused varied deficiencies and behavioral abnormalities suggesting that some interplay did still exist between brain regions and behavior (Yildirim & Sarikcioglu, 2004). An avalanche of research soon followed, characterizing and qualifying these interactions, along with the functions of a number of other brain and nerve components (Figure 2). Were it not for the early writings and claims of phrenology, the brain might have not been drawn into so many distinct components over the next two centuries.

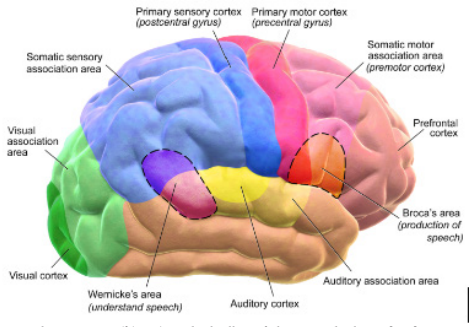

Figure 2: Blausen.com staff (2014). Medical gallery of Blausen Medical 2014 [png]. Retrieved from https://en.wikipedia.org/wiki/Human_brain#/media/File:Blausen_0102_Brain_Motor&Sensory_(flipped).png

Modular Theory Comes Under Scrutiny

Significant progress has been made over the last several decades in analyzing and characterizing brain regions and tissues. Our predecessor neurophysiologists of the late 1700s and 1800s lacked the sophisticated imaging technology we use today. Our imaging techniques provide a far more nuanced view of the brain, permitting us to see individual cells with profound resolution as seen in the Golgi staining technique (Finger, 2004). Golgi staining, developed by Camillo Golgi in 1873, entails the perfusing of silver nitrate into the cell bodies of neurons, the functional unit

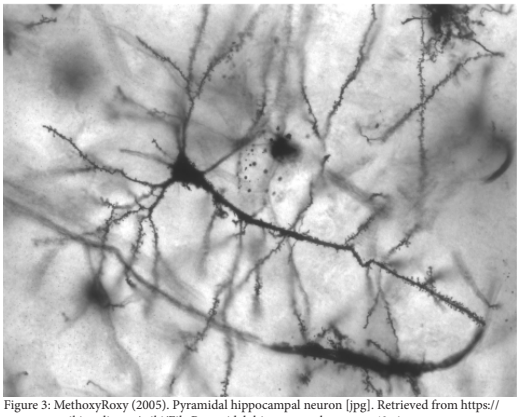

Figure 3: MethoxyRoxy (2005). Pyramidal hippocampal neuron [jpg]. Retrieved from https://commons.wikimedia.org/wiki/File:Pyramidal_hippocampal_neuron_40x.jpg

of the nervous system. The resulting stains depict darkened cell bodies and axons, the cellular projections that neurons use to communicate with one another (Figure 3). This advent in imaging technology allowed scientists to observe the actual connections and highways of communication between distant regions within the nervous system (Finger, 2004). Modular theory was beginning to be forced on the defense for the first time since its birth two centuries prior.

Cell imaging had its uses but had fairly limited applications when it came to in-vivo study of the brain and its operations. Cell and tissue isolation required the sacrifice of animal subjects and the collection of brain matter from cadavers. The first in-vivo studies of brain function and organization came about as the result of the invention of the x-ray in 1895 by Wilhelm Konrad Roentgen. The first images from this technology gave researchers a valuable opportunity to observe naturally-occurring brain deterioration in living human subjects and to relate the damage location and intensity with the behaviors and actions the subjects expressed (Finger, 2004). Early work demonstrated the lack of uniformity in brain tissue between humans. Regions thought to be related to language comprehension and speech production were found to differ in size and location between subjects. Furthermore, the degree of gyration of those and other brain regions was unique for everyone who was imaged (Triarhou, 2017). Overt dissimilarities in brain appearance began to give way to mounting criticism of the well-defined module mold of brain organization.

Both cell and brain imaging had important implications in research, but limited potential because each perspective provided only a snapshot of activity at a single given moment. It was not until the invention and implementation of imaging and even neurostimulator technologies that such a feat was possible. Positron emission tomography (PET) and magnetic resonance imaging (Figure 4) allowed scientists to observe the brain in action and directly measure the activity of brain regions through the circulation and exchange of blood and oxygen. These were complemented with experimental chemical stimulation, light stimulation through optogenetics, and Transcranial Magnetic Stimulation (Figure 5) to directly test relationships of stimulation and inhibition with brain activity (Badcock et al., 2019). These technologies revealed the limited importance of clusters of cells and tissues in action execution, and the greater relevance of their overarching and interconnected communication networks. However, a substantial disconnect still exists between what research has managed to reveal about the merits of network theory and what is being actively taught in classrooms.

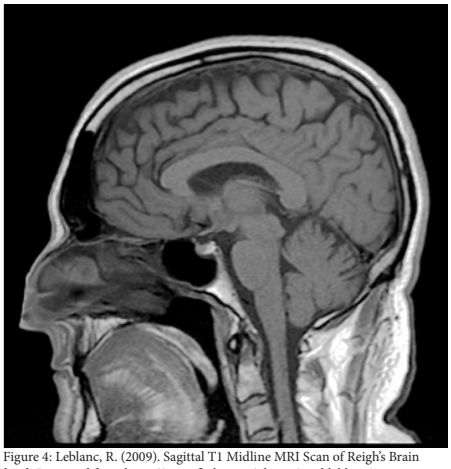

Figure 4: Leblanc, R. (2009). Sagittal T1 Midline MRI Scan of Reigh's Brain [jpg]. Retrieved from https://www.flickr.com/photos/reighleblanc/3854685038.

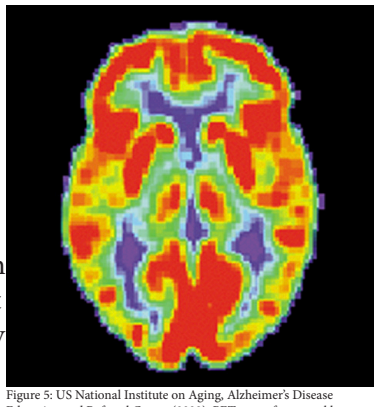

Figure 5: US National Institute on Aging, Alzheimer's Disease Education and Referral Center (2008). PET scan of a normal human brain [jpg]. Retrieved from https://commons.wikimedia.org/wiki/File:PET_Normal_brain.jpg.

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The Differences between ADHD Brains vs. Non ADHD Brains

Julia Gainski

There are many common misconceptions between differentiating ADHD brains and non ADHD brains, the cause of which largely stems from the stigmatization of mental health disorders. Though it is still debated whether or not ADHD is classified to be a disorder of the brain, inaccurate assumptions are often formed, leading to much confusion in the understanding of the disorder. ADHD includes symptoms such as forgetfulness, hyperactivity, irritability, impulsivity, and difficulty paying attention to details. Researchers have gathered evidence through scrutinizing various brain images and identifying structural differences that strongly convey the substantial differences between people who have ADHD in comparison to those who do not. These differences will be investigated throughout this paper.

Today, the reports estimate approximately eleven percent of children and five percent of adults to be diagnosed with ADHD in the United States. Alongside this, there is increased difficulty while completing tasks such as listening during a class period or during brief moments of instructions. ADHD stands for attention deficit hyperactivity disorder, and is classified as a common neuropsychiatric disorder. ADHD is not a severely rare disorder, but still "affects more than one in 20 people under 18 years old" (Radboud University Nijmegen Medical Centre 2017). It is important to note that about two-thirds of the people diagnosed with ADHD early on such as during their childhood continue to experience the symptoms of ADHD as adults. The main part of the brain that researchers are examining is the basal ganglia, a part of the brain that controls emotion, voluntary movement, and cognition. Researchers have "... found that the caudate and putamen regions within the ganglia are smaller in people with ADHD" (Radboud University Nijmegen Medical Centre 2017). Both the putamen and caudate make up the dorsal striatum, a functional structure that is directly involved in the decision-making process. More specifically, the things that encompass this would be action selection and initiation. The basal ganglia makes up the caudate, putamen, globus pallidus in the cerebrum, the substantia nigra in the midbrain, and the subthalamic nucleus in the diencephalon. It is important to note that the basal ganglia is known for its prominent role in movement, a critical aspect to pay attention to because many people with ADHD have issues with staying still. Therefore, the basal ganglia can be used as a strong indicator and an identifier of those who have ADHD. To add on to this finding, international studies are interested in examining the differences in the brain structure and density involving 1,713 people with a diagnosis of ADHD and 1,529 without the diagnosis. The age ranges for this study was between four and 63 years old. The purpose of the MRI scan was to measure the overall brain volume of each person. The scientists took specific percentages of each region of the brain and measured the density of each person's brain. Alongside this, the size of the seven regions of the brain that were associated with a possible linkage to ADHD are: the pallidum, thalamus, caudate nucleus, putamen, nucleus accumbens, amygdala, and hippocampus. Through the analysis of measuring the regions, scientists can use the differences in brain volume percentages to better understand how an individual's brain with ADHD differs from an individual's brain without ADHD. Scientists put more emphasis on scrutinizing the differences in each individual brain region in order to get a better idea on which regions are affected the most and the correlation they share with ADHD.

The conclusive results from this study were that people with ADHD had slightly smaller overall brain volumes, thus not allowing for some expansion of certain brain regions and therefore limiting the ability to concentrate. Alongside this, the regions that reported differences in size were the caudate nucleus, putamen, nucleus accumbens, amygdala, and hippocampus. The list is notably narrowed down because these were the regions that reported the most significant differences and were shown to have slightly smaller volumes in people with ADHD as opposed to the other regions.

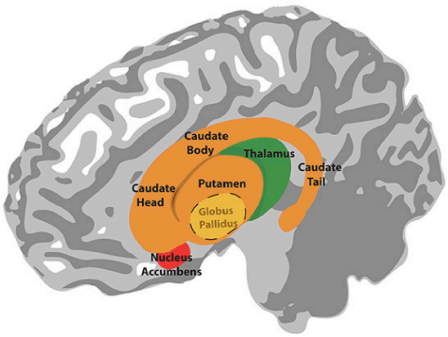

Figure 1: This image demonstrates the anatomy of the basal ganglia.

Another study identified specific locations of the differences in volumetric abnormalities within the basal ganglia through the use of LDDMM, which stands for large deformation diffeomorphic metric mapping. The anatomy of the basal ganglia is illustrated in Figure 1. The LDDMM mapping's purpose revolves around, "the effects of ADHD, sex, and their interaction on basal ganglia shapes" (Qiu 2009). The LDDMM mappings generated basal ganglia templates and Laplace-Beltrami basis functions in the template coordinates was used to demonstrate shape variations within each structure in relation to the template. The shape variations, "were modeled for each subject as a random field" (Qiu 2009). The results from this study encompassed that girls with ADHD did not depict any differences in terms of volume or shape. In contrast, "boys with ADHD showed significantly smaller basal ganglia volumes compared with typically developing boys, and LDDMM revealed the groups

remarkably differed in basal ganglia shapes" (Qiu 2009). One study encompassed the stigma behind ADHD not being classified as a real disorder of the brain. The study makes the argument that ADHD should not be treated differently than other disorders because of the similarities that ADHD presents and the similarities it shares with other disorders such as learning disorders. The brain images were collected from 3,200 people. Roughly half of the participants had some sort of diagnosis to ADHD in the past and half of the participants were never diagnosed with ADHD. The National Institutes of Health (NIH) worked with ENIGMA Consortium, an international multidisciplinary group that specializes in psychiatric disorders, to conduct this study. In a like manner, figure 2 denotes an image that is superimposed on an ICBM (International Consortium for Brain Mapping) standardized anatomical template.

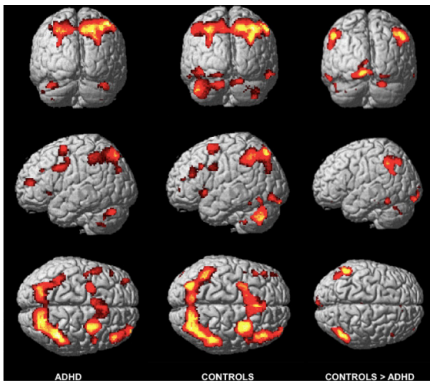

Figure 2. Differences in neural activity and functional brain patterns between controls and children who have never been medicated with ADHD.This image is superimposed on an ICBM (International Consortium for Brain Mapping).

One might wonder what these differences look like, and the answer is that on average, differences in brain volumes only range by a few percent between individuals who have ADHD with those who do not. ADHD is a disorder of the brain that primarily affects behavior and attention. Other brain disorders, such as bipolar disorder, affect mood. One study used an MRI scan, in which 455 people with ADHD received psychostimulant medication. Since there were[1] different volumes demonstrated within the five brain regions, it goes to say that ADHD is present regardless of the fact that people had taken medication. In essence, this suggests that differences in brain volumes had no correlation to the presence of psychostimulants.

[1] A psychostimulant medication is used to treat ADHD and narcolepsy. The purpose of psychostimulant is to increase alertness, attention, and energy.

Therefore, this study had a primary focus on measuring more of the effects of psychostimulants than ADHD. This finding presents the phenomenon that psychostimulants are not always proven to be effective as they have failed to produce any significant differences, if any. In terms of the amount of individuals who took them, there were 62 participants in each of the three trials. In a like manner, several studies encompassing the use of psychostimulants, used for treating individuals with depression, have shown how multiple trials and groups of participants have reported no significant differences with the use of psychostimulants (Candy 2008). It is important to weigh the benefits and costs before deciding if one should take psychostimulants. Not every individual who decides to take them will benefit and some ultimately face negative side effects such as mood swings and headaches. It is vital for an individual to note the progress he or she feels when taking psychostimulants. In order for this person to see if taking psychostimulants a good path for them to take, they should closely monitor their progress and check in with themselves everyday and then make the conclusion with their doctor on if they saw a consistent trend of improvement. As previously mentioned earlier in the article, the study conducted by a team of Dutch neuroscientists also analyzed over 3,200 MRI scans of the brains of people aged between four and 63 years old. Around half of the participants had a diagnosis of ADHD and the study analyzed overall brain volumes and inspected the regions most likely to be linked to ADHD. They meticulously differentiate between genetics and the differences between brain imaging. The study's results in brain scans "...revealed that five brain regions were smaller in people with ADHD" (Gregoire 2017). The study showed that the differences were more drastic in children in comparison to adults, leading the authors to derive that ADHD is associated with delayed brain development. The study illustrates that differences are seen to be much more significant in children rather than adults. This is because as an adult brain matures, the brain regions more closely resemble the brains of people who do not have ADHD. These differences become less and less distinct over time as opposed to the drastic differences seen between children with ADHD brains in comparison to children who do not have ADHD. Within the study, analyzing different brain volumes and different amounts of psychostimulants, 455 people with ADHD took a psychostimulant such (Adderall, for example), and then another 600 participants were not currently on any medication but had a history with taking the medication. The MRI imaging results demonstrated that the role of the stimulants did not at all correlate to the differences in brain volume. One researcher, Dr. Martine Hoogman, studying the effects of ADHD on the human brain, states her take on the role that the brain disorder plays in society: "The results from our study confirm that people with ADHD have differences in their brain structure and therefore suggest that ADHD is a disorder of the brain. We hope that this will help to reduce stigma that ADHD is just a label for difficult children or caused by poor parenting" (Paddock 2017). In essence, in today's world, mental health is constantly being stigmatized and overlooked.

In a like manner, brain disorders are being looked at as a rather secondary importance, which ignites the need for more conversations surrounding mental health. As seen in the studies described, certain paths and solutions work better for some than others. Individuals with ADHD must

be mindful of this when deciding on their personalized path in order to treat what they are experiencing, because one solution cannot fix all issues. Solutions ought to be approached with the mindset of needing to make collective changes such as dietary selections, having a conversation with a doctor on if psychostimulants are a promising option, and prioritizing the amount of exercise that is sufficient on a daily or weekly basis. On top of making lifestyle changes, one must begin to make internal changes as well, and adapt positive thinking patterns in order to better cope with their disorder. Alongside this, it is important to remain optimistic in the midst of daily obstacles; as a society, we must work together to break down these barriers and pay closer attention to how we can accommodate those who need extra assistance.

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Therapeutic techniques for Neural Regeneration in the Central Nervous System

Chloe Kim

Scientists have studied multiple approaches that have been thought to enhance neural regeneration. These approaches have led to the development of groundbreaking treatment for age-related diseases and nerve injuries. The development and use of these treatments are vital because spinal cord injuries and traumatic brain injuries alone affect 90,000 people every year; approximately 10,000 mostly young individuals are affected by acute spinal cord injury and 50,000 die from traumatic brain injury each year (Stabenfeldt et al., 2006). It is also important to note that neurodegenerative diseases, such as Alzheimer's or Parkinson's disease, are affecting a large portion of the aged population worldwide. As the average human lifespan is expected to increase over time, the number of people within the population affected by such diseases is projected to grow by mid-century (Alzheimer's Association, 2016). Thus, by recovering nerve functionality after injury, nerve regeneration techniques have great potential to conquer the problems that are projected to affect a significant amount of the general population. Therefore, techniques such as neural tissue engineering is a rapidly growing field of research that has the potential to achieve efficient nerve regeneration. Nevertheless, most clinical treatments are limited to symptomatic methods, as in vivo approaches in neural regeneration are yet to be utilized. In this article, current limitations and newly developed methods of neural regeneration are to be introduced, as well as suggestions on possible future improvements for clinical adaptations.

One of the greatest problems in neural injuries is that, in contrast to the peripheral nervous system, the central nervous system (CNS) is generally incapable of self-repair or regeneration. Spontaneous regeneration of the CNS is mainly due to functions of inhibitory factors, and little is uncovered about this mechanism of inhibition. Yet in the late twentieth century, an explanation for the functional recovery of the CNS was introduced based on the concept of neuroplasticity, the CNS's ability to anatomically and functionally adapt to changes. In addition, the concept of reactive synaptogenesis was also proposed in 1979. Reactive synaptogenesis is the process in which neighboring neurons form new synaptic contacts to replace those lost, contributing to a restoration of function following brain injury. As a result, several methods, including the use of stem cells, brain drug delivery, and implanting degradable biomaterial, have been actively researched to enhance regeneration in CNS. Studies have found that specific brain regions including the subventricular zone (SVZ), the adjacent rostral migratory stream (RMS), and the circumventricular organs (CVOs) might be responsible for modulating the regenerative ability of neural stem or progenitor cells. Neural stem cells that are possibly responsible for neurogenesis are expressed by filament proteins, nestin, vimentin, GFAP, and transcription factor Sox2 in the SVZ of the anterolateral ventricle and subgranular zone of the hippocampus. Similarly, studies using rat models identified Sox2 and the cell cycle-regulating protein Ki67 in CVOs, and therefore proposed that CVOs play important roles in stem-cell based neurogenesis as well as SVZ and RMS (Bennett et al., 2009).

SVZ, RMS, and CVOs share the common trait of lacking protection provided by the blood-brain barrier (BBB) compared to other parts of the brain. BBB is a unique form of cellular membrane that is relatively impermeable compared to the membranes of other body parts because its capillary walls have no pores and the capillaries are lined by astrocytes. Limited permeability of BBB has been one of the most limiting restrictions in brain drug delivery research. However, because SVZ, RMS, and CVOs have more "leaky" BBBs, they are more likely to perceive damage and engage in brain repair by producing new neurons which cross to other parts of the brain.

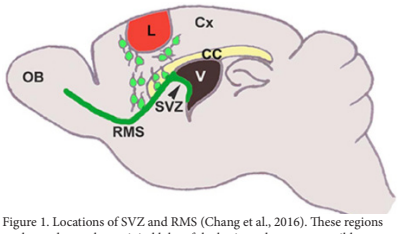

Figure 1. Locations of SVZ and RMS (Chang et al., 2016). These regions are located near the occipital lobe of the brain and serve as possible sources of stem cell regulation.

In addition, several neuroprotective and neuroregenerative drugs have been developed to treat neurodegenerative diseases. Nevertheless, most of them are not utilized because they are generally incapable of crossing the BBB, followed by rapid clearance from the blood circulation by the reticuloendothelial system (RES). For example, molecules like Z-DEVD-FMK and basic fibroblast growth factor (bFGF) were found to significantly induce neuroregeneration in in vitro studies. However, neither can pass the BBB in their free form or do so in very low amounts, displaying limited efficacy in potential clinical uses (Yemisci et al, 2015). Thus, to stimulate these brain regions and to utilize the drug molecules that have been found to contribute to neurogenesis, intravenous injection of nanoparticles (NP)

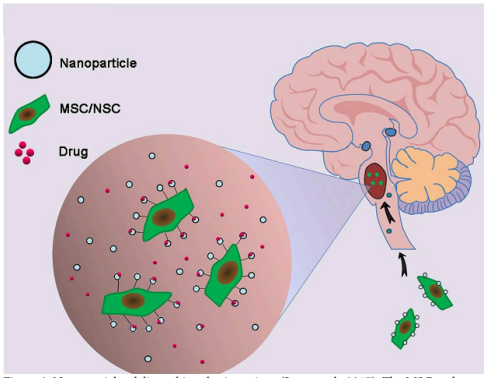

Figure 2. Nanoparticles delivered into brain regions (Long et al., 2017). The MSC and NSCs are types of stem cells that can carry nanoparticles into the brain and allow for transfusion and delivery of the desired drug, which has been experimented with for in vivo studies.

through.

NPs are well-defined particles ranging in sizes of approximately 10 to 1000 nm (1 μm) with a core-shell structure (nanocapsules) or a continuous matrix structure (nanospheres) (Kreuter, 2014). Researchers have uncovered that specific forms of NP (angiopep-conjugated poly(ethylene glycol)-copoly(ε-caprolactone) nanoparticles or ANG-PEG-NPs) pass through the BBB and accumulate in certain brain areas such as the ventricles, hippocampus, and cortical layer. Also, chitosan NPs and cationic bovine serum albumin-conjugated tanshinone IIA PEGylated NPs showed promising results in crossing the BBB and therefore increase drug efficacy. Moreover, these NPs have the inherent ability to elicit neuroprotective effects by themselves. For example, by down-regulating pro-inflammatory cytokines, up-regulating anti-inflammatory cytokines and transforming growth factor-β1 (TGF-β1) these NPs modulate inflammatory processes and neuronal signaling pathways (Saraiva et al., 2016).

More specifically, among other NP formulations, solid lipid nanoparticles (SLNs) are expected to enhance efficiency in brain-targeted drug delivery system. In the late 1900s, researchers found that surfactant coating on NPs increases blood NP level along with the total NP brain amount in in vivo studies. Several mechanisms were proposed to explain this increase, one being that increased NP retention in the brain blood capillaries, and their absorption into the capillary walls may create a higher concentration gradient, which enhances transportation across the BBB, leading to brain drug accumulation. Another explanation may be that NP endocytosis by endothelial cells can permit the drug release within these cells and the following drug diffusion in the brain parenchyma, or the transcytosis of NPs with the bound drug can release directly into the brain parenchyma, along with multiple other possible explanations. Although these mechanisms are still being studied, previous experimental results have shown that the use of surfactant-coated SLNs plays a role in brain-targeting drug delivery that induces neural regeneration as a possible treatment to neurodegenerative diseases (Blasi et al., 2007).

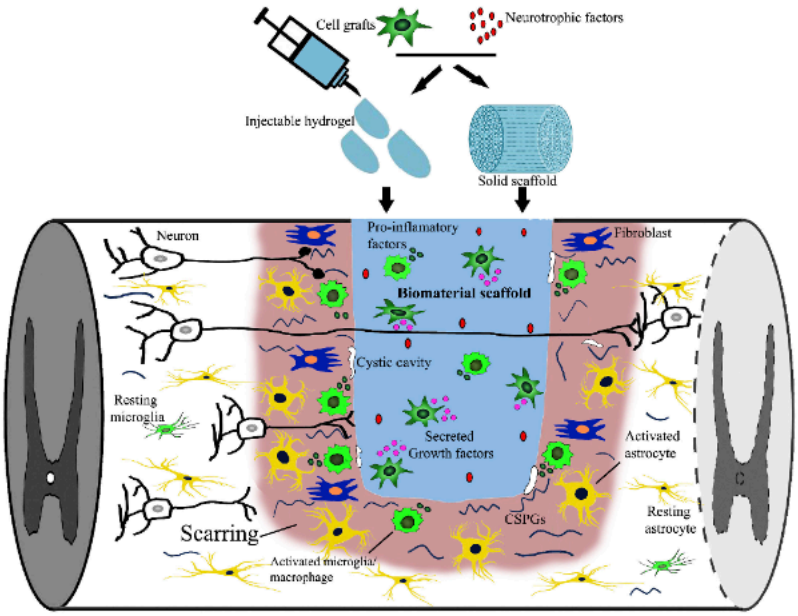

Figure 3. Mechanism of hydrogel-induced neural regeneration (Liu et al., 2018). The cell grafts and neurotrophic factors are injected via a hydrogel into the muscle scaffolding. The integration of the cells + neurotrophic factors lead to activation of astrocytes, microglia, and a variety of other neurons that are involved with the repair mechanism within the tissue.

Another way to induce enhance neuroregeneration is to directly implant active biomaterials such as hydrogels. Hydrogels are used in the same drug delivery system as NPs but act differently through inducing neurogenesis by mimicking neural growth conditions. Biomaterials can be useful because the systemic delivery of pharmaceuticals usually results in reduced efficacy over time. This is predominantly due to failure to meet the needs for continuous drug delivery, along with possible side effects followed by repeated drug administration (Gerndt et al., 1997). In treatments of spinal cord injury (SCI), the drug-releasing biomaterial has been proposed as a new solution to overcome these obstacles. Polymer-based materials, including hydrogels, particles, and fibers/conduits, are implantable or sometimes injectable; they can prevent detrimental side effects of drugs delivered systemically, such as a compromised immune system.

Such biomaterials are targeted to provide structural support to regenerating axons and glia migrating into the injury site. They also aim to provide a similar mechanical and biological environment as those of the nerve tissue matrix and degrade over time to be replaced by regenerating tissue. For instance, hydrogels are injected into the intrathecal space of the spinal cord, most commonly in treatments of contusive SCI. For an acute injury, hydrogels are injected onto the contusion injury site, and solidified gels onto the hemisection injury site. For secondary injury, hydrogels incorporating particles are injected onto the contusion injury site, and solidified gels with particles onto the hemisection injury site. A small cavity grows within the contusion injury during the proliferation and chronic injury phases. Fibers are positioned below the dura within the contusion injury space, while the conduit scaffolds within the hemisection injury connect to the healthy tissue. In a study conducted in 1995, Arg-Gly-Asp peptide-functionalized PHPMA hydrogels promoted angiogenesis and extension of axons and glial cells (Woerly et al., 1995). In addition, agarose is another injectable biodegradable material as it solidifies following injection according to changes in the environment such as temperature and pH. Brain-derived neurotrophic factors (BDNF)-formulated agarose can solidify when cooled post-injection; nevertheless, the appropriate mechanism to cool the material in situ should still be concerned (Nguyen & Lee, 2010).

Regenerative capability of biomaterials is based on

its ability to deliver appropriate growth factors or critical components of the extracellular matrix (ECM), bind the same receptor as their natural counterpart to promote cell attachment, spreading, and proliferation. These peptides, such as the most common examples, tripeptide RGD and multidomain peptide (MDP), are attached to syringe-deliverable hydrogels and are subcutaneously implanted into the injury site to provoke neurogenesis and angiogenesis resulting in the dense vascular network. As discussed above, these biomaterials predictably degrade over time and replaced with the regenerating cellular matrix.

One of the greatest concerns in this approach is the immune response to the implanted biomaterials. Injections generally lead to an acute inflammatory response as hydrogels are frequently recognized as foreign material (Moore et al., 2018). Several aspects such as the local context of biomaterials influence the innate properties of the implanted biomaterials that form the extent of the immune response (Sadtler et al., 2016). Thus, multiple approaches are being discovered to minimize the potentially harmful immune response in treatments involving biomaterial injection.

As both approaches, drug delivery via nanoparticles and direct injection of biomaterials, have distinct compatibility in treating different neuroregeneration-related diseases or injuries, combining these techniques can be a possible solution to overcome inherent problems in these methods (Schmidt & Leach, 2003). Followed by more extensive research in individual techniques, an appropriate combination of these could result in significant improvements of multiple neurological illnesses by inducing neural regeneration in different situations as needed.

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Language Acquisition Device and the Origin of Language

Briana Sobecks

In the early twentieth century, psychologists realized that language is not just understanding words, but also requires learning grammar, syntax, and semantics. Modern language is incredibly complex, but young children can understand it remarkably well. This idea supports Chomsky's idea that language learning is innate. According to his hypothesis, young children receive "primary linguistic data" from what is spoken around them, which helps them develop knowledge of that specific language (Cowie 2008). Children passively absorb language from adults, peers, and exposure to media. However, this data is not sufficient to explain how children can learn unique constructions of words and grammar patterns. Previously structuralists created a list of "phrase structure rules" to generate all possible grammar patterns. However, Chomsky argued that grammar must also include "transformations" that combine old sentence patterns and reorganize them. He called these patterns "generative grammars." For a child to understand patterns of this complexity, their language ability must be well developed. The primary linguistic data they're exposed to isn't enough to give them this complexity. The complexity of language allows Chomsky to refute B.F. Skinner's hypothesis that grammar is developed through operant conditioning. Too many usages of each individual word are needed for conditioning to be a viable option. Since people can say and understand unique sentences, language ability must transcend pure conditioning. Furthermore, the mechanism for operant conditioning is unlikely to take place in a child's language development. If a child is trying to learn a new grammar pattern and makes a mistake, he or she could either be corrected by their parents or hear the sentence said by a more competent speaker. However, parents may not correct the child, and even if one child hears the correct sentence, it is unlikely that all children will hear a similar phrase. This does not prove that an innate language learning faculty exists, but it does strongly disregard operant conditioning's role in language development.

Chomsky proposed a theory of "universal grammar," in which all grammar follows certain rules that humans implicitly understand. Since the data that a child is exposed to is finite, but the number of expressions possible in language is infinite, there must be a way for a child to generate new ideas independent of the vocabulary they have encountered. When first developing the theory, Chomsky thought that children would do a "scientific inquiry" to investigate the working patterns of language. Later, psychologists created a "parameter setting" model, saying that the device is a normal part of development, and as children grow, "switches" are activated to further their learning (Cowie 2008). Depending on the more specific patterns of a particular language, the universal grammar can be refined to fit a specific language. Even if some children may hear a specific language pattern more than others, the fact that all children know it indicates a poss ble innate language sense.

One of Chomsky's main tenants in his LAD theory is the Poverty of Stimulus argument. Though children do collect data to learn a language, it is unlikely that the data they are exposed to is enough to master an entire language. Instead, they must infer grammatical rules through an internal sense. There are several cognitive factors that support this argument. Underdetermination states that the finite data is applicable in infinite situations. In context, this means that children utilize the finite amount of data they hear to generate any possible sentence. Degeneracy is another important factor. In regular speech, people often use abbreviated or grammatically incorrect sentences, yet children still learn proper grammar. Idiosyncrasy is a third concept. Every child is exposed to a different sample of sentences, yet they all develop the same language abilities. This points to the idea that children possess an innate way to interpret these sentences and generate grammatical patterns. Fourth is positivity, which states that children only learn correct examples, and do not learn that "non-example" sentences are incorrect, since they are not exposed to incorrect sentences. In other types of learning, examples are paired with counterexamples to ensure full understanding of a concept. In addition, children do not receive feedback for their sentence usage in most cases, which contrasts most learning from parents or teachers, in which feedback is used to reinforce or correct behavior (Cowie 2008).

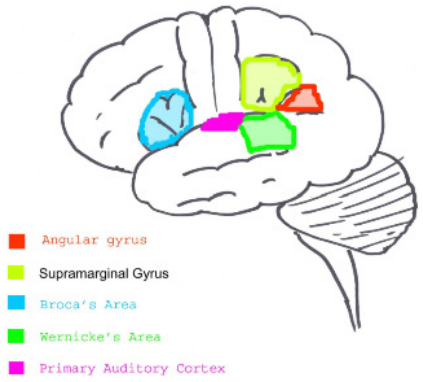

Figure 1: Chomsky's LAD theory corresponds with the localization of language skills in several brain regions, including Broca's and Wernicke's Areas.

Aside from cognitive factors, biological evidence supports the LAD hypothesis, since data suggests localization of language ability to certain regions of the brain. Broca's area is a section of the brain that is used for speech production. If this portion of the brain is impaired, then people are unable to utilize complex grammatical paterns. This indicates that Broca's area could contain a cognitive faculty for language development (Cowie 2008). All these observations indicate the validity of the LAD hypothesis.
Though B.F. Skinner's theory of cognitive development of

grammar because they can pick up on semantics and put information into the correct context. According to supporters of cognitive language development, children use innate perceptual and cognitive skills to learn language, but these skills are not language-specific, since they allow children to earn other interpersonal communication skills.

When children learn languages, their early linguistic abilities are constrained by their overall cognitive function. As a child increases their overall cognitive function, their language ability increases as well. Like the innate language theory, the cognitive language theory states that language learning ability increases from input data (Behme 2008). However, unlike the innate language theory, cognitive language theory states that children do receive negative evidence in language learning. If a child says a sentence that others do not understand, then the child will realize that their sentence does not make sense. In addition, if a child expects a certain grammar pattern but never hears it, they will realize that this pattern is probably incorrect. Parental feedback also shapes a child's linguistic ability. Demetras, Post, and Snow found that parents will repeat entire correct sentences from their child, but will not fully repeat incorrect ones. If they do repeat an incorrect sentence, they will say the correct version instead. Children are more likely to repeat their parent's corrections of incorrect sentences than to say the incorrect sentence again.

Figure 2: A mother reads to her child. As she reads sentences out loud, her daughter starts to pick up on patterns in the speech rhythms and grammar.

According to cognitive psychologists, cognitive development allows young children to learn complex grammar patterns because the development process starts early, even before birth. Fetuses can respond to sound at only 22 weeks old, and will postnatally recognize passages that were read to them while in the womb (Behme 2008). Newborn infants pick up on their own language more than other ones only a few days after birth. They are able to discriminate between languages with different rhythmic patterns, and can discriminate their own language from others after several months. Since this ability takes time to develop, it suggests that language learning is not innate in itself. Instead, it develops out of their innate auditory ability.

Studies have indicated that very young babies can learn patterns of speech, suggesting that the language learning process follows the same process of learning other things. Though young children learn language at an early age, it takes time for them to refine it and produce meaningful words. Children start by babbling in sounds from all languages, but narrow down to sounds from only their languages as they grow and mature. However, infants aren't necessarily corrected in their babbling, so the exact reason why theynarrow down is unclear. One explanation may be the exposure to their parents' grammar and speech patterns. This data can lead to their cognitive development of language. When parents speak to children, they use simpler grammar patterns that are easier for them to learn and comprehend. Researchers found that most of children's verbalizations are things they have previously said, suggesting that they practice these phrases to encode them in their brains. Just as cognitive linguistic ability is an application of auditory learning, it could also be an application of statistical learning. Statistical learning is a general ability that has been observed in other primates, not simply a separate, innate ability in humans. In a study done by Jenny Saffran, young children were able to sense the boundaries between words and the distribution of speech sounds (Behme 2008). They track that some words correspond to certain objects even before they know the meaning of the words, which would not have to occur if language learning was innate. Babies can also sense patterns in sounds that appear frequently at the beginning or the end of a word, which is another way for them to learn words.

However, the LAD theory is not without problems. It states that language is too complex for its syntax to be learned, but this research indicates that children can observe these differences through statistical information. Even young children pick up on patterns like verb endings that distinguish different parts of speech. Though this does not disprove the LAD theory, it does act against the poverty of stimulus argument.

Another theory of cognitive development, posed by John Macnamara, suggests that an infant learns meaning and language independently, and later combines them as they mature. Macnamara defines meaning as any idea that a person can express through language, while the language itself is a collection of rules and structures that are used to convey this meaning. Speech is a way to convey this meaning (MacNamara 1972). Language and meaning are almost always combined, but they are two separate ideas.For example, individuals with underdeveloped cognitive function are still able to use other cognitive facilities. Assigning words and objects is more complicated than one expects, since there are often

Figuer 3: A young boy plays with a toy truck. The boy knows that this is a "truck," but cannot recognize it as a "toy."

multiple words for objects, and it would be difficult to identify which word is being referenced. If an adult references a specific object by name directly, the infant will interpret this as the object's name. This also occurs even when the word is not the object name, but is used in the same context. For example, if a parent tells their child not to touch an object because "It's hot," the child will think the object is called "hot." After learning names of objects or other nouns, children tend to learn conditional attributes of an object, and finally, they learn permanent attributes. Children initially cannot discriminate between more and less descriptive words. For example, a child will know the word "truck," but will not recognize that his truck is also a "toy." However, he will also realize that a collection of toys are called "toys." He treats "toys" as a separate idea from his truck. Children learn more abstract words like "and" at a young age, suggesting that they need this word to give meaning to their thought processes. Many grammar patterns can express multiple ideas based on context, and many times, the same ideas can be expressed through multiple grammar patterns. Children can learn which patterns work in which contexts if they discover what the sentences mean independent of learning the grammar patterns.

Overall, there is compelling evidence for both the innate and cognitive theories of development. There is heavy evidence showing the development of linguistic ability through cognitive processes. Yet these processes do not disprove the existence of a language acquisition device. However, the poverty of stimulus argument does not prove its existence, either. Whether or not there is an innate language device in humans, it is clear that humans possess a remarkable ability to understand and produce complex grammar patterns and meaningful sentences.

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About Brain Matters & Meet the Editorial Board

The Undergraduate Neuroscience Society (UNS) is an academic student organization that strives to promote, educate, and hold events that help undergraduates gain a deeper understanding and appreciation for the field of neuroscience. The Neuroscience Journal Committee, a subsidiary of UNS, has created a journal entitled Brain Matters. This journal promotes a neuroscience dialogue on campus by publishing student research about topics ranging from neuroscience, psychology, and biology.

Fiza Bukhari
Chief Editor

Fiza is a sophmore majoring in Molecular and Cellular Biology on the pre-med track. In addition to her involvement in the Neuroscience Journal Committee, she communicates her Illinois experience by writing for the UIUC Admissions Blog. Just like her blog, she is thrilled to promote a neuroscience dialogue.

Laura Kilikevicius
Assistant-Chief Editor

Laura is a sophomore majoring in biology and hopes to one day move into work in genetics. She is thrilled to be working on "Brain Matters" and hopes to broaden the knowledge of current neuroscience research across campus. Outside of the journal, she is an orientation leader on campus and is a member of Catholic Illini.

Emerson Fister
Chief of Design/Editor

Emerson is a senior majoring in Psychology with a concentration in Behavioral Neuroscience and a minor in Integrative Biology. Outside of learning about Neuroscience, she is passionate about human-centered design and is an active member of the University of Illinois Design for America studio. She is delighted to collaborate and learn with the other students behind "Brain Matters".

Carolyn Oh
Editor

Carolyn is a sophomore majoring in Molecular and Cellular Biology and is currently conducting research in neurochemistry in Dr. Jonathan V. Sweedler's lab. Outside of academics, she is passionate about IlliniThon, the University of Illinois' Dance Marathon program that fundraises for St. John's Children's Hospital in Springfield, IL. She is excited to collaborate with the other students behind "Brain Matters" and promote brain awareness on campus.

Eva Cornman
Editor

Eva is a sophomore majoring in Molecular and Cellular Biology and minoring in Creative Writing. Aside from her passion for mental health and neuroscience awareness, she enjoys writing and dancing, and is a proud member of UIUC's Legend Dance Company. She is so excited to work with her fellow students to expand our campus's appreciation for neuroscience through Brain Matters!

Meet the Writers

Thomas Romanchek
Writer
Thomas is a junior double majoring in Bioengineering and Psychology and does research with the Cellular Neuroscience Imaging Lab on campus. He is an editor for IJOIS and an active member of the Beckman Journal Club, two experiences which inspired him to start this journal. He is very excited to introduce "Brain Matters" to the UIUC community and hopes to broaden undergraduate interest in neuroscience and other brain topics.

Julia Gainski
writer
Julia Gainski is a sophomore majoring in Integrative Biology with a minor in German. During the school year, she works as a personal assistant for students with physical disabilities. She is a part of the Illini Club Tennis team and the secretary and a mentor of the Pre-Physician Assistant Club. She also works as a research assistant in the Carla Cáceres Lab on campus. She is very excited to have her first article published in Brain Matters!

Chloe Kim
Writer
Chloe (Chaeyeon) Kim graduated U of I in 2019 with B.S. in chemical engineering and minor in psychology. She worked as an undergraduate researcher in Kong Lab from 2016 to 2018 to develop her interest in clinical neuroscience research. She looks forward to sharing interesting topics in the field of neuroscience through Brain Matters.

Briana Sobecks
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Activities: American Chemical Society, Newman Center Choir, Campus Honors Student Council