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Neuroscience

Review of Emerging and Existing Neurodiagnostic Technologies

Introduction

As the world's population ages, the prevalence of neurological disorders and the need for preserving brain health are on the rise. However, the current tools and methodologies available to front-line physicians and neurologists are limited, lacking accessible and sensitive solutions for early detection and differential diagnosis. This limitation hampers the effectiveness and accuracy of treatments. It is well established that early and precise diagnostic capabilities are crucial for achieving optimal treatment outcomes and quality, particularly in the field of neurology. As a result, focus and resources are being directed towards developing new, informative, and accessible tools for early and accurate diagnosis.

This report reviews existing and emerging technologies in brain health and neuro-diagnosis from a holistic perspective.

Neurodiagnostic methodologies and tools can be divided into three major categories which attempt to deal with different aspects of the most complex organ in our body, the brain. These tools are applied separately and are often combined to provide more comprehensive information.

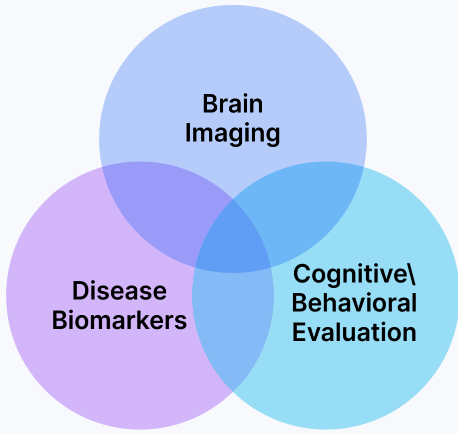

Figure 1: Neurodiagnostic methodologies and tools, 3 major classes.

Brain Imaging Technologies

Brain imaging technologies play a pivotal role in the diagnostic process and comprehension of brain diseases. Since the brain is an electrically functional organ, it is essential to image both its structure and activity to gain a complete understanding of disease status. Brain imaging tools encompass a range of technologies that can be categorized into two main subcategories: structural and functional imaging.

Structural imaging includes CT (computerized tomography) and MRI (magnetic resonance imaging). CT scans utilize X-ray technology and are commonly used to visualize brain structure in various neurological conditions such as stroke and brain tumors. MRI scans provide non-radiative and high-resolution images, making them valuable for detecting structural abnormalities and aiding in neuro-diagnosis. Both CT and MRI can incorporate the use of radioactive biomarkers, such as Pittsburgh amyloid CT (for Alzheimer's disease diagnosis), to target specific materials in the brain. While CT and MRI are widely used neurodiagnostic tools known for their objectivity and visual representation of the brain, their greatest limitation remains the fact that they provide only limited structural information. A fairly new advanced technology utilized in brain imaging is Diffusion Tensor Imaging (DTI), an MRI-based approach that measures the diffusion of water molecules in brain tissues. It provides information about the structural connectivity of white matter pathways in the brain, aiding in the study of brain development, connectivity changes in neurological disorders, and mapping neural networks. This technology is mostly used for research and is rarely used in the clinical setting.

Most innovations in this field focus on three main areas of improvement. The first involves the development of small and portable CT and MRI devices, aiming to make these technologies more accessible. The second area revolves around enhancing diagnostic capabilities through AI-based algorithms. Lastly, there is an emphasis on disease diagnosis using specific imaging brain biomarkers, aiming to enhance diagnostic specificity. Yet, these innovations remain constrained by the technological limitations that solely offer structural information.

Functional imaging incorporates various technologies and is a rapidly evolving field due to the significance of objective measurements of brain network function. The brain is an electrically functional organ, and in order to fully evaluate its health and wellness, a functional imaging and diagnosis tool is required. However, developing such a technology has proven to be extremely difficult given the constraints of safety, efficacy, and clinical everyday use. Functional brain imaging involves the direct or indirect measurement of brain function.

Indirect functional brain imaging tools include functional MRI (fMRI) and PET (positron emission tomography) scans, which assess brain blood flow or energy consumption/metabolism. These methods provide insights into the activation of specific brain areas but offer indirect information about brain function and health. They may also involve invasive and radiative materials. Both fMRI and PET are considered expensive and inaccessible, with fMRI primarily used for research purposes and PET employed when a specific brain disease is suspected. New technologies in this field include fNIRS and FUS. fNIRS is a non-invasive imaging method that uses near-infrared (NIR) light to estimate hemodynamic cortical changes, offering accessibility and mobility. However, its applications are limited to measuring indirect blood flow in superficial cortical areas. FUS (focused ultrasound) has shown superiority to fMRI in several studies, but it is still in its early stage of development.

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Direct functional brain imaging technologies involve invasive and non-invasive measurement of brain electrophysiology, which is the brain network electrical activity. Invasive methods employ depth and cortical electrode implants, offering high spatial and temporal resolution but are limited to cases requiring brain surgery. Non-invasive tools commonly used for direct electrophysiology include electroencephalography (EEG), which measures the electrical brain activity, and Magnetoencephalography (MEG), which measures the magnetically induced electrical brain activity. Both use sensors placed on the head surface. These technologies provide direct measurement of brain activity with increased temporal resolution. EEG is primarily used for epilepsy and sleep disorders, while MEG, although rarely used clinically, due to its expensive equipment and special requirements, surpasses EEG in both spatial and temporal resolution. Advances in EEG focus on ease of use, automated AI analytics for data analysis, and combination with cognitive tasks to obtain objective measures of brain response. MEG advancements aim to enhance accessibility, portability, and clinical informativeness. A new emerging technology in this field is Delphi-MD technology, which combines non-invasive direct measurement of brain neurophysiological response to focused-high resolution magnetic stimulation. This technology adds a new layer of insights into brain network comprehension, by directly pinging specific brain network hubs and analyzing brain network response. Similar to computer network analytics methodologies, where a specific 'ping' message is delivered and monitored, this technology is highly effective in analyzing network properties of connectivity, activity, and coherence. Delphi-MD significantly improves the signal-to-noise ratio and temporal resolution, opening new horizons in the field.

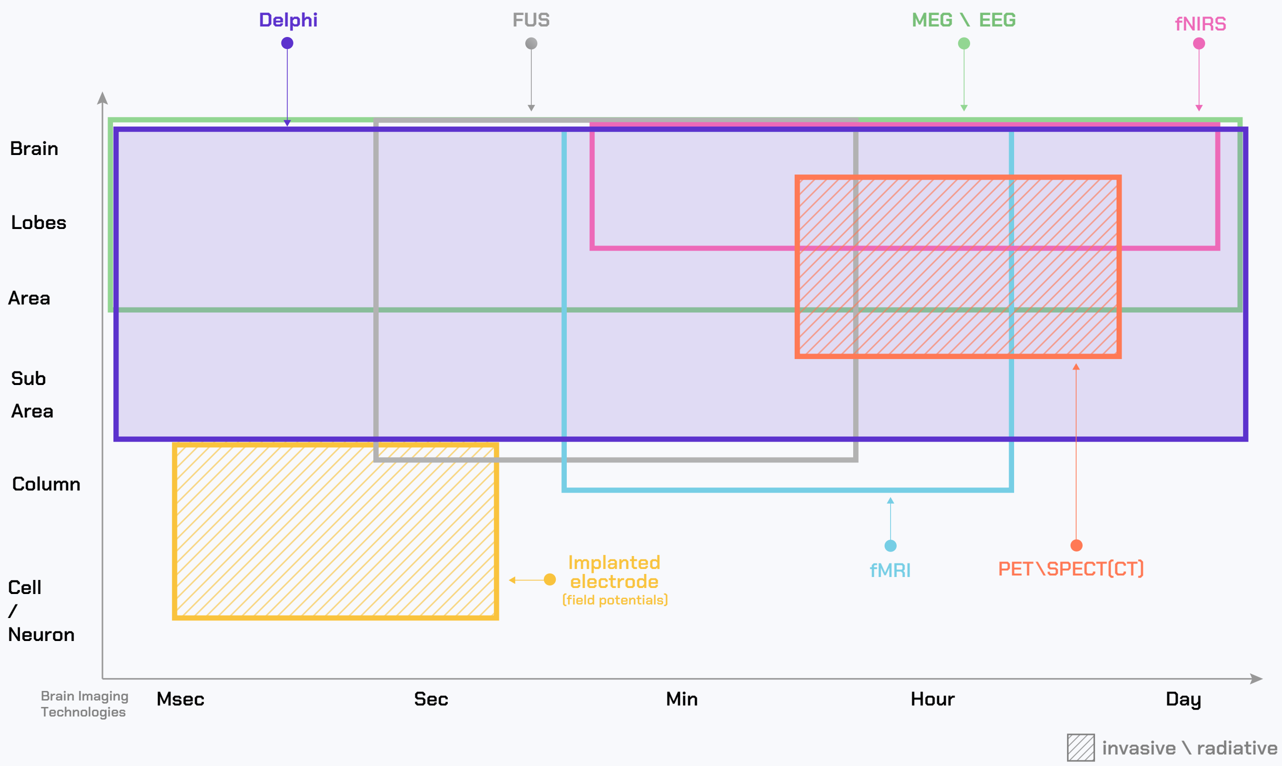

Figure 2. Each colored box represents the approximate spatiotemporal scope of the labeled imaging technique. Dashed boxes represent invasive technologies or technologies that require the use of radiative agents.

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Cognitive\Behavioral Based Methods and Technologies

This field incorporates a range of methodologies and applications that cover cognitive performance evaluation, daily behavior monitoring, and vital signs tracking. Assessing cognitive performance, including memory, executive function, and other domains, can be performed by computerized, or manual cognitive testing. This approach has been leading clinical diagnostics for many years and continues to improve with advancements in technology. It includes traditional pen and paper tests, conducted by neuropsychologists or physicians, which are considered best practice, as well as computerized testing.

The primary advantages of this approach are its cost-effectiveness, ease of use, safety, and its ability to provide valuable insights into brain function and health. As a result, it remains the preferred method for detecting and diagnosing various brain degenerative disorders like Alzheimer's and dementia. However, this approach has two main limitations that cannot be overcome. First, it is an indirect measure of brain function and is often subjective, influenced by factors such as the patient's state, mood, willingness to participate, or the physician's subjective opinion. Secondly, cognitive and behavioral abnormalities typically manifest in the later stages of a disease. The brain's ability to compensate for significant damage, known as "cognitive reserve," leads to the fact that cognitive or behavioral deficits are mostly apparent only in the advanced stages of the disease when substantial brain damage has already occurred. Consequently, this approach and technology are less effective for early detection and objective diagnosis.

Recent advancements in this field are primarily driven by computational developments, such as advanced processing techniques, AI-based methodologies, smartphones, and wearable devices. These advances pave the way for new, sensitive markers, including smartphone behavior analysis, accurate measurements, and remote monitoring of vital signs with direct analysis and interpretation provided to physicians. Overall, these technologies mainly focus on evaluating lifestyle, behavioral, and physiological measures associated with changes related to brain disorders.

Wearable devices consist of lightweight, wireless headsets or sensor electrodes. They can be employed for various purposes, such as monitoring sleep patterns, assessing cognitive performance, and detecting epileptic seizures. Wearables offer the advantage of portability and continuous monitoring but have significant limitations in terms of spatial resolution and signal quality.

Wearable brain diagnostics hold promise for monitoring brain health, studying brain function in real-world settings, and enabling personalized interventions. However, challenges remain in terms of data interpretation, accuracy, and the development of user-friendly devices that seamlessly integrate into everyday life.

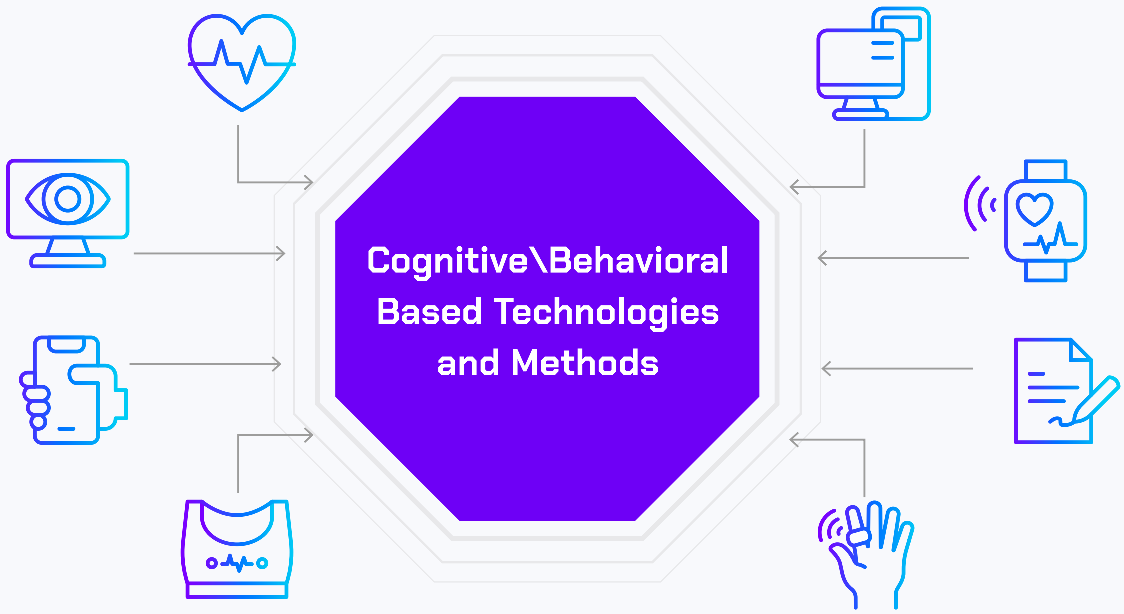

Figure 3. Cognitive/Behavioral Based Technologies and Methods

Disease Specific Biomarkers

This emerging neurodiagnostic field has become the center of attention in recent years due to the Alzheimer's disease amyloid and tauopathy hypothesis and newly developed anti-amyloid/ anti-Tau drugs for treatment of Alzheimer's Disease. It includes lab testing of disease specific markers (such as Amyloid beta 40/42; p-Tau; alpha-synuclein) that are either extracted via lumbar puncture (LP) CSF test (where patients' cerebrospinal fluid is drawn from the spine), a simple blood test or a genetic test. The greatest advantages of these tests are their specificity for diseases, objectiveness and in the case of a blood test, accessibility, and safety. The main disadvantages include the risk associated with an LP procedure and, more importantly, the fact that these tests do not provide a direct evaluation of the brain, making them unreliable as the sole tool for diagnosis. For example, a patient can be Amyloid positive in a blood / CSF test but lacking cognitive deficits. This patient might be diagnosed with Alzheimer's, while never progressing to the actual cognitive impairment and degeneration defining this disease. In addition, clinical and scientific evidence regarding these biomarkers' link to disease and its progression is still preliminary and under debate in the clinical community. In this field medical advances include finding and defining new biomarkers in blood tests for specific brain states and diseases.

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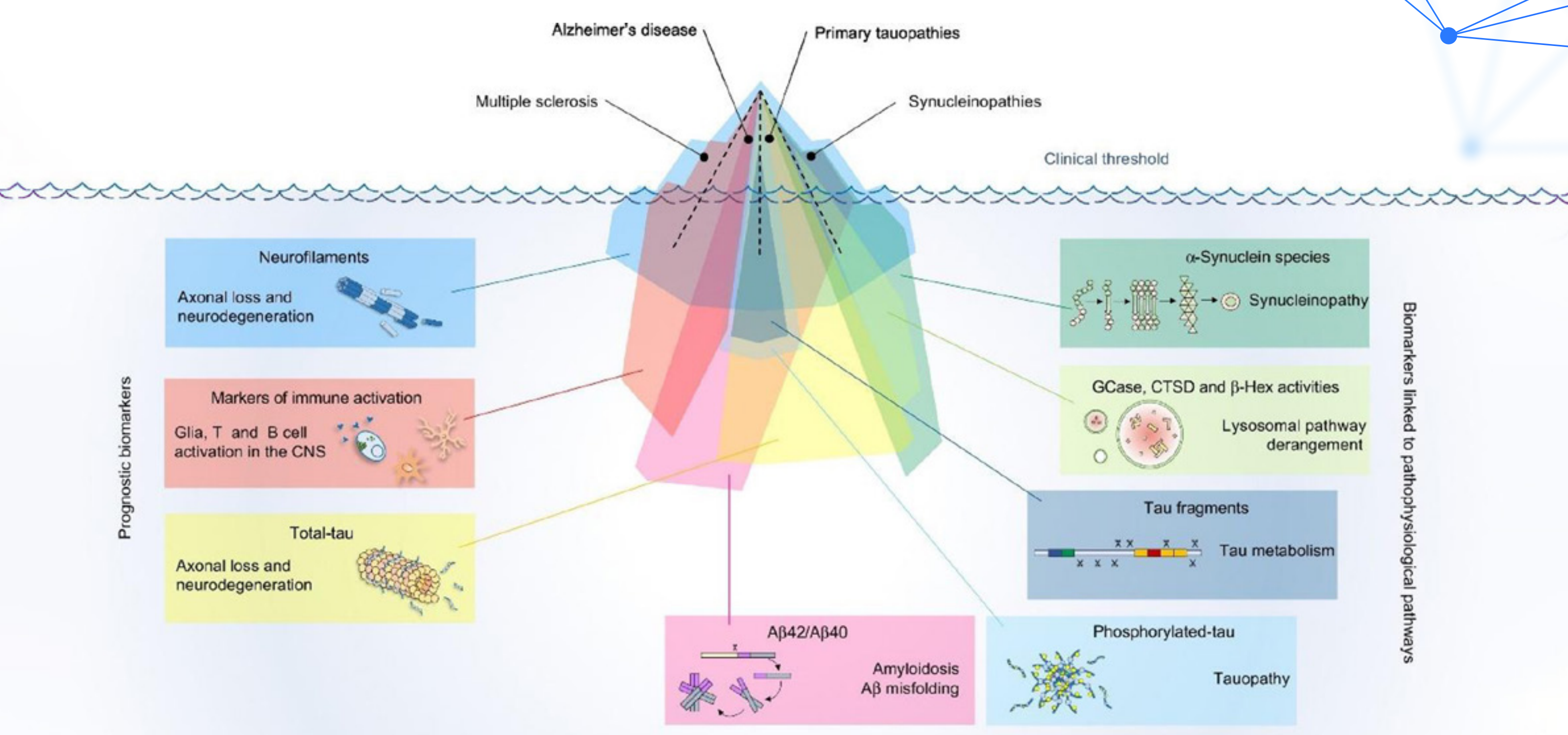

Figure 4. CSF and Blood Biomarkers in neuroinflammatory and Neurodegenerative Diseases (4)

Conclusion

Our understanding of the complex network of systems in the brain is forever growing and new information is being discovered daily. Research is progressing as is technology and the need for early detection in an aging population increases with it. This is specifically true today, as we witness the introduction of novel disease-modifying drugs like Biogen's (Leqembi) and Eli Lilly's (Donanemab) medications designed for mild cognitive impairment or early-stage Alzheimer's disease. These recent developments underscore the pressing requirement for convenient, accessible, cost-effective, and precise methods for early disease diagnosis. These advances are leading brain health toward a brighter future and will play a more significant role in how physicians approach diagnostics and make care decisions, ultimately improving patient care and, as a direct consequence, the overall healthcare system.

About QuantalX

QuantalX is medical device company led by Neuroscientists, who are committed to enhancing patient care and alleviating the burden on healthcare systems through objective, accurate, early detection and differential diagnosis of brain abnormalities, leveraging its novel Direct Electro-Physiology neurodiagnostic technology, the Delphi-MD device.

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