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Role of Structural and Functional Whole-Brain Imaging in the Assessment of Preterm Infants

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ABSTRACT

Approximately one in ten infants are born preterm, with each bearing some form of underdevelopment, ranging from behavioral problems to muscular disorders. These developmental issues can lead to increased healthcare costs, permanent injury, and even death. However, with the growth of whole-brain imaging, scientists have found new ways to study premature infants. Leading this overlapping of fields are magnetic resonance imaging (MRI), functional MRI (fMRI), diffusion MRI (dMRI), electroencephalography (EEG), and magnetoencephalography (MEG). These technologies give insight into a premature infant's disposition to lower brain mass, suboptimal learning, and neuropathological lesions. Although every technique has flaws, whether it be in its spatial or temporal resolution or just fundamental limits, each has its own unique benefits. In this paper, we will observe how different techniques are used to study the neurological health of premature infants.

1. Introducing the problem: Preterm Birth

Healthy birth usually takes place after 40 weeks of pregnancy[1]. However, more than 1 in 10 pregnancies results in preterm birth (PTB) – a birth that occurs before the 37th week of pregnancy. Scientists categorize PTB into four types: late preterm (born between 34 and 36 weeks), moderate preterm (born between 32 and 34 weeks), very preterm (born between 26 and 32 weeks), and extreme preterm (born before or at 25 weeks). The brain, arguably the most complex and important organ, gets less time to develop during PTB, leading to long-term neurological defects and even death. To address how the brain is analyzed in preterm infants using certain techniques, we must first cover the fundamentals of PTB: its causes, complications, and importance regarding neurological health.

PTB is a complex subject that stems from a multitude of causes and leads to numerous issues, but although it cannot be tied to a single source, scientists can utilize past research to explain certain contributing factors as well as the specific mechanisms of injury in premature born infants[2]. There are 2 main factors associated with PTB: general poor maternal health and direct damage to fetal development.

The relationship between poor maternal health and PTB is simple: when the mother's health is negatively affected, the body's limited resources must focus on repairing damage rather than developing the fetus, causing delivery to occur too soon. Poor maternal health is linked with harmful behaviors, such as smoking tobacco, drinking alcohol, illicit drug use, and malnutrition[3–6]. Usually, such behaviors occur in tandem and create heavy stress on the body, making physical injuries and disease more likely and further exacerbating poor health.

Although poor maternal health certainly increases the chances of PTB and is of much concern, disease and damage to the fetus is much more likely to create an immediate effect[7]. One in four cases of PTB involve some kind of microbial or viral inflammation to the amniotic/decidual lining, the main boundary between the mother's viscera and the fetal environment[8]. From an evolutionary perspective, dispelling infected tissue through delivery is an effective way to preserve maternal health and increase future reproductive success; at the same, this mechanism leads to premature delivery and compromises infant health. However, bleeding in the amniotic/decidual lining is much more pernicious because major uterine blood loss can draw vital nutrients away from both the fetus and the mother. To combat the internal bleeding, the immune system releases thrombin, an anticoagulant. Although it is helpful in preserving

blood supply, it can start inducing muscular contractions that, just like during an infection, can push the fetus out too early[7]. Another important factor in PTB is that the immune system recognizes the fetus as a foreign body. If the immune system does not suppress during pregnancy, its tolerance will fall and may consider the fetus as a threat, causing T cells to induce apoptosis in fetal cells and provoke myometrial contractions to push the fetus out[9].

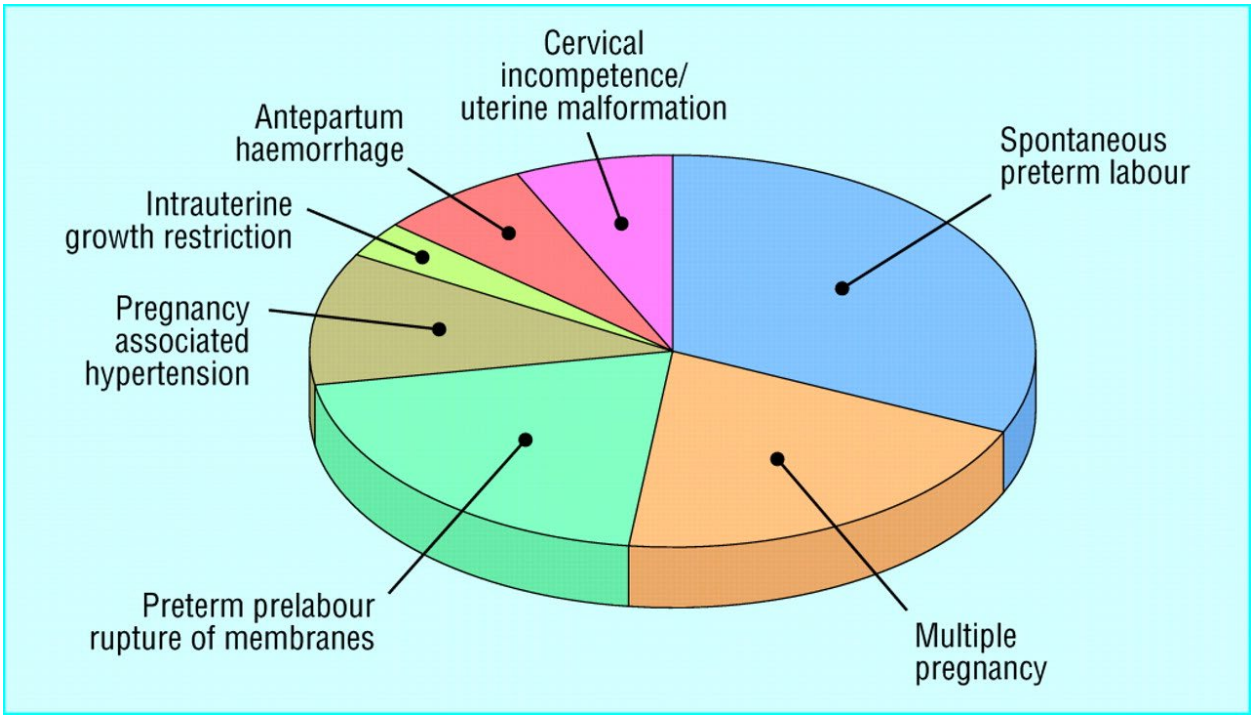

Figure 1[10] Pie-chart showing relative proportions for different causes of premature birth

This pie-chart model depicts the relative proportions of the different causes of PTB birth. Antepartum hemorrhage involves bleeding in the fetal wall; rupture of membranes involves the breakdown of the amniotic/decidual lining usually due to infection; maternal hypertension (unhealth blood pressure) and intrauterine growth restriction (decreased weight of an infant) are associated with poor behaviors, especially smoking. Multiple pregnancy involves the carrying of more than one baby at one time (twins, triplets, etc.) and leads to premature birth because nutrients are taken up faster than can be supplied.

2. Involvement of neuroimaging techniques in the assessment of premature birth

With so many potential causes, PTB has a very high chance of harming an infant, and the brain, as the most complex and fragile organ in the body, is at great risk of major irreversible damage. However, determining the mechanisms by which PTB affects neurological health can assist clinicians in preventing PTB-induced brain damage. To examine such injuries, scientists use certain neuroimaging techniques to address important changes in brain structure, activity, and health. In this paper, we will discuss how certain whole-brain imaging techniques (MRI, fMRI, dMRI, EEG, MEG) are used to analyze the premature brain.

2.1 Magnetic Resonance Imaging

Magnetic resonance imaging focuses on the phases of hydrogen protons, which are notable for the widespread presence in the body (water, fats, proteins, etc.)[11]. These protons have two directions, north and south (can be visualized as up and down) and precess along an axis. At rest, these protons precess randomly, but when the MRI machine inputs a magnetic field that matches or is a multiple of the Larmor frequency of a hydrogen proton (1 tesla/42.58 MHz), the hydrogen protons will start precessing around that field. Most protons will line up in the same direction as the MRI's magnetic field, but others in a high-energy state will line up in the exact opposite direction. Because most of the protons are in a low-energy state, they will create a strong magnetic field, deemed longitudinal magnetization, that aligns with the MRI's main magnetic field. However, when a radiofrequency (RF) pulse is emitted by the machine, some protons absorb the pulse and transition into a high-energy state, thereby lowering the longitudinal magnetization. At the same time, this RF pulse also makes every proton line up in phase, which creates a new magnetic field – the transverse magnetization – that is perpendicular to both the longitudinal magnetization and the MRI's main magnetic field. When the RF pulse is taken away, the protons start to repel and move out of phase, causing the transverse magnetization to diminish; this process is called T2 relaxation. Simultaneously, many high-energy protons fall back to a low-energy state, thereby regrowing the longitudinal magnetization back to its original state of lining up with the MRI's main magnetic field; this process is called the T1 relaxation. In the final image, different parts of the brain can be contrasted based on these types of relaxations. For example, when the RF pulse is taken away from an area with fat molecules, which have hydrogen protons fixed in place, the hydrogen protons quickly repel (causing a rapid T2 relaxation), and high-energy protons quickly return to a low-energy state (causing a rapid T1 relaxation). At any given moment, an MRI image will show a relatively strong longitudinal magnetization and weak transverse magnetization. On the other hand, when a RF pulse is taken away from an area with many water molecules, which have protons moving freely in space, the hydrogen ions repel slowly (causing a slow T2 relaxation), and high-energy protons will slowly return to a low-energy state (causing a slow T1 relaxation). The MRI image will show a relatively weak longitudinal magnetization and strong transverse magnetization. An image that shows the varying strengths of longitudinal magnetizations in different areas is called a T1-weighted image, while those showing the strengths of transverse magnetizations are called T2-weighted images.

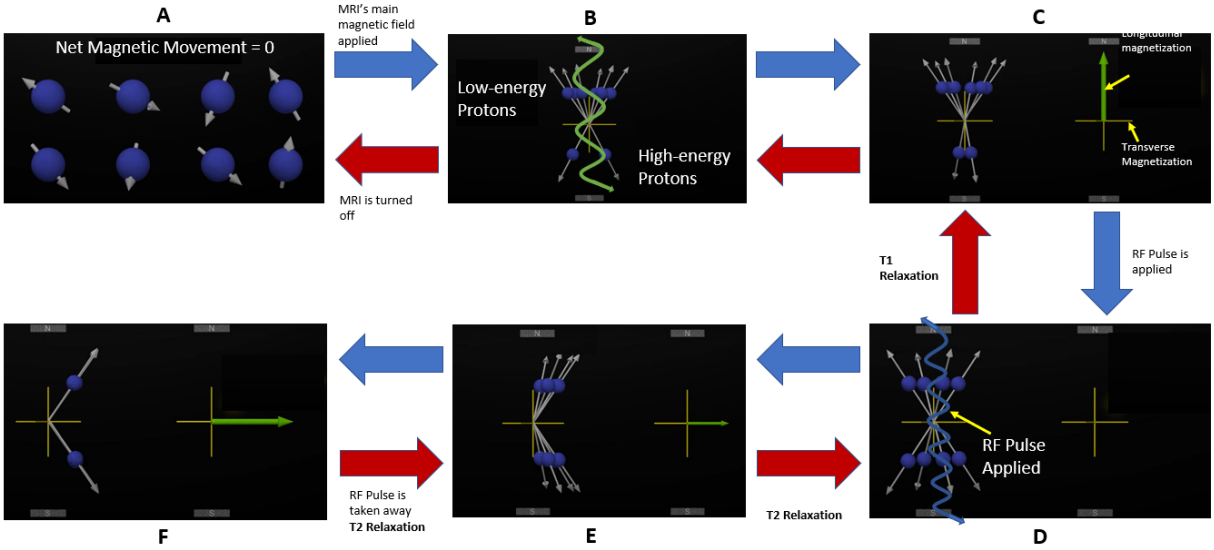

Figure 2[12] MRI Signaling process

A represents the random phases protons are in. **B** shows how these protons line up with the MRI's main magnetic field when the machine is turned on – those in a high-energy state will face directly opposite of the field (assume this

main magnetic field is always on for stages **B-F**). **C** shows how these protons lining up on a single axis create a new magnetic field, called longitudinal magnetization. **D** shows how low-energy protons shift into a high-energy state when an RF pulse is applied, thereby decreasing the longitudinal magnetization. E shows how the RF pulse also causes protons to get in-phase, which increases the transverse magnetization. Eventually, the environment will reach a state like that shown in **F**, with an equal number of protons (all of which are in-phase) in a high-energy state and a low-energy state. For imaging, the RF pulse is taken away, as shown by the red arrows going from **F** to **C**. T2-weighted images measure the transverse magnetization as the protons move out of phase, whereas T1-weighted images measure the longitudinal magnetization as the protons go back to a low-energy state. Typically, scientists will cycle through Stage **C** to **F** in order to get multiple images; the protons will only reach their original state, as seen in **A**, when the MRI machine and its main magnetic field is turned off.

When examining the effects of PTB on the brain, physicians can use an MRI to compare a premature infant's brain to that of a healthy infant, and any major structural differences can indicate which region has been harmed and help clinicians identify the areas more prone to damage[13]. The physical parts of the brain can be analyzed by MRI in 2 sections: the gray matter (which is composed of the cell bodies of neurons and makes up most of the surface of the brain) and the white matter (which is composed of the axonal appendages of neurons and makes up most of the interior of the brain).

Most PTB-induced white matter damage involves structural mishaps around the brain's ventricles, cavities that are filled with cerebrospinal fluid and located in the center of the brain[14]. Such damage is called Periventricular white matter (PVWM) damage. In preterm infants, the arteries tend to be too underdeveloped in the PVWM to provide adequate amounts of blood and oxygen[15]. The cells most affected by this hypoxia are oligodendrocytes, cells vital for axonal myelination and neuronal communication. The other contributing factor to PVWM damage is infection, which is heavily associated with PTB. Along with toxins produced by bacteria and viruses, the immune system's production of cytokine proteins can make blood flow unstable and create a dearth of nutrients for the PVWM[16]. These 2 main causes of PVWM damage create two types of sequelae: cystic and diffuse[14–20]. Cystic brain injury, also called periventricular leukomalacia, involves the formation of cysts and scars, lesions that can readily be assessed by MRI based on the site of the scarred tissue and the volume of the ventricles[16,21]. Diffuse damage, on the other hand, is characterized by a diminished number of oligodendrocytes and is typically seen as high intensity points on T1-weighted imaging. In very serious cases, PVWM damage can extend into the ventricles, the most common type of injury being Intraventricular hemorrhaging (IVH)[16]. If the IVH is very subtle, the best device to detect the damage would be through MRI, and the patient would need to receive immediate medical attention to stop the bleeding.

Although white matter analysis involves more urgent injuries, grey matter, which is necessary for almost all daily functions, should still undergo examination to help clinicians identify what areas are underdeveloped. Of course, the main observation under MRI is smaller cortical grey matter volume. However, certain areas tend to be more underdeveloped than others: the inferior occipital, sensorimotor, and parieto-occipital regions show markedly reduced volumes[22,23]. Such findings can help explain why motor function is impaired in preterm infants, as these areas are heavily involved in proper muscular control.

Ultimately, MRI is a very important tool for analyzing the brain of preterm infants, and certain forms of magnetic resonance technology can offer even more information regarding areas of interest. One variation is functional MRI (fMRI), which examines the activity of different brain regions. The next section will go in detail as to how fMRI operates and its role in analyzing PTB.

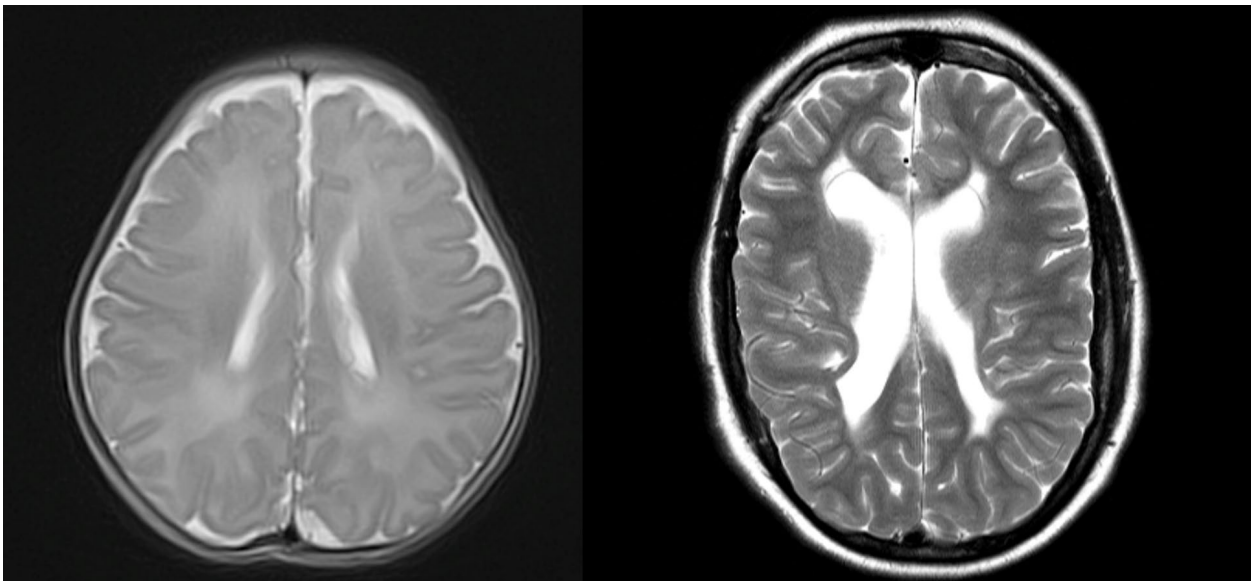

Figure 3[24] Health (left) vs Unhealthy premature brain (right)

The MRI image on the left shows the ventricles of a term-born, healthy infant. The image on the right shows the clear enlargement of the ventricles in a preterm-born infant, most likely due to periventricular leukomalacia (cystic PVWM damage).

2.2 Functional Magnetic Resonance Imaging

FMRI involves many of the same principles as MRI, yet it analyzes brain activity by focusing on the oxygen levels of blood in different regions[25]. When a neuron fires, surrounding blood vessels are forced dilate to supply adequate oxygen, as the brain has no close storage of nutrients. This oxygen is carried in the blood by the protein hemoglobin, which is read just like hydrogen protons on an MRI. Hemoglobin with oxygen has no immediate effect on the MRI's main magnetic field, while deoxygenated hemoglobin will create its own magnetic field that will destroy the main MRI field. As a result, oxygenated areas will appear stronger on T2-weighted imaging compared to deoxygenated areas. One drawback of fMRI, however, is its poor temporal resolution. Because it takes a lot of time for enough blood to move around an active area and create a significant signal, there is a strong delay that clinicians must consider when examining fMRI data. However, fMRI still provides very valuable insight into the brains of preterm infants since it allows scientists to examine how the brain processes information.

FMRI's ability to analyze brain activity makes it incredibly useful for physiological imaging when examining PTB's effect on the brain, and scientists will examine the premature brain in two ways: while the infant is performing a task (task-based fMRI or tb-fMRI) or while the infants is at rest (resting-based fMRI or rs-fMRI)[26]. Clinicians can use such variations to study multiple aspects of the brain, including cognition, emotional processing, and connectivity.

Based on tb-fMRI, preterm infants, when compared to term born controls, tend to use different regions of the brain whilst performing complex tasks; this change in the brain activity has a clear link with PTB, as the brain has less time to develop and therefore must adapt and change its functional structure (the core principle of neuroplasticity)[27,28]. In addition, brain suppression, which indicates the retaining of information, occurs at a relatively slow rate in preterm infants despite repeated stimuli, which explains why PTB impairs an infant's ability to improve at a task and learn[29,30]. Such regional brain suppression is associated with certain areas (cortex, temporal lobe, cerebellum) and certain activities (verbal fluency, motor planning, physical execution)[31,32].

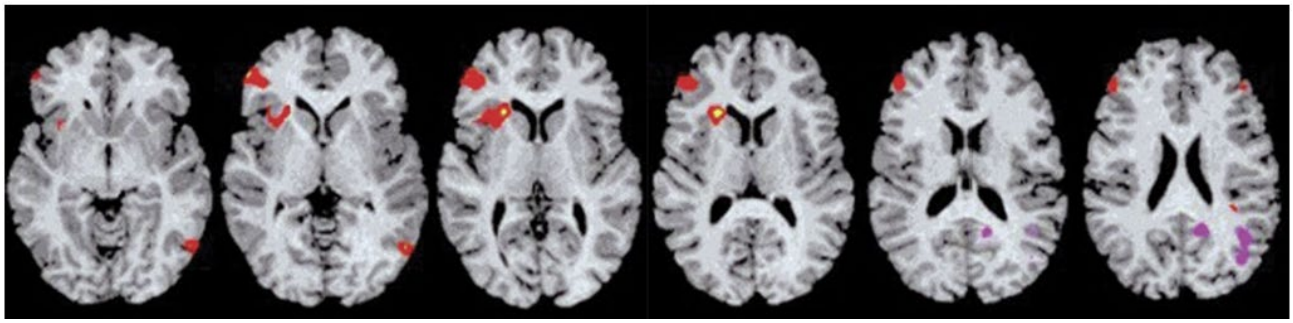

Figure 4[33]**.** Functional-MRI readings of PTB brain: Damaged/underdeveloped regions shown in red

Each image highlights the differences between preterm infants and term-born infants when given a semantic task (tb-fMRI). Areas of red and yellow show regions of the brain that were activated only by preterm infants. Throughout each image, it is clear there is a right frontal shift of activity, which indicates changes in the brain's language network. However, the changes in networks are not as defined as in rs-fMRI readings.

RS-fMRI tends to be easily applicable when analyzing preterm infants because of the physical and mental limitations, and although it does not allow for task-based experiments, rs-fMRI and its high spatial resolution make it incredibly useful for examining resting state networks, the functional connections that occur involuntarily between different regions of the brain[34,35]. Because the brain is a very complicated neural system of constantly interacting parts, analyzing different networks helps identify the specific parts of the brain responsible for impairment associated with PTB[35–39]. For example, the amygdala in preterm infants, the region responsible for emotional information processing, has been shown to have abnormally poor connectivity with the cingulate cortex and precuneus, resulting in poor emotional cognition and behavior. Similar kinds of PTB-induced disconnectivity can be found in areas responsible for attention, language ability, and behavioral outcome. It is important to note that network analyzation can also be applied when using tb-fMRI, as seen in FIG fMRI2.

Ultimately, fMRI's use of blood-flow analyzation to examine brain activity as well as its excellent spatial resolution makes it incredibly useful for observing not only how the brain is activated in different ways when performing a task but also the changes in fundamental brain networks. The next section, covering dMRI, will focus solely on the aspect of neural connectivity and its involvement with preterm birth.

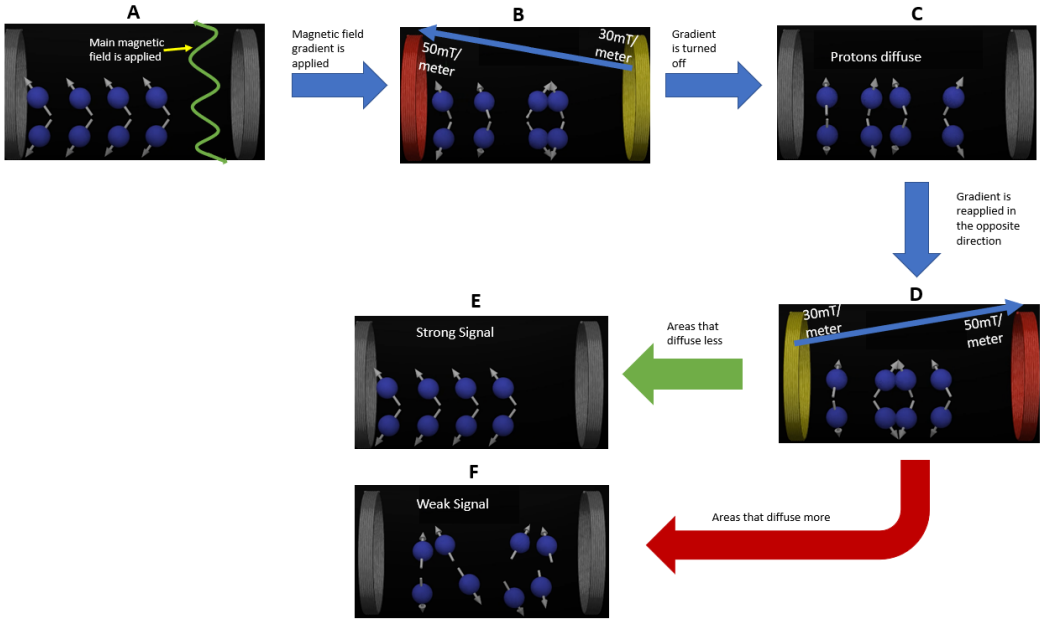

Figure 5.[36] DMRI signaling process

A shows the dMRI's main magnetic field lining up every proton, just like in MRI. **B** shows a magnetic gradient (like an MRI's RF pulse) being applied, with the left side having a stronger force than the right. **C** shows this gradient being taken away, allowing the protons to diffuse. Then, as seen in **D**, the gradient is reapplied but in the opposite direction. If the protons did not diffuse much, they would line up, and their signal would be strong, as shown in E; however, if they did diffuse significantly, their signal would be weak, as seen in F.

2.3 Diffusion Magnetic Resonance Imaging

DMRI is based on magnetic resonance technology, but rather than analyzing just the phases of protons, it examines how hydrogen atoms diffuse[36]. Like MRI, the process begins with hydrogen protons lining up with a longitudinal main magnetic field. Another magnetic field is applied across the transverse axis, but incorporates a gradient, where the power of the magnetic field changes linearly in one direction. This field is taken away and then reapplied but in the opposite direction – in the time where no field is applied, the protons can diffuse and grow out of phase. In areas of restrictive diffusion, the end signal of the hydrogen protons will be strong, whereas in areas of low diffusion, the end signal will be weak.

DMRI most commonly focuses on water molecules, which incorporate hydrogen protons and diffuse continuously in the brain through axons - the neural cell body extensions that make up the white matter. Such data can give very valuable clinical insight and be used in two ways when examining the premature brain: detecting white matter tract damage or analyzing the neural connectome[13,26].

Scientists can interpret neurological health based on dMRI readings of axonal fibers - in many preterm infants, small changes in important fibers are found throughout the brain, giving insight into poor structural development[38–40]. On top of microstructural changes, fluid movement readings can also reveal the lack of vital components: typically, certain developmental changes like axonal thickening or oligodendrocyte wrapping create a barrier for diffusion, making the flow stronger and the directionality sharper[15]. However, if such development is impaired, these natural barriers will not be formed and manifest on dMRI as weak diffusivity, leading not only to uncontrolled fluid movement but poor development in general[41].

One of the biggest uses of DMRI in the study of PTB is its ability to create a brain connectome, a mapping of neural connections that reveals how certain areas, despite having distinct functions, are heavily linked. The entire system is broken down into nodes and their interactions, with higher-level nodes responsible for connecting large regions and lower-level nodes responsible for more specialized tasks[42]. PTB has been shown to poorly influence the connectome's network efficiency, which explains why the ability for preterm infants to incorporate and use information is impaired[43]. This issue can be tied to the brain's natural development of neural connectivity: during the last trimester, many important high-level rich-club nodes start forming and are heavily prioritized. PTB, however, cuts this developmental stage short and can cause permanent brain network damage.

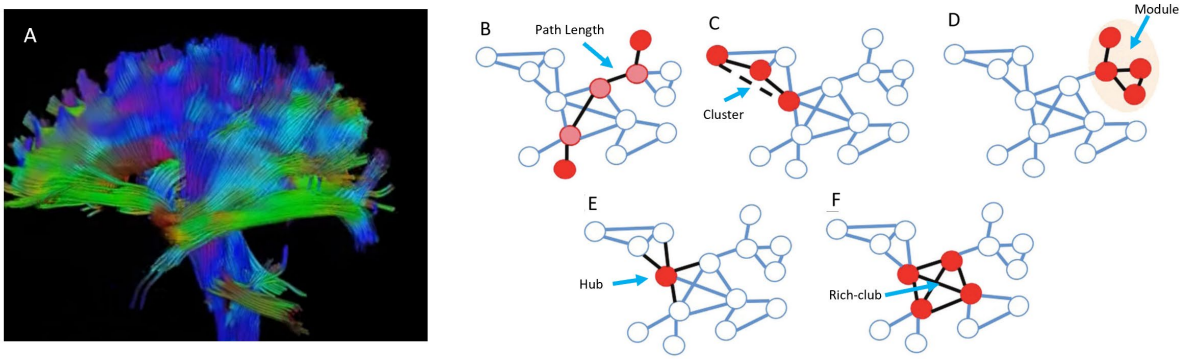

Figure 6. [26,37] Connectome visualization and denotations

A shows how dMRI readings can create a connectome, a map of the brain's neural connections based on axonal fibers. **B-F** shows how different regions can each be simplified into nodes (graph theory). **B** represents the path-length between different regions. **C** shows how nodes with short path lengths cluster with one another. In preterm infants, path length between regions tends to be longer and clustering decreases, causing communication to be slower. **D** shows modularity, with modules making up their own subnetwork – if modularity is too high, large regions communicate with each other poorly, but if modularity is too low, clustered nodes interact slowly. **E** shows a hub, which acts as the only nodal connection between a large module and the rest of the brain. **F** shows the rich-club, a centralized area where nodes meet up and connect many parts of the brain. When the rich-club hubs are damaged, important actions involving many regions of the brain are at risk of dysfunctionality.

2.4 Electroencephalography

EEG find which regions of the brain are active and to what extent by analyzing the electrical signals of neurons[44]. When a neuron fires, there is a rush of negatively charged particles that move across the axons. When the end of the neuron is negatively charged enough, it will release neurotransmitters that activate another neuron, which fires and repeats the process. By attaching electrodes tangentially onto a subject's scalp, scientists can compare brain activity coming from different parts of the brain. Typically, these neural signals are categorized based on rhythmic frequency and properties: Gamma (30-90 Hz) correlates with sensory integration, Beta (15-30 Hz) correlates with alertness, Alpha (8-13 Hz) correlates with waking states, Theta (4-8 Hz) correlates with sleeping and waking states, and Delta (less than 4Hz) correlates with deep sleep. This method does have poor spatial resolution: only electrical signals that hit the electrode perpendicularly are detectable and they tend to be diminished by the natural barriers (skull, scalp, etc.). However, EEG does have very high temporal resolution unlike Resonance Imaging, as electrical signals are readily apparent after neural activation.

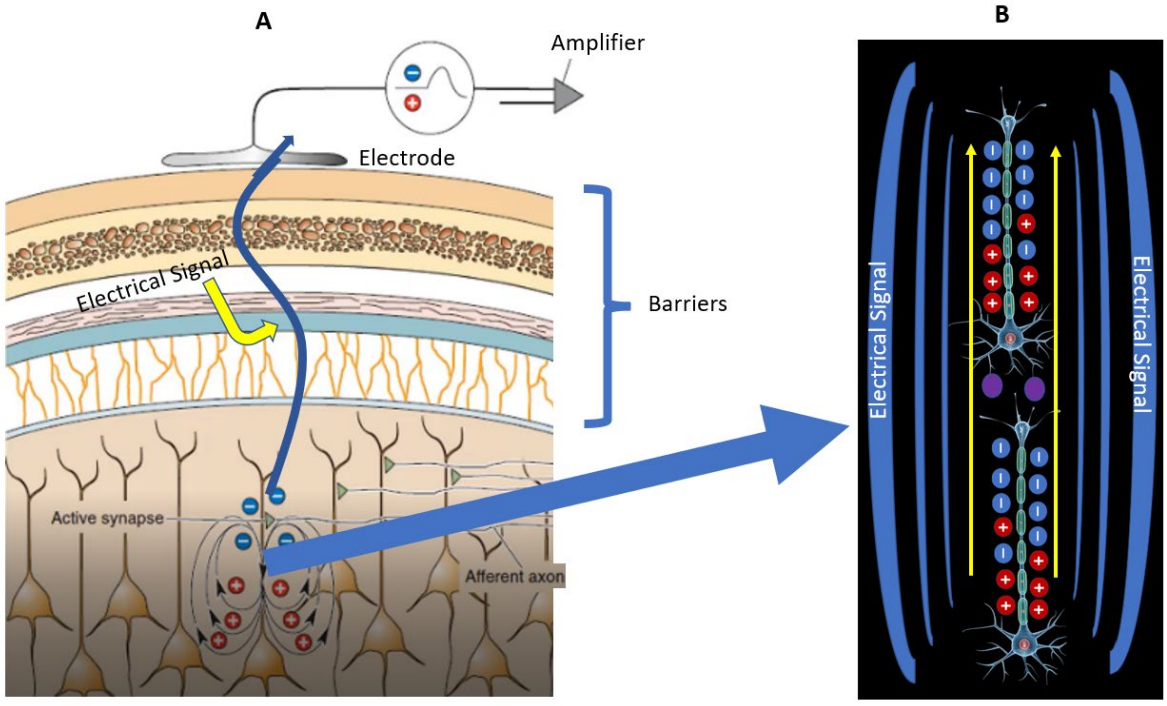

Figure 7. Electrical signal passing through neuron and head

As seen in **B,** when a neuron fires, anions move across the axon extension, forcing the release of neurotransmitters that diffuse and activate the adjacent neuron. As seen in **A**, this neural cascade creates a negatively charged field that, when strong enough to penetrate the body's natural barriers, reaches the electrode that then outputs the signal for scientists to read. It is important to note that these signals can only be detected if they hit the electrode perpendicularly.

By analyzing voltage signals in different regions of the brain through the noninvasive, undemanding attachment of electrodes, EEG helps scientists deduce certain patterns and types of harm that occur in the preterm brain[45]. There are two characteristics of brain abnormality that can be readily assessed with EEG: the level of damage and time of injury.

Brain damage can be split into two types: acute and chronic. Brain damage can be split into two groups: acute and chronic. Acute damage is characterized by sudden injury and can be detected by 3 types of atypical EEG readings: discontinuity, frequency, and voltage. Discontinuity refers to gaps between wave patterns, frequency refers to the prevalence of different types of waves (not rhythmic frequency), and voltage refers to the amplitude of certain waves. More discontinuity, lower frequency of alpha and theta waves, and lower neuron-signaling voltage all stem from abnormal acute damage[46,47]. Chronic damage will usually follow acute damage and leads to long term brain damage, which, in some cases, is irreversible. A very common sign of chronic damage on EEG is dysmaturity, readings that would typically be found on younger infants[48]. Such findings are nearly always associated with white matter brain damage and neurological disorders.

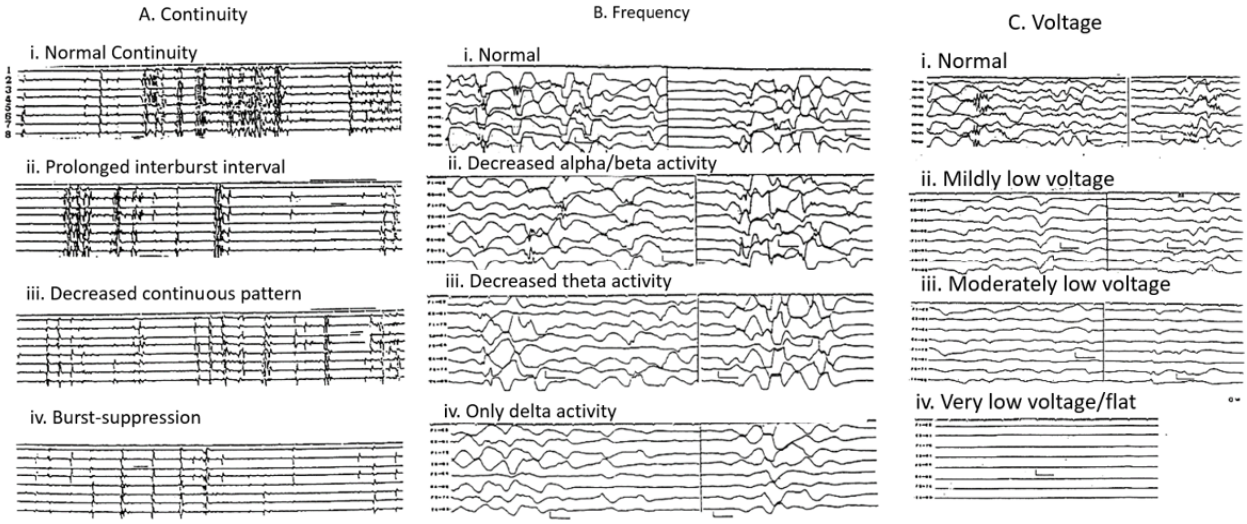

Figure 8. EEG results of damaged PTB brain[45]

Each column represents the variables involved in brain damage when using EEG: Continuity, Wave frequency (types of waves), and Voltage. The lower levels of each column represent increasing severity of injury[49,50].

2.5 Magnetoencephalography

Magnetoencephalography analyzes, as implied by the name, magnetic signals instead of electrical signals[51]. However, it still relies on action potentials of firing neurons since the electrical fields produce a corresponding magnetic field that, instead of being oriented parallel to the axon, is oriented perpendicularly to the axon. The MEG machine's receptors, which are raised above the scalp to detect magnetic signals, still need to be parallel to the scalp for the same noninvasiveness as the EEG, axons facing perpendicular to the cortex send a detectable signal. The main advantage of MEG is that it has the same temporal resolution as EEG, but the magnetic signals are not by natural obstacles (hair,

scalp, skull, etc.), giving much better spatial resolution and more information on specific neural networks. Ultimately, MEG can help clinicians understand more about PTB by analyzing spatially accurate neural signals, thereby giving insight into the changes in functional connectivity.

MEG's neural network analyzation is like that of rs-fMRIs and dMRI but involves the waves examined with EEG (alpha, beta, theta, delta, and gamma). MEG evaluates the connectivity between regions by examining neural synchrony – the synchrony established when many neurons' electrical signals start oscillating in phase (i.e., if two different regions start oscillating in phase, they are said to be connected). There are 2 main types of network activities that are impaired by PTB: the thalamocortical interactions and cognitive/memory control.

The thalamus is a section of the brain that acts as a transfer station: it takes information from throughout the brain and moves it to different areas, like a rich-club node. A very important section of the brain the thalamus interacts with is the cortex; such interactions are called thalamocortical interactions and play a major role in many networks throughout the brain. For example, under healthy conditions, both the thalamus-cortex region and the region encompassing the limbic system both produce theta oscillation. Thalamocortical interactions also influence the basal ganglia through gamma-based synchrony: the entire structure is called the cortico-basal ganglia-thalamo-cortical loop and is important for allowing cognitive, sensorimotor, and goal-based processes to occur simultaneously[52]. If PTB damages any involved region, these processes and network systems become erratic and possibly lead to the loss of many important functions.

Cognitive control involves many systems but is tied heavily to two main networks: the frontoparietal network (FPN) and the cingulo-opercular network (CON) (Title). These 2 networks are involved in cognition through perceptual binding – the process of turning packs of information into logical rendering[53,54]. Regions such as the dorsolateral prefrontal cortex, which is responsible for processing of goals, the insula, which communicates with other regions and processes important information, and the anterior cingulate, which helps in outcome monitoring, are all involved in the FPN and CON networks based on MEG recording. With so many areas involved in basic cognition, PTB can easily impair the entire system and damage brain processing.

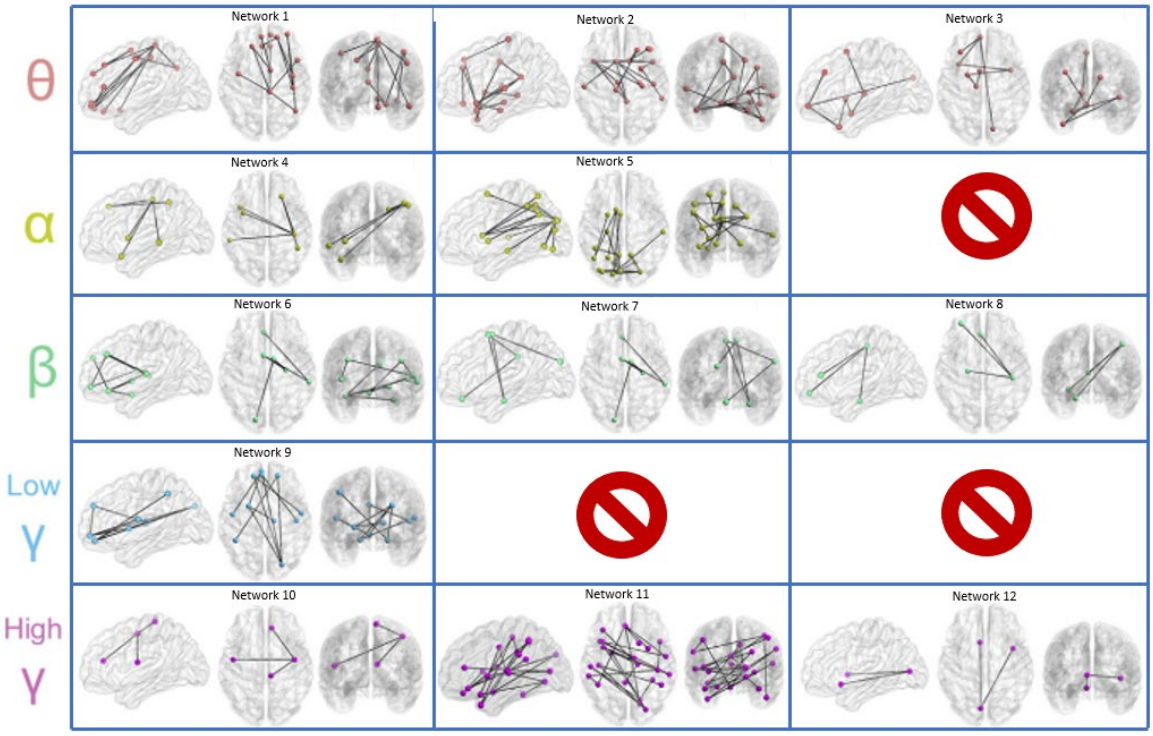

Figure 9. Damage-prone *c*ommunication networks

Each dot and edge-line represent areas of decreased connectivity in relation to the analyzed wave. As connectivity decreases, communication and processing becomes slower and less efficient.

3. Discussion

3.1 Technique comparisons

Although we have discussed the intricacies of each technique, understanding the different applications is vital for proper use. With such a variety of cases possible involving the analysis of the preterm brain, whether it be a life-or-death emergency or an extensive experimental research project, even small advantages in certain techniques can provide groundbreaking insight. There are multiple metrics by which scientists rate neuroimaging techniques to deduce what moment calls for a specific method: temporal resolution, spatial resolution, structural analysis, and functional connectivity.

Temporal resolution refers to the amount of time required for a certain technique to acquire the data needed to create an image. Lower temporal resolution typically indicates that a given technique requires a relatively long time to produce analyzable images, making them poor choices for emergency care. All types of magnetic resonance imaging have relatively slow temporal resolution, with fMRI being one of the poorest – the delay between brain activity and an associated hemodynamic response takes nearly 9 seconds. Encephalography, on the other hand, can transmit data in the realm of milliseconds.

The spatial resolution of a certain technique depends on the amount of information conveyed in a single image pixel, just like rendering quality of digital art or videos. Ultimately, spatial resolution can indirectly tell scientists how well a certain technique can decipher structural deformities in the preterm infant brain. DMRI and MRI have poor spatial resolution whereas fMRI, EEG, and MEG can reveal structures that are just millimeters apart. More accurate spatial resolution is especially useful in analyzing incredibly subtle deformities around the ventricular areas that form due to PTB.

A neuroimaging technique can be classified as structural (able to reveal anatomical structures) or functional (able to image physiological activities). Functional techniques can provide structural data, but techniques that are solely structural, like MRI, can only record brain anatomy. Because so many neurological actions are dictated by connections between different brain regions, there are a multitude of functional neuroimaging techniques (fMRI, dMRI, EEG, MEG) used to analyze such activities in the brain of preterm infants. Typically, proper practice will start with an MRI test to study a mental misbehavior in a preterm infant, and if clinicians cannot deduce a discernible cause, a functional technique is then ordered.

Although it seems that certain techniques seem superior, other facts must be considered, especially physical limitations and costs. FMRI, with advanced spatial resolution, or MEG, known for having incredible temporal and spatial resolution, seem to be the best approach to studying PTB; however, these techniques come with major financial costs: a single MEG or fMRI machine can cost millions of dollars, making testing very expensive. EEG or MRI systems, on the other hand, can cost less than $100,000. Of course, infants, especially those born prematurely, may suffer from disabilities preventing them from staying still for long periods of time, making immobilizing techniques like MRI or MEG unusable. Ultimately, it is the job of the leading physicians or researchers to deduce what technique is most reasonable for different cases.

3.2 Future applications

With preterm birth becoming ever more common in nations - even as they develop - infants must sustain serious injuries, many of which affect the brain. Because the brain is, of course, incredibly delicate, non-invasive techniques are the only way of analyzing neural damage that occurs due to PTB. Although there are several possible techniques

that analyze the brain, complex cases typically call for more advanced methods of study, particularly Resonance Imaging (MRI, fMRI, dMRI) and Encephalography (EEG, MEG). Ultimately, if the scientific community is to ever take the next step towards addressing the effects of premature birth, understanding not only how such neuroimaging techniques work but also how they are used to specifically study the PTB brain will only become more necessary.

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