NEXEON

DATA IS DRIVING THE FUTURE OF NEUROTECHNOLOGY WITH CRANIALCLOUD

Will Rosellini, Chairman and Chief Executive Officer, Nexeon Medsystems, and Pierre-Francois D'Haese, PhD, Founder and Chief Executive Officer, Neurotargeting, discuss the neurotechnology market and how the Internet of Medical Things is creating exciting opportunities in the space. Looking at the collaboration centring Nexeon's Deep Brain Stiumulation technology and Neurotargeting's CrainialCloud, they expand on the untapped potential in the sector and how it might be realised by a platform type business model.

INTRODUCTION

The past decade has ushered in an explosion of neurotechnology designed to measure, improve and repair nervous system function in patients suffering from chronic diseases. Newly developed implantable neurostimulators, wearable stimulators and imaging techniques provide rich data to fuel further refinement of therapies. In parallel, a global rise in the "Quantified Self" concept has gained traction, enabled by Internet of Things (IoT) technology. More recently, leaders of the neurotech revolution are adopting an emerging sub-sector of IoT for use in neurotechnology – the Internet of Medical Things (IoMT).

IoMT refers to a connected infrastructure of medical devices and software applications that can communicate with various healthcare IT systems. IoMT is being leveraged to improve medical care by integrating neurological data with other biometric diagnostics, thus providing medical professionals with richer information with which to make their decisions. Successful usage of IoMT will require a vast and layered database of neurological information, including real-time neural recordings that enable medical treatment to be customised to specific patients. Linking nervous system recordings with the IoMT facilitates the alleviation of chronic pain, stopping of tremors or improvement of mood disorders, all at the touch of a button. Once this level of connectivity is achieved, the addressable neurotechnology market is expected to widen significantly as these therapies start to improve patient outcomes whilst also reducing the overall burden of management.

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DEEP BRAIN STIMULATION

Deep Brain Stimulation (DBS) therapy is one of the most common technologies that modulates a patient's neuronal activity. Worldwide, it has been prescribed in over 150,000 patients with Parkinson's disease (PD), a neurodegenerative disorder

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which leads to a progressive deterioration of motor function. DBS has also shown great potential in alleviating symptoms of patients suffering from other movement disorders. Unfortunately, evaluation of long term studies shows that neuromodulation technologies, such as DBS, have not received major improvement since arriving on the market 30 years ago.

While DBS therapy does improve a patient's quality of life, compared with other medical technologies such as pacemakers, it is in a state far removed from its potential. At present, DBS involves empirically selected stimulation parameters arrived at through trial and error over a number of clinical visits. Identification of the appropriate DBS stimulation parameters can take up to six months, followed by up to twelve months of intermittent adjustments during outpatient visits. Oftentimes the stimulation parameters are not fully optimised to maximise patient outcomes, falling short of the potential improvements a patient could receive. To date, DBS device manufacturers have yet to provide neurologists with the robust tools needed to assess a patient's quality of life continuously and enable them to fine tune the stimulation parameters. The technology implanted for the last 30 years provides a static or pseudo-static stimulation scheme that does not adjust to a patient's disease state, medication status or side-effects. DBS therapy will only reach its full potential once the therapeutic output adapts to a patient's neurological state automatically.

Recognising this gap in the market, Nexeon MedSystems has created a DBS device that records local field potentials (LFPs) of the neuronal activity where known biomarkers of the disease can be detected (Figure 1). These recordings can then be extracted, analysed and used to create self-adjusting algorithms that automatically optimise the therapy. Stimulation will be delivered and signals will be collected using a bidirectional DBS system instead of setting static parameters that do not account for the numerous changes a person goes through during the course of a day. Just as a pacemaker dynamically adjusts to keep the heart at a healthy, appropriate rate, the Nexeon DBS system adjusts to keep the brain in a healthy, optimally functioning state. It will also enable physicians to manage patients remotely to reduce or avoid disruption to quality of life.

Thus far, the benefits of LFPs have remained a mystery, since no DBS devices have enabled robust, sustained recordings of these LFP biomarkers. Physicians and neuro-engineers are cautiously optimistic that this never before collected data will provide the basis for "closed-loop" systems that automatically adapt to a patient's clinical state, therefore improving the efficacy of the therapy and minimising undesirable side-effects.

Furthermore, as the MedTech world is connecting us to an ever increasing number of wearable sensors, Nexeon is setting up the path for the brain stimulator to correlate its data with external information about a patient's state or actions in order to produce more sophisticated insights to how a specific disease effects a patient. Observing directly how the brain reacts to stimulation in real-time opens the door to closed-loop control, refining stimulation to the true physiological state. Such control is preferable to using manual adjustments, which are time consuming, prolonged and often subjective.

Nexeon's vision is for neurotechnology to integrate with IoMT technologies that address all aspects of medical treatment to maintain a comprehensive picture of patient health. This means neurological data will combine with the IoMT system that tracks patient medications, hospital visits, data from wearable devices, caregiver input, patient vital signs and other key indicators for comorbidity management (i.e. diabetes, COPD, dysphagia, etc). The goal is not the singular treatment of, for example, Parkinsonian tremor, the goal is complete interconnectivity on all aspects of a patient's healthcare to improve their overall wellbeing.

Figure 1: Nexeon's synapse device.

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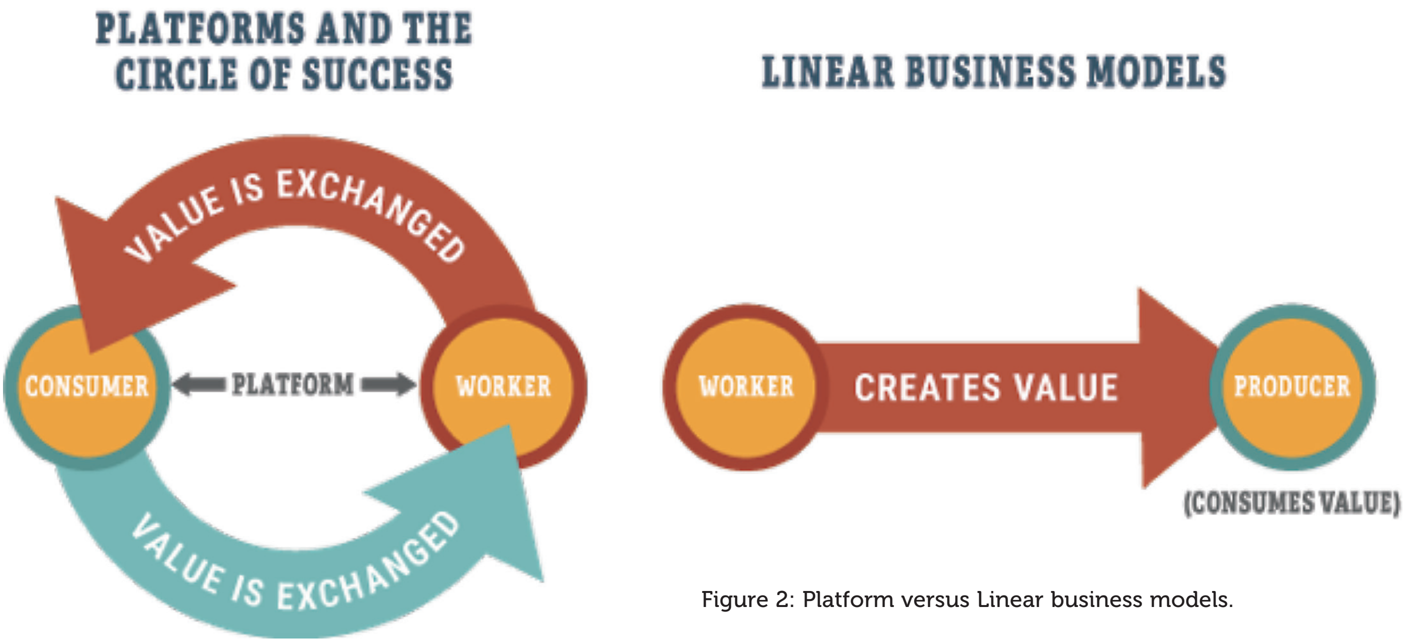

Figure 2: Platform versus Linear business models.

DATA-DRIVEN NEUROTECHNOLOGY PLATFORMS

Revolutionising neurotechnology requires a new way of doing business. The 20th century was dominated by the factory business model, in which companies create a commodity and push it in one direction toward the customer at the end of the supply chain. Internally owned and controlled resources are a factory's most valuable assets. It is now the case that platform business models are starting to replace these traditional linear models by enabling a multi-directional exchange of value between two or more user groups. Platform businesses use external networks, such as the IoMT technology, data and users, as the aggregator of business value rather than investing in and growing their internal resources or supply chain (Figure 2).

A useful analogy would be General Motors, which manufactures cars, versus Uber, which "manufactures" transactions between drivers and riders. Uber does not provide the ride service, instead it merely facilitates the exchange of value between drivers and passengers. When a linear business gains a new customer, it adds only one new relationship. But when a platform adds a new user, that person adds potential relationships with all the platform's users. Platform companies grow exponentially rather than linearly, which is why platform businesses can expand at an unprecedented pace. This is how Alibaba, Facebook and Google continue to grow at an exponential rate regardless of their current size.

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Although a platform model enables transactions, it does not directly control the behaviour of its users. In the context of neurotechnology, the users are patients, caregivers, researchers and healthcare providers. The challenge for neurotech companies going forward is directing user behaviour toward effectively improving patient care.

The answer lies in the four core functions of a platform:

1. Audience building
2. Matchmaking
3. Providing core tools and services
4. Setting rules and standards.

If a neurotech platform can handle these four functions well, it would be able to facilitate transactions that reduce the burden of neurological diseases.

Data-driven decision making is the revolutionary neurotechnology platform upon which improved neurological disease management can be delivered. With the development of IoMT connected neurotechnology, data collected on patient disease management will facilitate an outpouring of analytics to improve decision making by healthcare providers. Leveraging data on patient disease holds the potential to eliminate redundant or predictable decisions, saving valuable physician time and focusing their attention on what only they can do: diagnose, plan treatments, perform procedures and care for patients. With these tools, quality patient care can expand beyond specialised centres into more rural or underserved areas. Smart neurotech devices, paired to data supported decision making algorithms, could support physicians who are less experienced or less knowledgeable about a therapy by providing therapeutic parameters developed from the data of thousands of other patients managed by leading physicians worldwide.

THE CRANIALCLOUD PLATFORM

Nexeon has combined its state-of-the-art neurostimulaton with an IoMT platform called CranialCloud designed by Neurotargeting, a specialist software company. The primary goal of the collaboration is to achieve data-driven decision making in neurology and neurosurgery. More specifically, CranialCloud is a centralised neurotechnology data platform that enables the visualisation and exchange of clinical data between researchers and healthcare providers. At its core, CranialCloud handles the management of neurological diseases by collecting images of a patient's brain and spatially relating their information to these images, facilitating improved clinical decision making. It consists of a network of databases and associated processing pipelines that are fully integrated into the clinical flow.

The CranialCloud framework permits spatial normalisation of the data, data sharing across institutions and handles the issue of data ownership, privacy and compliance with the US Health Insurance Portability and Accountability Act (HIPAA). Each research group or medical centre owns a single CranialCloud account in which clinical data is stored. Neurotargeting works with each account owner to create contracts and analyse risk, thereby integrating CranialCloud smoothly into the hospital workflow. To assuage industry concerns of safety in data management, Neurotargeting maintains compliance with HIPAA and ISO-27001 standards, as ensured by the monitoring of two external companies. Once CranialCloud accounts are opened by a hospital or research group, the platform becomes a legal extension of that institution's IT network. Because data within the platform is managed on the institutional level, any stakeholder within that institution (clinician, researcher, etc) can store their data in a structured way during the clinical care or clinical research.

The integration of CranialCloud into healthcare IT networks allows access to patient data collected with regulated neurotechnology and other medical devices. Key patient data include (but are not limited to):

- Signals recorded directly from the patient's brain
- Images from surgical planning systems to extract lead locations and location in the brain of electrophysiological data
- Patient responses to therapy.

Neurotargeting has developed multiple applications that feed into CranialCloud to utilise these data sources.

CranialSuite is the surgical planning tool used for patients who require neurosurgery to implant neurostimulators, such as DBS devices. It combines basic trajectory planning to obtain frame settings with advanced planning and navigation capabilities that improve operating room workflow and localisation of anatomical and functional areas.

The CranialDrive application is a client-based application used to acquire and transfer data to the archive. Similar to file hosting platforms like DropBox, CranialDrive runs on a computer and listens for new clinical and research data to sync with the archive. The CranialDrive application has a complex mechanism of data anonymisation and multi-level encryption to ensure HIPAA compliance.

Sharing anonymised patient data across institutions is perhaps the most crucial component of CranialCloud, because advancing the treatment of neurological diseases cannot be done in a vacuum. CranialCloud collects data from CranialSuite and CranialDrive, which then enables cross-institutional data collection and analysis. Neurotargeting has developed effective methods for data sharing by incorporating requirements or constraints on data structure to enable a common data storage and labelling. These standard structures are able to acquire and manage complex, multi-dimensional data, including real-time LFPs streamed from implantable neurostimulators.

The CranialCloud platform enables multidirectional flow of value between healthcare providers, between companies and patients, from patients to healthcare providers and from healthcare providers to companies. As clinicians grow and share their patient database, companies can access data that will enable them to refine features of their technology. Clinicians can share smart algorithms to deliver more efficient and effective patient care. Patients can provide improved, less subjective feedback to their caregivers and providers. By combining neurotechnology and IoMT through platforms like CranialCloud, connectivity can be increased, opening up possibilities for unprecedented advances in healthcare.

ABOUT THE COMPANY

Nexeon Medsytems is a global medical device company focused on providing innovative neurostimulation products that improve the quality of life of patients suffering from debilitating neurological disease. It was originally founded in 2005 with the goal of changing how innovative ideas in the medical device industry move from concept to reality with a focus on creating solutions for clinicians in their pursuit of improving patient outcomes.

ABOUT THE AUTHORS

Will Rosellini is a 15 year veteran of the neurotechnology space with expertise in accelerating the development of emerging technologies using minimal at-risk capital, holding five Master's degrees and a law degree. From 2005 to 2012, he was a founder and CEO of Microtransponder, a company developing vagal nerve stimulation therapies for treatment of stroke and tinnitus. He went on to serve in other Board and C-level positions for various biomedical device companies and research programmes. Mr Rosellini joined Nexeon MedSystems in 2016.

Pierre-Francois D'Haese conceived of and became the key architect of the CranialCloud system as part of his PhD, already having Master's degrees in Electrical Engineering and Business Administration. He co-founded Neurotargeting in 2007 and successfully secured funding from the US NIH to translate this technology to create a product that would impact patient care. Dr D'Haese also holds a faculty position at Vanderbilt University (Nashville, TN, US) as Research Assistant Professor in Electrical Engineering and Computer Science, as well as in Neurological Surgery.