Chapter

An Evolutionary Perspective for Network Centric Therapy through Wearable and Wireless Systems for Reflex, Gait, and Movement Disorder Assessment with Machine Learning

Robert LeMoyne and Timothy Mastroianni

Abstract

Wearable and wireless systems have progressively evolved to achieve the capabilities of Network Centric Therapy. Network Centric Therapy comprises the application of wearable and wireless inertial sensors for the quantification of human movement, such as reflex response, gait, and movement disorders, with machine learning classification representing advanced diagnostics. With wireless access to a functional Cloud computing environment Network Centric Therapy enables subjects to be evaluated at any location of choice with Internet connectivity and expert medical post-processing resources situated anywhere in the world. The evolutionary origins leading to the presence of Network Centric Therapy are detailed. With the historical perspective and state of the art presented, future concepts are addressed.

Keywords: wearable systems, wireless systems, accelerometers, gyroscopes, smartphones, portable media devices, machine learning, reflex, gait, movement disorder

1. Introduction

Quantifying human movement characteristics can provide a significant foundation for enabling optimized rehabilitation therapy, for which the advent of wearable and wireless inertial sensor systems provides considerable opportunity [1–12]. The quantification of inertial sensor systems have been proposed for the measurement and quantification of human movement characteristics since approximately the mid-20th century. However, sufficient miniaturization and reliability regarding that timeframe had not been achieved for associated biomedical applications [11–15]. Motivating research, development, testing, and evaluation for the evolution of inertial sensors derived from industries extrinsic relative to the biomedical field, such as the automotive industry for regulation of airbag deployment [11–13, 15]. Upon the achievement of a sufficient threshold for miniaturization and reliability these inertial sensors have been successfully applied to numerous human movement scenarios, such as the quantification of reflex, gait, and movement disorder. Furthermore, these inertial sensors were noted as functionally wearable with wireless in capability, which ushered the presence of wearable and wireless inertial sensor systems for quantifying human movement [1–12]. A historical and evolutionary perspective leading to the amalgamation of inertial sensors that are functionally wearable with wireless connectivity to Cloud computing resources in conjunction with machine learning classification as an advanced post-processing technique, which is known as Network Centric Therapy, for the biomedical domain is presented.

2. Ordinal methodologies for quantifying reflex response, gait, and movement disorder

Prior to the advent of wearable and wireless inertial sensor systems, the diagnosis of a subject's health status was essentially derived from the expert although subjective interpretation of a skilled clinician. The clinician is generally tasked with the responsibility to interpret the health of the patient and apply the observation to an ordinal scale criteria methodology. This ordinal scale process is ubiquitous to the clinical domain, and this approach is relevant to the scope of reflex response, gait, and movement disorder. However, the ordinal scale strategy encompasses contention regarding reliability, and there generally does not exist a means for translating between various available ordinal scales [1, 3, 11, 12, 16–30].

Further issues with the ordinal scale approach are evident with respect to the imperative need for patient-clinician interaction. From a logistical perspective a patient is required to travel to a clinical appointment, which in the case of a specialized expert may require relatively long-distance travel. Additionally, the clinician is only provided with a short duration of time to interpret the patient's health status, which may be in dispute to the true health condition of the patient. The ordinal scale approach intuitively only provides limited insight of patient health, for which sensor signal data may provide a more revealing historical perspective.

3. Electro-mechanical systems providing signal data for quantifying reflex response, gait, and movement disorder

The acquisition of quantified sensor signal data enables more pertinent clinical acuity regarding the health status with respect to reflex response, gait, and movement disorder [1–12]. With respect to the quantification of reflex response an assortment of electro-mechanical sensor systems have been proposed. These devices generally have consisted of the means for evoking the reflex through a provisional reflex hammer and quantifying the correlated reflex response [17, 18, 31–38]. By temporally synchronizing the input quantification device eliciting the reflex and output quantification sensor of the reflex response a functional reflex latency can be derived [17, 18, 39, 40].

The quantification of the input that commences the reflex has been demonstrated through instrumented provisional reflex hammers and motorized devices. These devices enable measuring of the intensity of the eliciting impact and the time stamp regarding the start of the reflex respective of the neurological pathway. The reflex response, such as deriving from the patellar tendon, can be measured through electromyograms (EMGs), strain gauges, optical motion cameras, force sensors, and wired inertial sensors in addition to the associated time stamp. The temporal differential between the evoking reflex input time stamp and the reflex response time stamp can derive a functional latency of the reflex under consideration, such as the latency of the patellar tendon reflex [17, 18, 31–44].

Electro-mechanical systems have been applied for the quantified assessment of gait, which also pertains to movement disorder conditions. Representative electro-mechanical apparatus for quantifying gait consist of EMGs, optical motion cameras, force plates, foot switches, electrogoniometers, and metabolic analysis devices. These devices are generally reserved for clinical gait laboratories and imply supervision from expert clinical resources [11, 12, 45–48].

The acquired sensor signal data can be post-processed and applied to sophisticated techniques, such as machine learning, for distinguishing between various states of health during gait. Two particular types sensor signal are the force plate and optical motion camera [49–54]. The force plate provides kinetic signal data, and the optical motion camera provides kinematic signal data. The force plate and optical motion camera can be operated in tandem and synchronicity to derive clinically significant information about gait, such as ankle torque derived during stance [48].

These electro-mechanical systems enable quantification of human movement features, such as reflex response, gait, and movement disorders, through the acquired sensor signal data [31–38, 41–54]. Although these electro-mechanical systems are clinically standard, they are generally constrained to a clinical laboratory. Furthermore, the majority of these devices both require specialized resources for their experimental operation, and they are predominantly not portable [1–4, 6–12, 47, 48].

By contrast, the functionally wearable with wireless inertial sensor system considerably alleviates the constraints of specialized resources through simplified means of activating the inertial sensor signal recording. These devices constitute portable systems, and they are functionally wearable [1–12]. The origins of the advent of Network Centric Therapy commence with the research, development, testing, and evaluation for quantifying reflex response and latency, which subsequently lead to the extrapolation to the domains of wearable and wireless inertial sensors for gait and movement disorder quantification.

4. Evolutionary pathway for Network Centric Therapy with respect to quantification of reflex response and latency

The global evolutionary pathway for Network Centric Therapy derives from the Ph.D. Dissertation research conducted by Dr. LeMoyne, which lead to the progressive development of a device known as the Wireless Quantified Reflex Device through the incremental develop of four generations. The preliminary success involved the quantification of reflex response through locally wireless accelerometers. In order to measure the response of the patellar tendon reflex, the wireless accelerometers were mounted proximal to the lateral malleolus, which signified their wearable capability [17, 18, 40].

The original wireless accelerometers were provided through internal UCLA research, and they were referred to as MedNodes. The MedNodes required specialized operation, as they were the scope of graduate-level research at UCLA. These wireless accelerometer nodes that were noted as conveniently wearable were applied to the first and second generations of the Wireless Quantified Reflex Device, and the quantification of the patellar tendon reflex was measured in an accurate and reliable manner. The collected signal data of the wireless accelerometer was transmitted to a locally situated computer for post-processing [55, 56]. Central to all four generations of the Wireless Quantified Reflex Device was the integration of a quantified potential energy impact pendulum to consistently evoke the patellar tendon reflex [17, 18, 39, 40, 55, 56].

The third and fourth generations of the Wireless Quantified Reflex Device included a second wireless accelerometer to determine the time of impact for the quantified potential energy impact pendulum. The first wireless accelerometer was mounted to the ankle to quantify reflex response and time of response. Using the temporal offset of the wireless accelerometer mounted on the impact pendulum evoking the patellar tendon reflex and the wireless accelerometer mounted about the lateral malleolus mounted about the ankle to measure reflex response, a functional patellar tendon reflex latency was derived. The third and fourth generations of the Wireless Quantified Reflex Device incorporated the G-link wireless accelerometer developed by Microstrain [17, 18, 39, 40].

The third generation Wireless Quantified Reflex Device utilized streaming signal data to the locally situated portable computer for acquisition of the accelerometer signal data and subsequent post-processing. The third generation Wireless Quantified Reflex Device was the first evolution to feature the ability to derive functional reflex latency through the tandem wireless accelerometers with one wireless accelerometer located on the potential energy impact pendulum that evokes the patellar tendon reflex and the other wireless accelerometer mounted proximal to the lateral malleolus of the ankle for also acquiring reflex response. The research findings demonstrated that patellar tendon reflex response and associated functional latency could be both quantified with considerable accuracy and reliability [39].

The observations of the third generation Wireless Quantified Reflex Device established opportunity for improvement, such as increasing the sampling rate for the tandem accelerometers. This improvement would implicate better acuity with respect to the derived functional latency of the patellar tendon reflex. An artificial reflex device was applied as intermediary before the development of the fourth generation Wireless Quantified Reflex Device. This intermediary device utilized the data logger of the G-link wireless accelerometers, which permitted augmented sampling rates, while retaining wireless connectivity to a local portable computer for accelerometer signal data downloading and post-processing [57–59].

The fourth generation Wireless Quantified Reflex Device successful applied a longitudinal study for multiple subjects. With the wireless accelerometer set to data logger configuration with subsequent wireless transmission, the Wireless Quantified Reflex Device successfully acquired patellar tendon reflex response and functional latency with considerable accuracy, reliability, and reproducibility [40]. Subsequent evolutions encompass the application of more robust wearable and wireless inertial sensor systems and conjunction with machine learning to distinguish a hemiplegic reflex pair regarding affected patellar tendon reflex and associated unaffected patellar tendon reflex [60–62].

The next improvement incorporated the use of the portable media device and smartphone for the quantification of reflex response as a functional wireless accelerometer platform using the potential energy impact pendulum to evoke the patellar tendon reflex [63, 64]. The portable media device was suited for facilities with local wireless internet zones [63]. For locations requiring broad telecommunication access, the smartphone provides better benefit [64]. Both applications feature a common software application that enables a discrete recording of the accelerometer signal for quantifying the reflex response, and the signal data can be attached to an email for wireless transmission to the Internet for post-processing anywhere in the world [63, 64].

For example, LeMoyne and Mastroianni conducted an experiment to quantify reflex response using a portable media device applying supramaximal stimulation of the patellar tendon reflex in Lhasa, Tibet of China. The signal data was wirelessly transmitted to the Internet as an email attachment, which served as a provisional

Cloud computing resource. The data was later downloaded in Flagstaff, Arizona of the United States of America, which is effectively on the other side of the world, for post-processing [65].

Further advancements of the concept of quantifying reflex response, such as the patellar tendon, pertained to using the accelerometer signal, such as through a portable media device, to differentiate between a hemiplegic reflex pair. The hemiplegic affected leg's patellar tendon reflex response is notably more amplified relative to the patellar tendon reflex response of the unaffected leg. By consolidating the respective accelerometer signals to a feature set for machine learning classification using the support vector machine available through the Waikato Environment for Knowledge Analysis (WEKA) considerable machine learning classification accuracy was attained [60]. This achievement is notable, since subjective clinical observations to distinguish between a hemiplegic reflex pair is a matter of contention [21].

The gyroscope was eventually incorporated in the inertial sensor package of portable media devices and smartphones. The gyroscope provides a clinical representation for rotational characteristics of a joint, which represents the response of the patellar tendon reflex. Successfully demonstration of the gyroscope to quantify the patellar tendon reflex was demonstrated in the context of the Wireless Quantified Reflex Device through the potential energy impact pendulum [61, 62, 66–68].

Using both the potential energy impact pendulum and supramaximal stimulation to evoke the patellar tendon reflex response multiple machine learning algorithms using WEKA have achieved considerable classification accuracy [60–62, 66, 67]. **Figures 1** and **2** represent the gyroscope signal for the reflex response of the hemiplegic affected leg and unaffected leg, respectively. Machine learning algorithms, such as the J48 decision tree, provide a visualized basis for the most prevalent numeric attributes to establish classification accuracy, such as the time disparity between maximum and minimum angular rate of rotation for the patellar tendon reflex response, as illustrated in **Figure 3** [67].

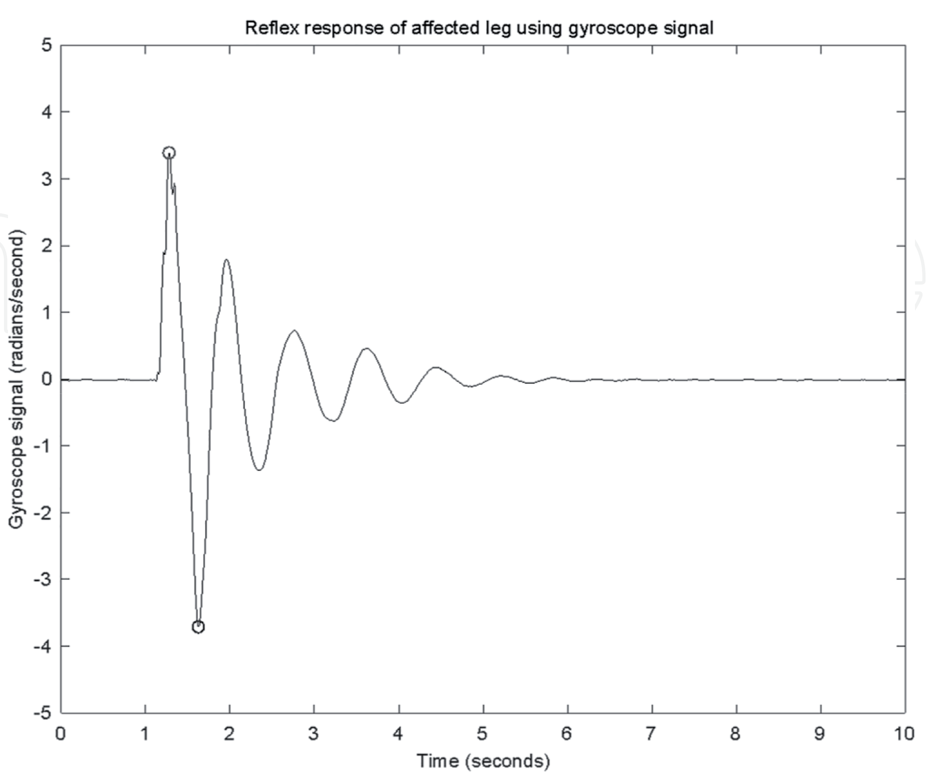

Figure 1.
The gyroscope signal of the patellar tendon reflex response for the hemiplegic affected leg using the potential energy impact pendulum to evoke the reflex [67].

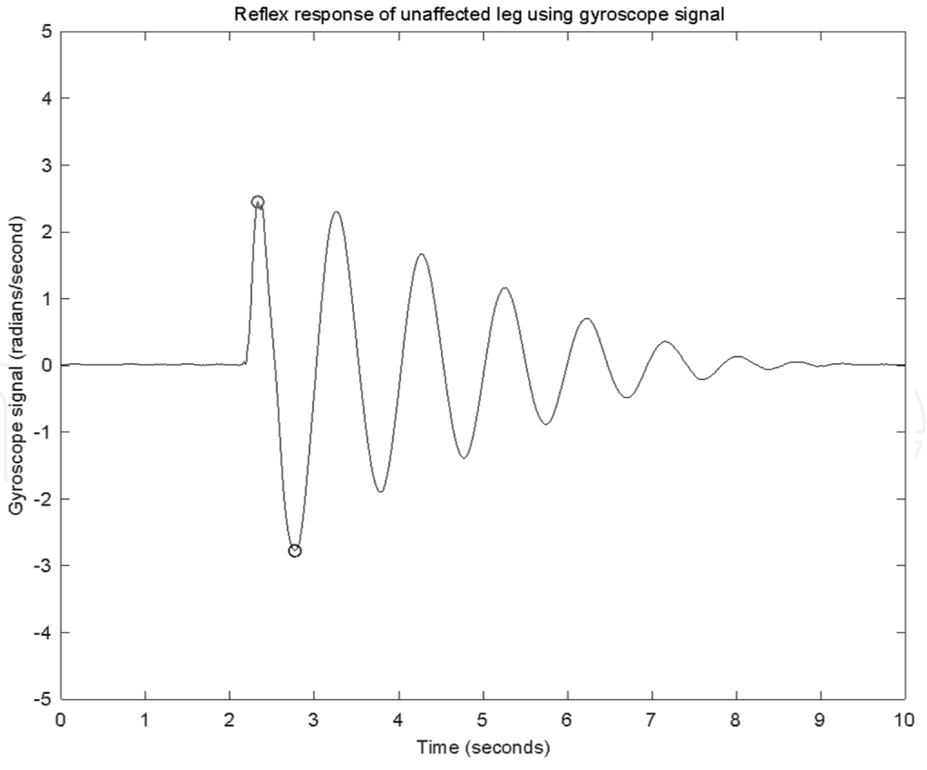

Figure 2.
The gyroscope signal of the patellar tendon reflex response for the unaffected leg using the potential energy impact pendulum to evoke the reflex [67].

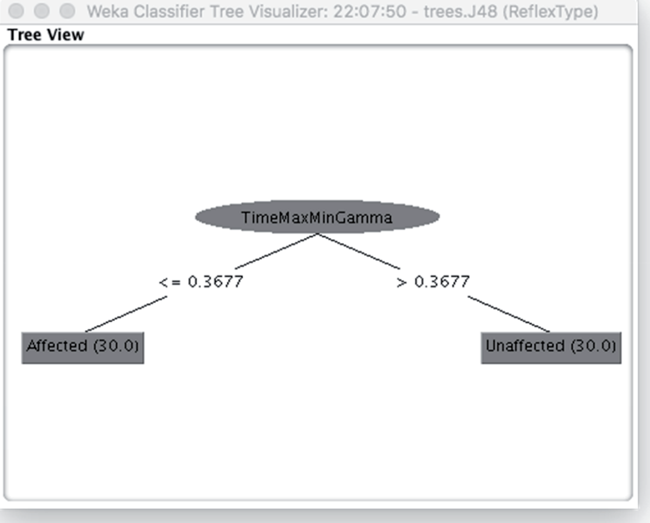

Figure 3.
The J48 decision tree to distinguish between a hemiplegic affected leg and unaffected leg, for which the time disparity between maximum and minimum angular rate of rotation for the patellar tendon reflex response numeric attribute is illustrated as the most prevalent for establishing classification accuracy [67].

5. Lessons learned through the research, test, and evaluation of the Wireless Quantified Reflex Device for the broader evolution of Network Centric Therapy, such as gait and movement disorder quantification

A readily noted capability observed by LeMoyne and Mastroianni was that since the wireless accelerometer was functionally wearable for the quantification of reflex response through mounting about the lateral malleolus of the patellar tendon, likewise the same mounting procedure could be applied for quantifying gait patterns [11, 12, 17]. Alternative mounting configurations, such as the lateral epicondyle proximal to the knee, were also feasible for assessing gait in a quantified context [11]. Additionally, the smartphone and portable media device were suitable candidates to represent functionally wearable and wireless inertial sensor systems (both accelerometers and gyroscopes) for gait quantification and eventually machine learning classification [3–10]. These concepts were also applied to the quantification of movement disorders through the mounting of wearable and wireless inertial sensor systems about the dorsum of the hand [1, 2, 5–10].

6. Evolutionary pathway for Network Centric Therapy with respect to quantification of gait

Preliminary attempts to apply functionally wearable wireless accelerometers to measure gait characteristics consisted of segmented subsystems and in some cases complex mounting techniques exceeding the knowledge of the common user [69–72]. The highly miniaturized, portable, and non-intrusive nature of the G-link wireless accelerometer developed by Microstrain demonstrate its robust capability for quantifying gait characteristics [11]. Proof of concept from an engineering perspective was demonstrated for the identification of quantified disparity of hemiplegic gait and Virtual Proprioception to enable real-time rehabilitation of hemiplegic gait [73–76].

Preliminary research, development, testing, and evaluation by LeMoyne et al. applied the G-link Microstrain wireless accelerometer to ascertain quantified disparity of hemiplegic gait. The wireless accelerometer nodes were effectively wearable. They could be mounted about the lateral epicondyle proximal to the knee through an elastic band or about the lateral malleolus near the ankle using the elastic band of a sock [74, 75].

The wireless accelerometer achieved connectivity to a locally situated personal computer, which would then serve as the basis for post-processing. Using the acceleration magnitude of the three-dimensional orthogonal acceleration signal, characteristic spikes of the acceleration magnitude signal represented the initiation of stance. The time averaged acceleration from stance to stance enabled the quantification of gait characteristics [74, 75]. Furthermore, through the ratio of the hemiplegic affected leg to the unaffected leg using the time averaged acceleration from stance to stance, the quantified disparity of hemiplegic gait could be quantified with the potential for deriving therapeutic intervention for rehabilitation [74]. Functionally wearable and locally wireless accelerometers have also been applied to successfully contrast hemiplegic gait with respect to the frequency domain [73]. Other applications of wireless accelerometer systems that are functionally wearable have been successfully demonstrated for the context of effectively autonomous gait analysis based on quantified data derived from the acceleration signal [11, 12, 69–72].

Virtual Proprioception expanded the capabilities of functionally wearable wireless accelerometers for real-time modification of hemiplegic gait based on accelerometer signal data. The wireless accelerometers were mounted by flexible elastic bands proximal to the lateral epicondyle of the knee for both the unaffected leg and hemiplegic affected leg. Based on a visual feedback strategy the person with hemiplegic gait was able to modify the hemiplegic affected leg to a more representative acceleration signal representative of the unaffected leg [76].

During 2010 LeMoyne and Mastroianni sought to expand the availability of wearable and wireless accelerometer systems for quantifying gait in the context of more commercially available systems. The smartphone of that timeframe was equipped with an internal accelerometer. Additionally, the smartphone is inherently capable of wirelessly accessing the Internet. A software application for recording the accelerometer data for a prescribed duration and sampling rate with wireless transfer to the Internet as an email attachment enables the smartphone to function as a wearable and wireless inertial sensor system. The email resource represents a provisional representation of a Cloud computing resource. These characteristics enable the smartphone to quantify gait features in the context of a wearable and wireless inertial sensor system [77]. These preliminary capabilities constitute the origins of Network Centric Therapy for the domain of gait analysis [3–7, 78].

Preliminary testing and evaluation of the smartphone as a wearable and wireless inertial sensor system for gait analysis was conducted in region of Pittsburgh, Pennsylvania. The experimental gait analysis accelerometer data was conveyed wirelessly to the Internet as an email attachment for subsequent post-processing in the general area of Los Angeles, California. The implications were that experimental and post-processing locations could be geographically separated anywhere in the world with Internet connectivity [77].

The preliminary gait experiment of 2010 implementing the smartphone as a wearable and wireless inertial sensor system through the internal accelerometer involved mounting the smartphone proximal to the lateral malleolus of the ankle joint by an elastic band. Two primary gait characteristics were quantified, such as the temporal duration between stance to stance and time averaged acceleration from stance to stance. These parameters acquired by the smartphone functioning as a wearable and wireless inertial sensor system through the available accelerometer demonstrated considerable accuracy and reliability [77].

Additional and similar themed experiments pertained to quantification of gait through other mounting applications, which underscores the flexibility of the smartphone as a wearable and wireless inertial sensor system. The two other mounting positions involved the lateral epicondyle near the knee joint and lumbar-sacral aspect of the spine through an elastic band. The temporal duration between stance to stance cycle displayed considerable accuracy and reliability and successfully elucidated predominant frequencies in the context of the frequency domain with respect to both mounting strategies [79, 80].

Another device that is similar to the smartphone for applications as a wearable and wireless inertial sensor system for the quantification of gait is the portable media device. The portable media device can utilize the same software application as relevant to the smartphone. Although the portable media device is generally restricted to an area with local internet connectivity, this device has a lighter mass and is more affordable for tandem applications involving both legs for gait analysis [3–10, 78].

Preliminary, testing of the portable media device was successfully demonstrated with mounting about the lateral malleolus of the leg by an elastic band. The accelerometer of the portable media device successfully quantified gait in an accurate and consistent manner. The experimental data was conveyed by wireless transmission through the Internet as an email attachment, and the experimental and post-processing resources were situated on opposite sides of the continental United States. Post-processing emphasized the derivation of step cycle time (stance to stance) and time averaged acceleration (stance to stance) [81].

An observation of the portable media device is that it is more affordable than the smartphone, such as for the application of two tandem operated portable media devices for quantifying the disparity of hemiplegic gait. LeMoyne and Mastroianni incorporated two portable media devices in the context of a wearable and wireless inertial sensor system, such as an accelerometer, for quantifying hemiplegic gait respective of the unaffected leg and the hemiplegic affected leg. The devices were mounted about the lateral malleolus of the ankle joint through an elastic band for both the unaffected leg and the hemiplegic affected leg. The tandem activated portable media devices successfully demonstrated the ability to quantitatively identify stance to stance temporal duration and stance to stance time averaged acceleration of the hemiplegic affected leg and unaffected leg with statistical significance. Also, the ratio of stance to stance time averaged acceleration less the offset for the hemiplegic affected leg and unaffected leg demonstrated quantified disparity [82].

Eventually a strategy for using a singular smartphone to quantify hemiplegic gait and its associated disparity was established with the incorporation of a treadmill to maintain constant velocity. The smartphone functioning as a wearable and wireless accelerometer platform was mounted about the lateral malleolus of the ankle by an elastic band. Automated post-processing software emphasized the rhythmic characteristics of gait and acquired gait parameters, such as stance to stance temporal disparity and stance to stance time averaged acceleration. The stance to stance temporal disparity did not display statistical significance, because of the treadmill velocity constraint. Statistical significance was achieved for stance to stance time averaged acceleration with respect to comparing the hemiplegic affected leg to the unaffected leg. This experimental configuration enables the evaluation and quantification of gait in an autonomous environment [83].

Evolutionary trends eventually enabled the smartphone to quantify gait through the internal gyroscope, which offers a more clinically representative kinematic signal. The strategy of conducting gait analysis constrained to a constant velocity by a treadmill was applied. A smartphone functioning as a wearable and wireless gyroscope platform quantified hemiplegic gait in terms of both the affected leg and unaffected leg with mounting about the lateral malleolus near the ankle joint through an elastic band. The gyroscope signal was consolidated to a feature set during the post-processing phase, which consisted of five numeric attributes: maximum, minimum, mean, standard deviation, and coefficient of variation. Using the multilayer perceptron neural network considerable classification accuracy was attained for distinguishing between the hemiplegic affected leg and unaffected leg during gait [84].

Additionally, the smartphone through its internal inertial sensor system has been applied to other applications pertaining to the domain of gait analysis and associated mobility. Smartphones have been successfully incorporated for augmenting the acuity of clinically standard evaluations, such as the Timed Up and Go and 6-Minute Walk Test [85–87]. An observed utility of the strategy of augmenting clinically standard evaluation techniques with functionally wearable and wireless inertial sensor systems, such as the smartphone, is the ability to evolve a clinical method rather than inventing a new methodology.

During this phase of the evolutionary process that lead to the realization of Network Centric Therapy a new observation occurred. Smartphones and portable media devices can function as representative and effective wearable and wireless inertial sensor systems. However, their evolutionary pathway is not consistent with the biomedical and healthcare domain. A new perspective for wearable and wireless inertial sensor systems was developed, which incorporated inertial sensor nodes with local wireless connectivity to a device, such as a smartphone or tablet, with considerably expanded wireless access to the Internet. This paradigm shift enabled considerable reduction in mass and volumetric profile for the wearable and wireless inertial sensor system. This strategy enabled segmented wireless access of the inertial signal data for connectivity to a Cloud computing resource [88].

During 2016 LeMoyne et al. utilized a wearable and wireless inertial sensor system architecture in the context of Network Centric Therapy for the evaluation of gait for subject's with Friedreich's ataxia. The system applied local wearable and wireless inertial sensor nodes with local wireless connectivity to a tablet with global wireless access to a Cloud computing environment. A multilayer perceptron neural network achieved considerable classification accuracy to distinguish between a person with healthy gait and gait for a person with Friedreich's ataxia [89].

The current state of the art for demonstrating the capability of Network Centric Therapy involves the recent test and evaluation of the BioStamp nPoint, which represents a conformal wearable and wireless inertial sensor system. The BioStamp nPoint achieves wireless connectivity for acquiring signal data for quantifying gait in a segmented manner through wireless systems, such as a tablet for operation and smartphone for Cloud computing access. **Figure 4** presents the supporting apparatus for the BioStamp nPoint conformal wearable and wireless inertial sensor system [90].

Recently, during 2020 LeMoyne and Mastroianni applied the BioStamp nPoint to quantify hemiplegic gait with distinction through machine learning. The BioStamp nPoint conformal wearable and wireless inertial sensor system was mounted by adhesive medium to both the hemiplegic affected leg and unaffected leg about the femur and proximal to the patella as shown in **Figure 5**. The subject walked on a treadmill for the experiment [91].

Figure 4.
The BioStamp nPoint conformal wearable and wireless inertial sensor system and supporting devices, such as docking station, tablet, and smartphone [90].

Figure 5.
The BioStamp nPoint conformal wearable and wireless inertial sensor system mounted about the femur for the quantification of hemiplegic gait [91].

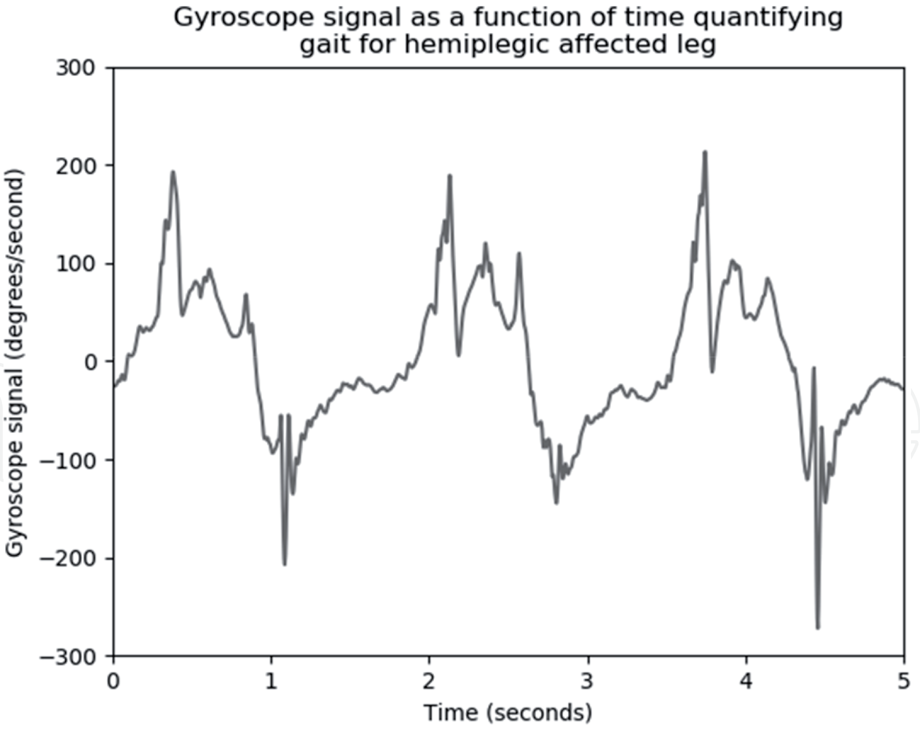

Figure 6.
The BioStamp nPoint conformal wearable and wireless inertial sensor signal for the hemiplegic affected leg [91].

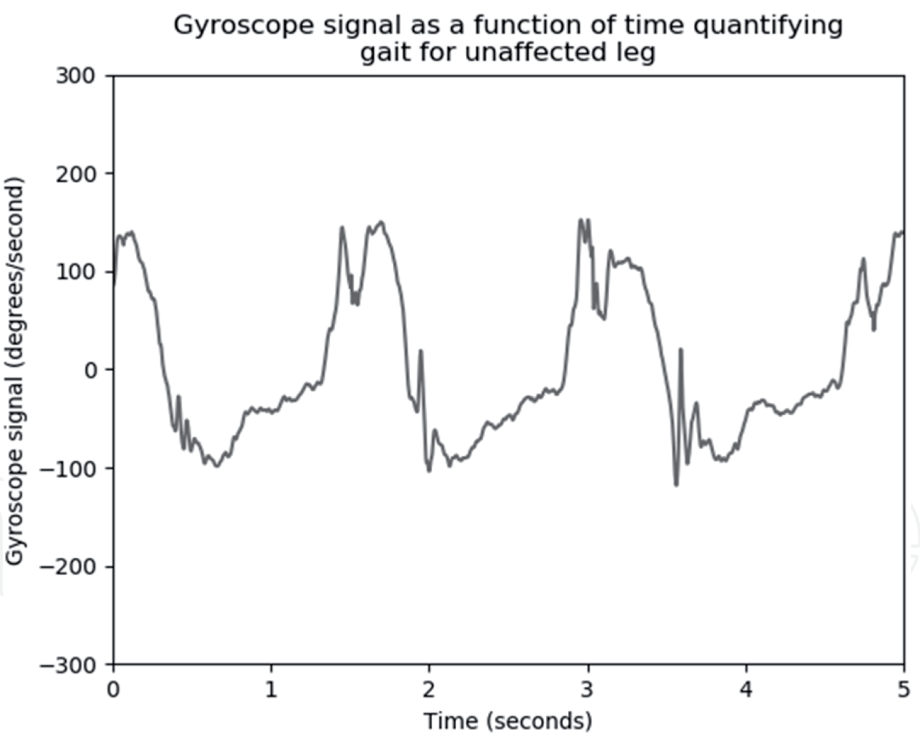

Figure 7.
The BioStamp nPoint conformal wearable and wireless inertial sensor signal for the unaffected leg [91].

The gyroscope signal revealed notable disparity respective of the affected leg and unaffected leg during gait as presented in **Figures 6** and 7 respectively. Post-processing of the gyroscope signal data consolidated a feature set consisting of five numeric attributes based on descriptive statistics, such as maximum, minimum, mean, standard deviation, and coefficient of variation. Multiple machine learning classification algorithms, such as the support vector machine and multilayer perceptron neural network, achieved considerable classification accuracy to distinguish between the hemiplegic affected leg and unaffected leg [91, 92].

7. Evolutionary pathway for Network Centric Therapy with respect to quantification of movement disorders, such as Parkinson's disease and Essential tremor

Functionally wearable accelerometer systems have been demonstrated for the quantification of movement disorder and also their response to intervention strategy [11, 12, 93–98]. With the evolution of wireless technology other traditional inertial signal data transfer strategies have become effectively obsolete [99]. Intuitively, the G-link wireless accelerometer was a candidate for testing and evaluating the quantification of tremor associated with movement disorders [11, 12, 100–103].

Preliminary demonstration of the G-link wireless accelerometer showed the ability to quantify simulated Parkinson's disease hand tremor by mounting the device to the dorsum of the hand [100, 101]. Eventually simulated Parkinson's disease tremor was contrasted to a static condition. Post-processing of the signal data involved the time averaged acceleration, for which statistical significance was achieved [100]. A similar wireless inertial sensor system configuration was successfully demonstrated for the quantification of Parkinson's disease hand tremor within this timeframe [104].

LeMoyne and Mastroianni during 2010 extended the capability of wearable and wireless inertial sensor systems for quantifying Parkinson disease hand tremor through the application of a smartphone. A software application enabled the smartphone to quantify hand tremor for a prescribed temporal duration through the smartphone's internal accelerometer. The accelerometer signal data was conveyed by wireless connectivity to the Internet as an email attachment. Statistical significance was achieved with respect to the subject with Parkinson's disease hand tremor and subject without Parkinson disease. Notably, the experiment occurred in metropolitan Pittsburgh, Pennsylvania and the post-processing was conducted in the general area of Los Angeles, California [105]. The research team observed that experimental and post-processing resources could be geographically separated anywhere in the world with Internet access [1, 2, 5–10, 105, 106]. This observation constitutes the origins of Network Centric Therapy with regards to movement disorders [1, 2, 5–7, 106].

Using the smartphone as an inertial sensor platform with wearable properties the recorded signal data can represent instrumental feedback with respect to the efficacy of therapy response. For example, with machine learning classification the smartphone functioning as a wearable and wireless inertial sensor platform can distinguish between deep brain stimulation set to 'On' and 'Off' status. A person with Essential tremor performed a reach and grasp task with a smartphone mounted to the dorsum of the hand by a latex glove. Post-processing consolidated the inertial signal data to a feature set amenable for machine learning classification, and considerable classification accuracy was achieved through the application of a support vector machine to differentiate between deep brain stimulation set to 'On' and 'Off' status [107]. In conjunction with the preliminary success of the research with respect to Essential tremor and deep brain stimulation set to 'On' and 'Off' status the multilayer perceptron neural network also attained considerable machine learning classification accuracy for differentiating these deep brain stimulation settings [108].

Another extrapolation of this research perspective involved considering six machine learning algorithms: multilayer perceptron neural network, support vector machine, K-nearest neighbors, logistic regression, J48 decision tree, and random forest. The reach and grasp task was applied for a subject with Essential tremor treated by deep brain stimulation with respect to 'On' and 'Off' status. Three feature set scenarios were addressed to determine the most appropriate machine learning algorithms: accelerometer and gyroscope signal recordings, accelerometer signal recordings, and gyroscope signal recordings. The multilayer perceptron neural network, support vector machine, K-nearest neighbors, and logistic regression achieved the highest classification accuracy in consideration of these three feature set scenarios [109].

The accelerometer and gyroscope intrinsic to the smartphone was also applied for the evaluation of deep brain stimulation efficacy for the treatment of Parkinson's disease. Deep brain stimulation was set to 'On' and 'Off' status with the hand tremor response measured by a smartphone mounted to the dorsum of the hand through a latex glove. Multiple machine learning algorithms were evaluated: multilayer perceptron neural network, support vector machine, K-nearest neighbors, logistic regression, J48 decision tree, and random forest. The feature set consisted of descriptive statistics for both the accelerometer and gyroscope signal data. Two performance parameters were considered, such as classification accuracy and time to develop the machine learning model. The support vector machine and logistic regression best satisfied these two performance parameters [110]. The multilayer perceptron neural network achieved considerable classification accuracy to distinguish between the deep brain stimulation set to 'On' and 'Off' status for Parkinson's disease hand tremor, but the time to develop the model was considerably protracted [110, 111].

Network Centric Therapy was further realized for the domain of movement disorders through the BioStamp nPoint. The BioStamp nPoint is a conformal wearable and wireless inertial sensor system with segmented operation and wireless transmission of signal data to a secure Cloud computing environment with wireless connectivity to a smartphone and tablet. The conformal sensors also have a mass less than ten grams and a profile on the order of a bandage. Additionally, the BioStamp nPoint is certified as an FDA 510(k) medical device for the acquisition of medical grade data [5, 90]. These attributes of the BioStamp nPoint ideally accommodate the quantification of movement disorder tremor response, such as for Parkinson's disease, based on deep brain stimulation intervention through mounting about the dorsum of the hand using an adhesive medium as illustrated in **Figure 8** [112].

Multiple sets of deep brain stimulation parameter configurations have been evaluated for the treatment of Parkinson's disease using the BioStamp nPoint to quantify the response and machine learning to distinguish the respective parameter configurations [112–115]. The BioStamp nPoint was mounted to the dorsum of

Figure 8.
The BioStamp nPoint conformal wearable and wireless inertial sensor system mounted about the dorsum of the hand for quantifying movement disorder tremor response, such as for Parkinson's disease, as a result of deep brain stimulation intervention [112].

the hand through an adhesive medium. The deep brain stimulation amplitude was evaluated at multiple settings, such as 'Off' status as a baseline, amplitude set to 1.0 mA, 2.5 mA, and 4.0 mA. The acceleration signal derived from the BioStamp nPoint conformal wearable and wireless inertial sensor system was post-processed to present the acceleration magnitude as illustrated in **Figures 9**–**12** [112].

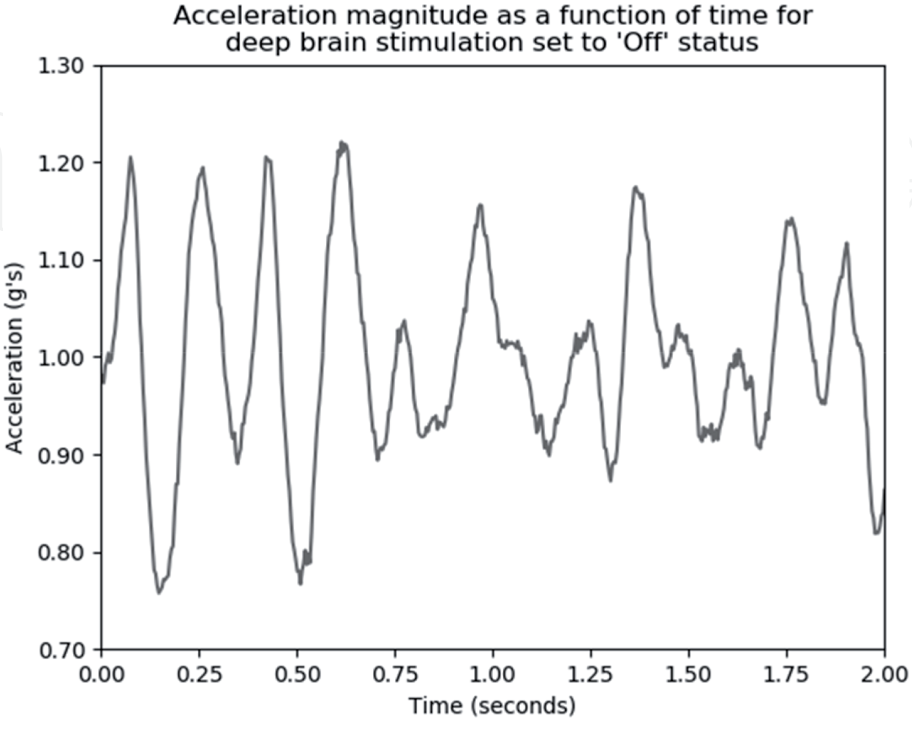

Figure 9.
Acceleration magnitude derived from the BioStamp nPoint conformal wearable and wireless inertial sensor system for hand tremor from a subject with Parkinson's disease with deep brain stimulation set to 'Off' status [112].

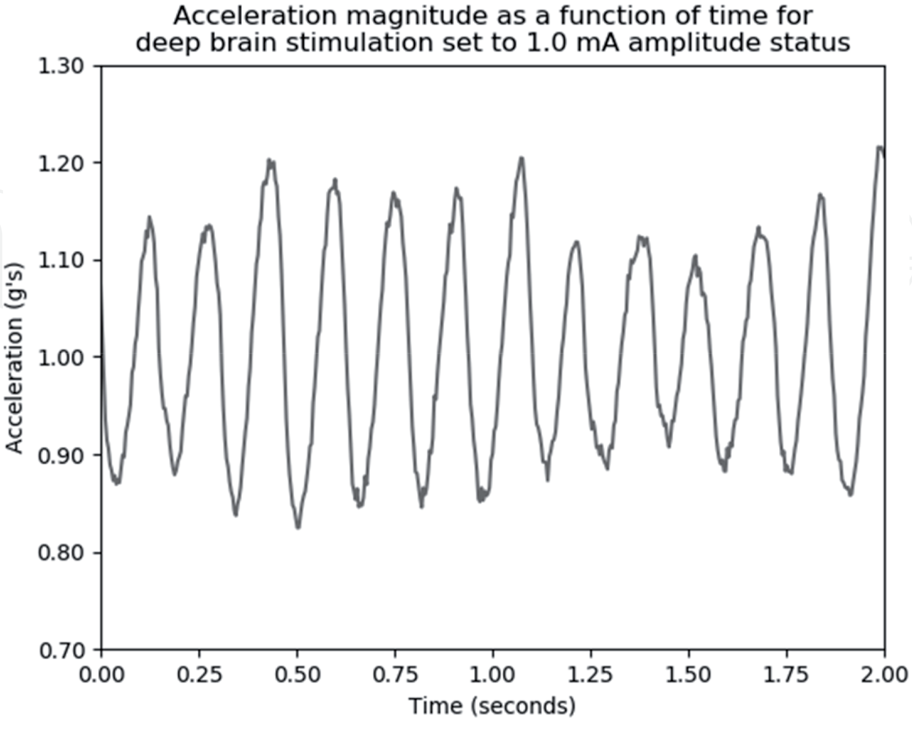

Figure 10.
Acceleration magnitude derived from the BioStamp nPoint conformal wearable and wireless inertial sensor system for hand tremor from a subject with Parkinson's disease with deep brain stimulation set to amplitude equal to 1.0 mA [112].

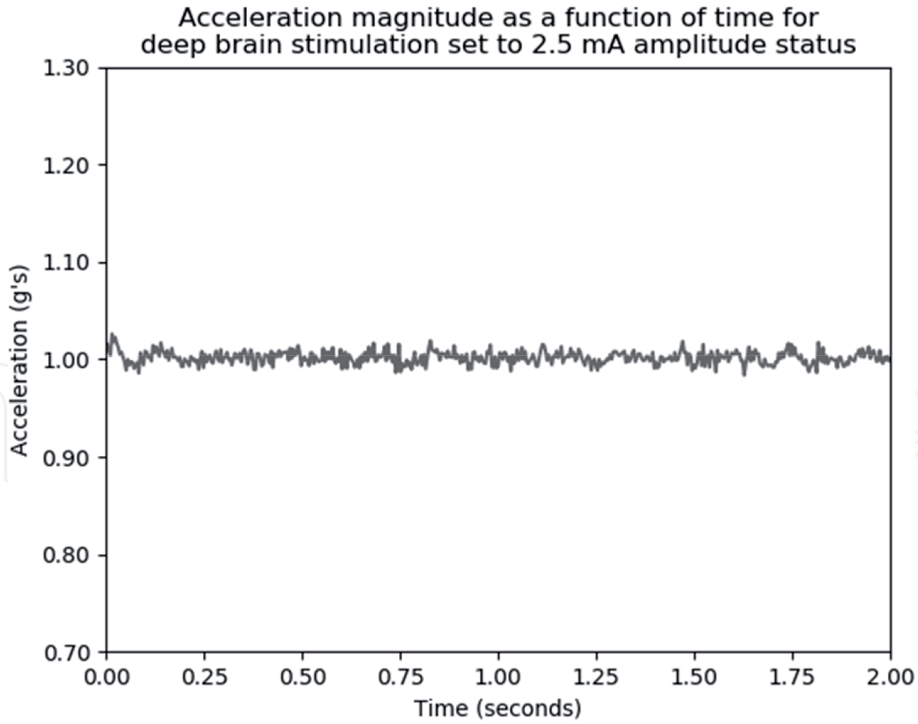

Figure 11.
Acceleration magnitude derived from the BioStamp nPoint conformal wearable and wireless inertial sensor system for hand tremor from a subject with Parkinson's disease with deep brain stimulation set to amplitude equal to 2.5 mA [112].

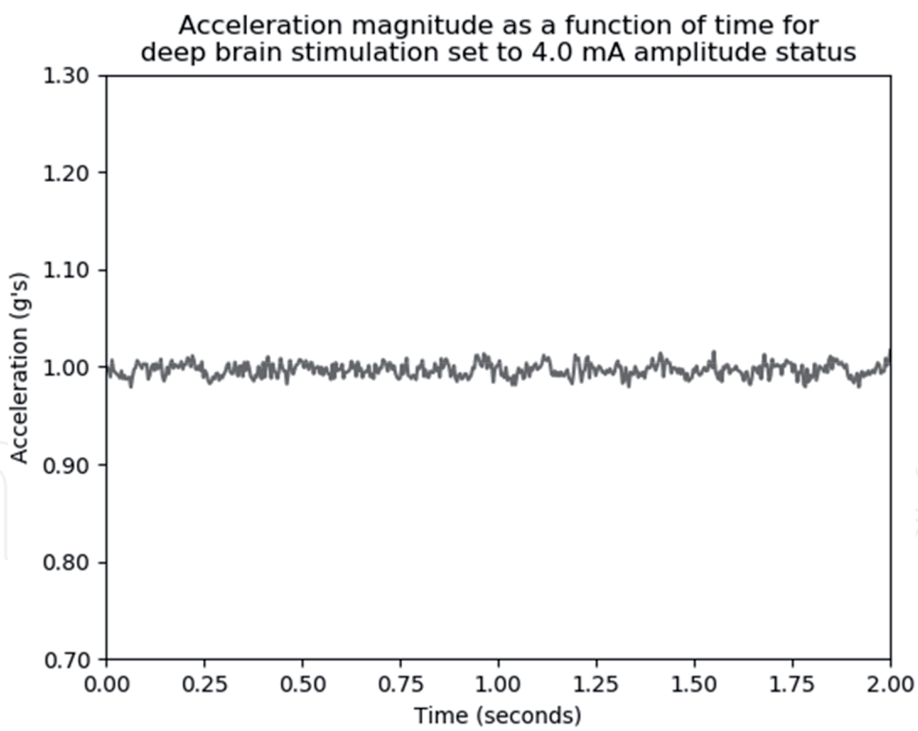

Figure 12.
Acceleration magnitude derived from the BioStamp nPoint conformal wearable and wireless inertial sensor system for hand tremor from a subject with Parkinson's disease with deep brain stimulation set to amplitude equal to 4.0 mA [112].

The acceleration magnitude signal data was consolidated to a feature set though Python. The feature set was composed of numeric attributes, such as maximum, minimum, mean, standard deviation, and coefficient of variation. Machine learning algorithms, such as J48 decision tree, K-nearest neighbors, support vector machine, logistic regression, and random forest were contrasted in terms of their classification accuracy and time to develop the machine learning model. Based on these criteria the K-nearest neighbors machine learning algorithm displayed the optimal satisfaction of classification accuracy in conjunction with time to develop the machine learning model and the support vector machine achieved the optimal classification accuracy [112]. The multilayer perceptron neural network also demonstrated considerable classification accuracy [113].

Deep learning was then applied to distinguish between deep brain stimulation parameter configuration settings for the treatment of Parkinson's disease, such as 'Off' status as a baseline, amplitude set to 1.0 mA, amplitude set to 1.75 mA, amplitude set to 2.5 mA, amplitude set to 3.25 mA, and amplitude set to 4.0 mA. The BioStamp nPoint conformal wearable and wireless inertial sensor system provided the accelerometer signal data. The post-processing was facilitated by Google Colab and TensorFlow to implement a convolutional neural network. The convolutional neural network achieved considerable classification accuracy to distinguish between all six of these parameter configurations [116, 117].

8. Future perspectives for Network Centric Therapy for reflex, gait, and movement disorder assessment with machine learning

Network Centric Therapy is anticipated to have a transformative influence on the healthcare and biomedical industry. Conformal wearable and wireless inertial sensor systems are envisioned to enable historical and distinctly quantified data for subjects undergoing rehabilitation and subjects with neurodegenerative movement disorders, such as Parkinson's disease and Essential tremor. Data science methodologies can be incorporated to optimize the respective therapy strategy. With the amalgamation of machine learning and eventually deep learning conformal wearable and wireless inertial sensor systems are predicted to considerably advance augmented clinical situational awareness for diagnostic and prognostic capabilities. In particular, with the Cloud computing accessibility intrinsic to Network Centric Therapy, the most talented clinical resources from anywhere in the world can provide optimal patient specific rehabilitation and therapy to subjects from the convenience of a homebound setting. Additionally, the inherent aspects of Network Centric Therapy, such as conformal wearable and wireless inertial sensor systems, machine learning, and Cloud computing access, imply a plausible pathway to the closed-loop optimization of deep brain stimulation parameter configurations.

9. Conclusion

The evolutionary perspective for the advent of Network Centric Therapy for the domains of assessing reflex, gait, and movement disorders have been thoroughly discussed. Inherent aspects pertaining to Network Centric Therapy involve wearable and wireless inertial sensor systems, machine learning, and Cloud computing access for the acquired inertial sensor signal data. The implications are that expert clinicians can access a patient's health status based on the wearable and wireless inertial sensor system signal data from anywhere in the world. These achievements constitute a significant evolution relative to traditional ordinal scale methodologies and electro-mechanical signal data obtained by clinical laboratory resources. Conformal wearable and wireless inertial sensor systems have further evolved the capabilities of Network Centric Therapy. In the future Network Centric Therapy is envisioned to augment clinical diagnostic and prognostic acuity, optimize rehabilitation, and enable closed-loop optimization of deep brain stimulation parameter configurations.

Author details

Robert LeMoyne[1]* and Timothy Mastroianni[2]

1 Department of Biological Sciences, Northern Arizona University, Flagstaff, AZ, USA

2 Founder of Cognition Engineering, Pittsburgh, PA, USA

*Address all correspondence to: robert.lemoyne@nau.edu; rlemoyne07@gmail.com

References

[1] LeMoyne R, Mastroianni T, Whiting D, Tomycz N. Wearable and Wireless Systems for Healthcare II: Movement Disorder Evaluation and Deep Brain Stimulation Systems. Springer, Singapore; 2019.

[2] LeMoyne R, Mastroianni T, Whiting D, Tomycz N. Wearable and Wireless Systems for Movement Disorder Evaluation and Deep Brain Stimulation Systems. Wearable and Wireless Systems for Healthcare II: Movement Disorder Evaluation and Deep Brain Stimulation Systems 2019 (pp. 1-15). Springer, Singapore.

[3] LeMoyne R, Mastroianni T. Wearable and Wireless Systems for Healthcare I: Gait and Reflex Response Quantification. Springer, Singapore; 2018.

[4] LeMoyne R, Mastroianni T. Wearable and Wireless Systems for Gait Analysis and Reflex Quantification. Wearable and Wireless Systems for Healthcare I: Gait and Reflex Response Quantification 2018 (pp. 1-20). Springer, Singapore.

[5] LeMoyne R, Mastroianni T. Machine Learning Classification for Network Centric Therapy Utilizing the Multilayer Perceptron Neural Network. Multilayer Perceptrons: Theory and Applications 2020 (pp. 39-76). Nova Science Publishers, Hauppauge, NY.

[6] LeMoyne R, Mastroianni T. Chapter 7 Network Centric Therapy for Wearable and Wireless Systems. Smartphones: Recent Innovations and Applications, 2019 Nova Science Publishers, Hauppauge, NY.

[7] LeMoyne R, Mastroianni T. Smartphone and portable media device: a novel pathway toward the diagnostic characterization of human movement. Smartphones from an Applied Research Perspective. 2017 (pp. 1-24). InTech, Rijeka, Croatia.

[8] LeMoyne R, Mastroianni T. Wearable and wireless gait analysis platforms: smartphones and portable media devices. Wireless MEMS Networks and Applications 2017 (pp. 129-152). Elsevier, New York.

[9] LeMoyne R, Mastroianni T. Telemedicine perspectives for wearable and wireless applications serving the domain of neurorehabilitation and movement disorder treatment. Telemedicine 2016 (pp. 1-10). SMGroup, Dover, Delaware.

[10] LeMoyne R, Mastroianni T. Use of smartphones and portable media devices for quantifying human movement characteristics of gait, tendon reflex response, and Parkinson's disease hand tremor. Mobile Health Technologies: Methods and Protocols 2015 (pp. 335-358). Springer, New York.

[11] LeMoyne R, Coroian C, Mastroianni T, Opalinski P, Cozza M, Grundfest W. The merits of artificial proprioception, with applications in biofeedback gait rehabilitation concepts and movement disorder characterization. Biomedical Engineering 2009 (pp. 165-98). InTech Vienna.

[12] LeMoyne R, Coroian C, Mastroianni T, Grundfest W. Accelerometers for quantification of gait and movement disorders: a perspective review. Journal of Mechanics in Medicine and Biology. 2008 Jun;8(02):137-152.

[13] Culhane KM, O'connor M, Lyons D, Lyons GM. Accelerometers in rehabilitation medicine for older adults. Age and Ageing. 2005 Nov;34(6):556-560.

[14] Inman VT, Eberhart HD. The major determinants in normal and pathological gait. The Journal of Bone and Joint Surgery. 1953 Jul;35(3):543-558.

[15] LeMoyne R, Mastroianni T. The rise of inertial measurement units. Wearable and Wireless Systems for Healthcare I: Gait and Reflex Response Quantification 2018 (pp. 45-58). Springer, Singapore.

[16] LeMoyne R, Mastroianni T. Traditional Clinical Evaluation of Gait and Reflex Response by Ordinal Scale. Wearable and Wireless Systems for Healthcare I: Gait and Reflex Response Quantification 2018 (pp. 21-29). Springer, Singapore.

[17] LeMoyne R, Mastroianni T, Coroian C, Grundfest W. Tendon reflex and strategies for quantification, with novel methods incorporating wireless accelerometer reflex quantification devices, a perspective review. Journal of Mechanics in Medicine and Biology. 2011 Jun;11(03):471-513.

[18] LeMoyne RC. Wireless Quantified Reflex Device. University of California, Los Angeles (Ph.D. Dissertation); 2010.

[19] Litvan I, Mangone CA, Werden W, Bueri JA, Estol CJ, Garcea DO, Rey RC, Sica RE, Hallett M, Bartko JJ. Reliability of the NINDS myotatic reflex scale. Neurology. 1996 Oct;47(4):969-972.

[20] Manschot S, Van Passel L, Buskens E, Algra A, Van Gijn J. Mayo and NINDS scales for assessment of tendon reflexes: between observer agreement and implications for communication. Journal of Neurology, Neurosurgery & Psychiatry. 1998 Feb;64(2):253-255.

[21] Stam J, Van Crevel H. Reliability of the clinical and electromyographic examination of tendon reflexes. Journal of Neurology. 1990 Nov;237(7):427-431.

[22] Perry J, Garrett M, Gronley JK, Mulroy SJ. Classification of walking handicap in the stroke population. Stroke. 1995 Jun;26(6):982-989.

[23] Lord SE, Rochester L. Measurement of community ambulation after stroke: current status and future developments. Stroke. 2005 Jul;36(7):1457-1461.

[24] Ferrarello F, Bianchi VA, Baccini M, Rubbieri G, Mossello E, Cavallini MC, Marchionni N, Di Bari M. Tools for observational gait analysis in patients with stroke: a systematic review. Physical Therapy. 2013 Dec;93(12):1673-1685.

[25] Brunnekreef JJ, Van Uden CJ, van Moorsel S, Kooloos JG. Reliability of videotaped observational gait analysis in patients with orthopedic impairments. BMC Musculoskeletal Disorders. 2005 Dec;6(1):17.

[26] LeMoyne R, Mastroianni T, Whiting D, Tomycz N. Traditional Ordinal Strategies for Establishing the Severity and Status of Movement Disorders, Such as Parkinson's Disease and Essential Tremor. Wearable and Wireless Systems for Healthcare II: Movement Disorder Evaluation and Deep Brain Stimulation Systems 2019 (pp. 25-36). Springer, Singapore.

[27] Ramaker C, Marinus J, Stiggelbout AM, Van Hilten BJ. Systematic evaluation of rating scales for impairment and disability in Parkinson's disease. Movement Disorders. 2002 Sep;17(5):867-876.

[28] Post B, Merkus MP, de Bie RM, de Haan RJ, Speelman JD. Unified Parkinson's disease rating scale motor examination: are ratings of nurses, residents in neurology, and movement disorders specialists interchangeable? Movement Disorders. 2005 Dec;20(12):1577-1584.

[29] Goetz CG, Stebbins GT, Chmura TA, Fahn S, Poewe W, Tanner CM. Teaching program for the movement disorder society-sponsored revision of the

Unified Parkinson's Disease Rating Scale:(MDS-UPDRS). Movement Disorders. 2010 Jul;25(9):1190-1194.

[30] Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. The unified Parkinson's disease rating scale (UPDRS): status and recommendations. Movement Disorders. 2003 Jul;18(7):738-750.

[31] Van de Crommert HW, Faist M, Berger W, Duysens J. Biceps femoris tendon jerk reflexes are enhanced at the end of the swing phase in humans. Brain Research. 1996 Sep;734(1-2):341-344.

[32] Faist M, Ertel M, Berger W, Dietz V. Impaired modulation of quadriceps tendon jerk reflex during spastic gait: differences between spinal and cerebral lesions. Brain. 1999 Mar;122(3):567-579.

[33] Cozens JA, Miller S, Chambers IR, Mendelow AD. Monitoring of head injury by myotatic reflex evaluation. Journal of Neurology, Neurosurgery & Psychiatry. 2000 May;68(5):581-588.

[34] Pagliaro P, Zamparo P. Quantitative evaluation of the stretch reflex before and after hydro kinesy therapy in patients affected by spastic paresis. Journal of Electromyography and Kinesiology. 1999 Apr;9(2):141-148.

[35] Zhang LQ, Wang G, Nishida T, Xu D, Sliwa JA, Rymer WZ. Hyperactive tendon reflexes in spastic multiple sclerosis: measures and mechanisms of action. Archives of Physical Medicine and Rehabilitation. 2000 Jul;81(7):901-909.

[36] Koceja DM, Kamen GA. Conditioned patellar tendon reflexes in sprint-and endurance-trained athletes. Medicine and Science in Sports and Exercise. 1988 Apr;20(2):172-177.

[37] Kamen G, Koceja DM. Contralateral influences on patellar tendon reflexes in young and old adults. Neurobiology of Aging. 1989 Jul;10(4):311-315.

[38] Lebiedowska MK, Fisk JR. Quantitative evaluation of reflex and voluntary activity in children with spasticity. Archives of Physical Medicine and Rehabilitation. 2003 Jun;84(6):828-837.

[39] LeMoyne R, Coroian C, Mastroianni T, Grundfest W. Quantified deep tendon reflex device for response and latency, third generation. Journal of Mechanics in Medicine and Biology. 2008 Dec;8(04):491-506.

[40] LeMoyne R, Mastroianni T, Kale H, Luna J, Stewart J, Elliot S, Bryan F, Coroian C, Grundfest W. Fourth generation wireless reflex quantification system for acquiring tendon reflex response and latency. Journal of Mechanics in Medicine and Biology. 2011 Mar;11(01):31-54.

[41] Mamizuka N, Sakane M, Kaneoka K, Hori N, Ochiai N. Kinematic quantitation of the patellar tendon reflex using a tri-axial accelerometer. Journal of Biomechanics. 2007 Jan;40(9):2107-2111.

[42] Tham LK, Osman NA, Abas WA, Lim KS. The validity and reliability of motion analysis in patellar tendon reflex assessment. PLoS One. 2013 Feb;8(2):e55702.

[43] Tham LK, Osman NA, Lim KS, Pingguan-Murphy B, Abas WW, Zain NM. Investigation to predict patellar tendon reflex using motion analysis technique. Medical Engineering & Physics. 2011 May;33(4):407-410.

[44] Chandrasekhar A, Osman NA, Tham LK, Lim KS, Abas WA. Influence of age on patellar tendon reflex response. PLoS One. 2013 Nov;8(11):e80799.

[45] Dobkin BH. The Clinical Science of Neurologic Rehabilitation. Oxford University Press, New York; 2003.

[46] Winter DA. Biomechanics and Motor Control of Human Movement. Wiley-Interscience, New York; 1990.

[47] LeMoyne R, Mastroianni T. Quantification Systems Appropriate for a Clinical Setting. Wearable and Wireless Systems for Healthcare I: Gait and Reflex Response Quantification 2018 (pp. 31-44). Springer, Singapore.

[48] LeMoyne R. Testing and Evaluation Strategies for the Powered Prosthesis, a Global Perspective. Advances for Prosthetic Technology 2016 (pp. 37-58). Springer, Tokyo.

[49] Begg R, Kamruzzaman J. A machine learning approach for automated recognition of movement patterns using basic, kinetic and kinematic gait data. Journal of Biomechanics. 2005 Mar;38(3):401-408.

[50] Begg RK, Palaniswami M, Owen B. Support vector machines for automated gait classification. IEEE transactions on Biomedical Engineering. 2005 Apr;52(5):828-838.

[51] LeMoyne R, Mastroianni T. Classification of software control architectures for a powered prosthesis through conventional gait analysis using machine learning applications. Journal of Mechanics in Medicine and Biology. 2019 Sep;19(06):1950044.

[52] LeMoyne R, Mastroianni T, Hessel A, Nishikawa K. Application of a multilayer perceptron neural network for classifying software platforms of a powered prosthesis through a force plate. In Proceedings of IEEE 14th International Conference on Machine Learning and Applications (ICMLA) 2015 Dec (pp. 402-405).

[53] LeMoyne R, Mastroianni T, Hessel A, Nishikawa K. Implementation of machine learning for classifying prosthesis type through conventional gait analysis. In Proceedings of 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2015 Aug (pp. 202-205).

[54] LeMoyne R, Kerr W, Mastroianni T, Hessel A. Implementation of machine learning for classifying hemiplegic gait disparity through use of a force plate. In Proceedings of IEEE 13th International Conference on Machine Learning and Applications 2014 Dec (pp. 379-382).

[55] LeMoyne R, Jafari R, Jea D, Srivastava M, Sarrafzadeh M. Fully quantified evaluation of myotatic stretch reflex. In Proceedings of 35th Society for Neuroscience Annual Meeting; Washington D.C. 2005 Nov.

[56] LeMoyne R, Dabiri F, Jafari R. Quantified deep tendon reflex device, second generation. Journal of Mechanics in Medicine and Biology. 2008 Mar;8(01):75-85.

[57] LeMoyne R, Mastroianni T, Coroian C, Grundfest W. Wireless three dimensional accelerometer reflex quantification device with artificial reflex system. Journal of Mechanics in Medicine and Biology. 2010 Sep;10(03):401-415.

[58] LeMoyne R, Coroian C, Mastroianni T. Evaluation of a wireless three dimensional MEMS accelerometer reflex quantification device using an artificial reflex system. In Proceedings of IEEE ICME International Conference on Complex Medical Engineering 2009 Apr (pp. 1-5).

[59] LeMoyne R, Mastroianni T, Grundfest W. iPhone wireless accelerometer reflex quantification system using an artificial tendon reflex device. In Proceedings of 43rd Society for Neuroscience Annual Meeting; San Diego, CA 2013 Nov.

[60] LeMoyne R, Kerr WT, Zanjani K, Mastroianni T. Implementation of an iPod wireless accelerometer application

using machine learning to classify disparity of hemiplegic and healthy patellar tendon reflex pair. Journal of Medical Imaging and Health Informatics. 2014 Mar;4(1):21-28.

[61] LeMoyne R, Mastroianni T. Smartphone wireless gyroscope platform for machine learning classification of hemiplegic patellar tendon reflex pair disparity through a multilayer perceptron neural network. In Proceedings of IEEE Wireless Health (WH) 2016 Oct (pp. 1-6).

[62] LeMoyne R, Mastroianni T. Implementation of a smartphone wireless gyroscope platform with machine learning for classifying disparity of a hemiplegic patellar tendon reflex pair. Journal of Mechanics in Medicine and Biology. 2017 Sep;17(06):1750083.

[63] LeMoyne R, Mastroianni T, Grundfest W. Quantified reflex strategy using an iPod as a wireless accelerometer application. In Proceedings of 34th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2012 Aug (pp. 2476-2479).

[64] LeMoyne R, Mastroianni T, Grundfest W, Nishikawa K. Implementation of an iPhone wireless accelerometer application for the quantification of reflex response. In Proceedings of 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2013 Jul (pp. 4658-4661).

[65] LeMoyne R, Mastroianni T. Quantification of patellar tendon reflex response using an iPod wireless gyroscope application with experimentation conducted in Lhasa, Tibet and post-processing conducted in Flagstaff, Arizona through wireless Internet connectivity. In Proceedings of 44th Society for Neuroscience Annual Meeting; Washington D.C. 2014 Nov.

[66] LeMoyne R, Mastroianni T. Implementation of a multilayer perceptron neural network for classifying a hemiplegic and healthy reflex pair using an iPod wireless gyroscope platform. In Proceedings of 46th Society for Neuroscience Annual Meeting; San Diego, CA 2016 Nov.

[67] LeMoyne R, Mastroianni T. Machine learning classification of a hemiplegic and healthy patellar tendon reflex pair through an iPod wireless gyroscope platform. In Proceedings of 45th Society for Neuroscience Annual Meeting; Chicago, IL 2015 Oct.

[68] LeMoyne R, Mastroianni T. Implementation of a smartphone as a wireless gyroscope application for the quantification of reflex response. In Proceedings of 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2014 Aug (pp. 3654-3657).

[69] Bamberg SJ, Benbasat AY, Scarborough DM, Krebs DE, Paradiso JA. Gait analysis using a shoe-integrated wireless sensor system. IEEE Transactions on Information Technology in Biomedicine. 2008 Jul;12(4):413-423.

[70] Lee JA, Cho SH, Lee JW, Lee KH, Yang HK. Wearable accelerometer system for measuring the temporal parameters of gait. In Proceedings of 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2007 Aug (pp. 483-486).

[71] Saremi K, Marehbian J, Yan X, Regnaux JP, Elashoff R, Bussel B, Dobkin BH. Reliability and validity of bilateral thigh and foot accelerometry measures of walking in healthy and hemiparetic subjects. Neurorehabilitation and Neural Repair. 2006 Jun;20(2):297-305.

[72] Kavanagh JJ, Morrison S, James DA, Barrett R. Reliability of segmental accelerations measured

using a new wireless gait analysis system. Journal of Biomechanics. 2006 Jan;39(15):2863-2872.

[73] LeMoyne R, Mastroianni T, Grundfest W. Wireless accelerometer system for quantifying disparity of hemiplegic gait using the frequency domain. Journal of Mechanics in Medicine and Biology. 2013 Jun;13(03):1350035.

[74] LeMoyne R, Coroian C, Mastroianni T, Grundfest W. Wireless accelerometer assessment of gait for quantified disparity of hemiparetic locomotion. Journal of Mechanics in Medicine and Biology. 2009 Sep;9(03):329-343.

[75] Lemoyne R, Coroian C, Mastroianni T. Wireless accelerometer system for quantifying gait. In Proceedings of IEEE ICME International Conference on Complex Medical Engineering 2009 Apr (pp. 1-4).

[76] LeMoyne R, Coroian C, Mastroianni T, Grundfest W. Virtual proprioception. Journal of Mechanics in Medicine and Biology. 2008 Sep;8(03):317-338.

[77] LeMoyne R, Mastroianni T, Cozza M, Coroian C, Grundfest W. Implementation of an iPhone as a wireless accelerometer for quantifying gait characteristics. In Proceedings of 32nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2010 Aug (pp. 3847-3851).

[78] LeMoyne R, Mastroianni T. Smartphones and Portable Media Devices as Wearable and Wireless Systems for Gait and Reflex Response Quantification. Wearable and Wireless Systems for Healthcare I: Gait and Reflex Response Quantification 2018 (pp. 73-93). Springer, Singapore.

[79] LeMoyne R, Mastroianni T, Cozza M, Coroian C. Quantification of gait characteristics through a functional iPhone wireless accelerometer application mounted to the spine. In Proceedings of Frontiers in Biomedical Devices 2010 Sep (Vol. 49453, pp. 87-88). American Society of Mechanical Engineers.

[80] LeMoyne R, Mastroianni T, Cozza M, Coroian C. iPhone wireless accelerometer application for acquiring quantified gait attributes. In Proceedings of Frontiers in Biomedical Devices 2010 Sep (Vol. 49453, pp. 19-20). American Society of Mechanical Engineers.

[81] LeMoyne R, Mastroianni T, Grundfest W. Wireless accelerometer iPod application for quantifying gait characteristics. In Proceedings of 33rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2011 Sep (pp. 7904-7907).

[82] LeMoyne R, Mastroianni T. Implementation of an iPod application as a wearable and wireless accelerometer system for identifying quantified disparity of hemiplegic gait. Journal of Medical Imaging and Health Informatics. 2014 Aug;4(4):634-641.

[83] LeMoyne R, Mastroianni T. Implementation of a smartphone as a wireless accelerometer platform for quantifying hemiplegic gait disparity in a functionally autonomous context. Journal of Mechanics in Medicine and Biology. 2018 Mar;18(02):1850005.

[84] LeMoyne R, Mastroianni T. Implementation of a smartphone as a wearable and wireless gyroscope platform for machine learning classification of hemiplegic gait through a multilayer perceptron neural network. In Proceedings of IEEE 17th International Conference on Machine Learning and Applications (ICMLA) 2018 Dec (pp. 946-950).

[85] Capela NA, Lemaire ED, Baddour N. Novel algorithm for a smartphone-based

6-minute walk test application: algorithm, application development, and evaluation. Journal of Neuroengineering and Rehabilitation. 2015 Dec;12(1):19.

[86] Galán-Mercant A, Barón-López FJ, Labajos-Manzanares MT, Cuesta-Vargas AI. Reliability and criterion-related validity with a smartphone used in timed-up-and-go test. Biomedical Engineering Online. 2014 Dec;13(1):156.

[87] Mellone S, Tacconi C, Chiari L. Validity of a smartphone-based instrumented Timed Up and Go. Gait & Posture. 2012 May;36(1):163-165.

[88] LeMoyne R, Mastroianni T. Bluetooth Inertial Sensors for Gait and Reflex Response Quantification with Perspectives Regarding Cloud Computing and the Internet of Things. Wearable and Wireless Systems for Healthcare I: Gait and Reflex Response Quantification 2018 (pp. 95-103). Springer, Singapore.

[89] LeMoyne R, Heerinckx F, Aranca T, De Jager R, Zesiewicz T, Saal HJ. Wearable body and wireless inertial sensors for machine learning classification of gait for people with Friedreich's ataxia. In Proceedings of IEEE 13th International Conference on Wearable and Implantable Body Sensor Networks (BSN) 2016 Jun (pp. 147-151).

[90] MC10Inc. [https://www.mc10inc.com/our-products#biostampnpoint].

[91] LeMoyne R, Mastroianni T. Network Centric Therapy for machine learning classification of hemiplegic gait through conformal wearable and wireless inertial sensors. In Proceedings of IEEE 8th E-Health and Bioengineering Conference (EHB) 2020 Oct. Oct (pp. 1-4).

[92] LeMoyne R, Mastroianni T. Conformal wearable and wireless inertial sensor system for the machine learning classification of hemiplegic gait using a multilayer perceptron neural network. 2020 8th International Conference on Bioinformatics and Computational Biology (ICBCB) 2020 May.

[93] Gurevich TY, Shabtai H, Korczyn AD, Simon ES, Giladi N. Effect of rivastigmine on tremor in patients with Parkinson's disease and dementia. Movement Disorders. 2006 Oct;21(10):1663-1666.

[94] Keijsers NL, Horstink MW, Gielen SC. Ambulatory motor assessment in Parkinson's disease. Movement Disorders. 2006 Jan;21(1):34-44.

[95] Kumru H, Summerfield C, Valldeoriola F, Valls-Solé J. Effects of subthalamic nucleus stimulation on characteristics of EMG activity underlying reaction time in Parkinson's disease. Movement Disorders. 2004 Jan;19(1):94-100.

[96] Obwegeser AA, Uitti RJ, Witte RJ, Lucas JA, Turk MF, Wharen Jr RE. Quantitative and qualitative outcome measures after thalamic deep brain stimulation to treat disabling tremors. Neurosurgery. 2001 Feb;48(2):274-284.

[97] Keijsers NL, Horstink MW, Van Hilten JJ, Hoff JI, Gielen CC. Detection and assessment of the severity of Levodopa-induced dyskinesia in patients with Parkinson's disease by neural networks. Movement Disorders. 2000 Nov;15(6):1104-1111.

[98] Schrag A, Schelosky L, Scholz U, Poewe W. Reduction of parkinsonian signs in patients with Parkinson's disease by dopaminergic versus anticholinergic single-dose challenges. Movement Disorders. 1999 Mar;14(2):252-255.

[99] Patel S, Park H, Bonato P, Chan L, Rodgers M. A review of wearable sensors and systems with application in rehabilitation. Journal of Neuroengineering and Rehabilitation. 2012 Dec;9(1):1-17.

[100] LeMoyne R, Mastroianni T, Grundfest W. Wireless accelerometer configuration for monitoring Parkinson's disease hand tremor. Advances in Parkinson's Disease. 2013 May; 2(2):62-67.

[101] LeMoyne R, Coroian C, Mastroianni T. Quantification of Parkinson's disease characteristics using wireless accelerometers. In Proceedings of IEEE ICME International Conference on Complex Medical Engineering 2009 Apr (pp. 1-5).

[102] LeMoyne R, Coroian C, Mastroianni T. 3D wireless accelerometer characterization of Parkinson's disease status. Plasticity and Repair in Neurodegenerative Disorders (Conference) 2008.

[103] LeMoyne R. Gradient optimized neuromodulation for Parkinson's disease. 12th Annual UCLA Research Conference on Aging 2007.

[104] Giuffrida JP, Riley DE, Maddux BN, Heldman DA. Clinically deployable Kinesia™ technology for automated tremor assessment. Movement Disorders. 2009 Apr;24(5):723-730.

[105] LeMoyne R, Mastroianni T, Cozza M, Coroian C, Grundfest W. Implementation of an iPhone for characterizing Parkinson's disease tremor through a wireless accelerometer application. In Proceedings of 32nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2010 Aug (pp. 4954-4958).

[106] LeMoyne R, Mastroianni T, Whiting D, Tomycz N. Wearable and Wireless Systems with Internet Connectivity for Quantification of Parkinson's Disease and Essential Tremor Characteristics. Wearable and Wireless Systems for Healthcare II: Movement Disorder Evaluation and Deep Brain Stimulation Systems 2019 (pp. 79-97). Springer, Singapore.

[107] LeMoyne R, Tomycz N, Mastroianni T, McCandless C, Cozza M, Peduto D. Implementation of a smartphone wireless accelerometer platform for establishing deep brain stimulation treatment efficacy of essential tremor with machine learning. In Proceedings of 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2015 Aug (pp. 6772-6775).

[108] LeMoyne R, Mastroianni T, Tomycz N, Whiting D, Oh M, McCandless C, Currivan C, Peduto D. Implementation of a multilayer perceptron neural network for classifying deep brain stimulation in 'On' and 'Off' modes through a smartphone representing a wearable and wireless sensor application. In Proceedings of 47th Society for Neuroscience Annual Meeting (featured in Hot Topics; top 1% of abstracts); Washington D.C. 2017 Nov.

[109] LeMoyne R, Mastroianni T, McCandless C, Whiting D, Tomycz N. Evaluation of Machine Learning Algorithms for Classifying Deep Brain Stimulation Respective of 'On' and 'Off' Status. In Proceedings of 9th International IEEE/EMBS Conference on Neural Engineering (NER) 2019 Mar (pp. 483-488).

[110] LeMoyne R, Mastroianni T, McCandless C, Currivan C, Whiting D, Tomycz N. Implementation of a smartphone as a wearable and wireless inertial sensor platform for determining efficacy of deep brain stimulation for Parkinson's disease tremor through machine learning. In Proceedings of 48th Society for Neuroscience Annual Meeting (Nanosymposium); San Diego, CA 2018 Nov.

[111] LeMoyne R, Mastroianni T, McCandless C, Currivan C, Whiting D, Tomycz N. Implementation of a smartphone as a wearable and wireless accelerometer and gyroscope platform for ascertaining deep brain stimulation

treatment efficacy of Parkinson's disease through machine learning classification. Advances in Parkinson's Disease. 2018 May;7(2):19-30.

[112] LeMoyne R, Mastroianni T, Whiting D, Tomycz N. Distinction of an assortment of deep brain stimulation parameter configurations for treating Parkinson's disease using machine learning with quantification of tremor response through a conformal wearable and wireless inertial sensor. Advances in Parkinson's Disease. 2020 Aug;9(3):21-39.

[113] LeMoyne R, Mastroianni T, Whiting D, Tomycz N. Parametric evaluation of deep brain stimulation parameter configurations for Parkinson's disease using a conformal wearable and wireless inertial sensor system and machine learning. In Proceedings of 42nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2020 Jul (pp. 3606-3611).

[114] LeMoyne R, Mastroianni T, Whiting D, Tomycz N. Preliminary Network Centric Therapy for machine learning classification of deep brain stimulation status for the treatment of Parkinson's disease with a conformal wearable and wireless inertial sensor. Advances in Parkinson's Disease. 2019 Nov;8(4):75-91.

[115] LeMoyne R, Mastroianni T, McCandless C, Currivan C, Whiting D, Tomycz N. Network Centric Therapy for deep brain stimulation status parametric analysis with machine learning classification. In Proceedings of 49th Society for Neuroscience Annual Meeting (Nanosymposium); Chicago, IL 2019 Oct.

[116] LeMoyne R, Mastroianni T, Whiting D, Tomycz N. Application of deep learning to distinguish multiple deep brain stimulation parameter configurations for the treatment of Parkinson's disease. In Proceedings of IEEE 19th International Conference on Machine Learning and Applications (ICMLA) 2020 Dec (pending publication).

[117] LeMoyne R, Mastroianni T, Whiting D, Tomycz N. Deep learning for differentiating parameter configurations of deep brain stimulation for treating Parkinson's disease incorporating conformal wearable and wireless inertial sensors as an evolution for Network Centric Therapy, Society for Neuroscience Global Connectome: A Virtual Event 2021 Jan.