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USE OF DYNAMICS IN MEDICAL RESEARCH: EFFECT OF DEEP BRAIN STIMULATION ON GAIT IN PARKINSON'S DISEASE PATIENTS

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INTRODUCTION

For many years dynamic systems analysis techniques have been used to study the human body. Historically, the focus has been to understand how the body functions and what can be done to improve human performance. The focus was on the science of human movement. In contrast, medicine evolved over a different pathway. Typically, treatments were discovered and adopted before the mechanism was fully understood. In some cases, even the efficacy of the treatment was not proven. This eventually led to a shift to evidence based medicine.

The foundation of evidence based medicine is that treatments are scientifically tested to evaluate efficacy prior to making these treatments the standard of practice. One challenge with evidence based medicine is that there must be a quantitative parameter for which to measure the effectiveness of the treatment. Traditional methods such as visual observation are difficult to quantify and objectively compare. Dynamic system analysis is able to provide objective measurements and may be a useful tool in unlocking the mysteries of musculoskeletal, neuromuscular and neurological disorders. These measured biomechanical parameters can be used to determine if treatment was effective or to compare the outcome of alternate treatments.

In this abstract, we present an approach for applying biodynamics in medical research. We demonstrate how to set up a study for evaluation of treatment outcome and to compare two different treatments. In addition, we show how the integration of human subject testing and mathematical modeling can have a synergistic advantage. The objective of this presentation is to demonstrate a general approach that may be used as a model for engineers and clinicians working in collaboration.

As an example, we will apply these methods to study the effect of deep brain stimulation (DBS) on patients suffering from Parkinson's disease (PD). The main concern with these patients is a loss of stability during standing and walking leading to falls and secondary injury. Falls among the elderly often result in broken bones which may begin a chain of events ultimately leading to death of the patient.

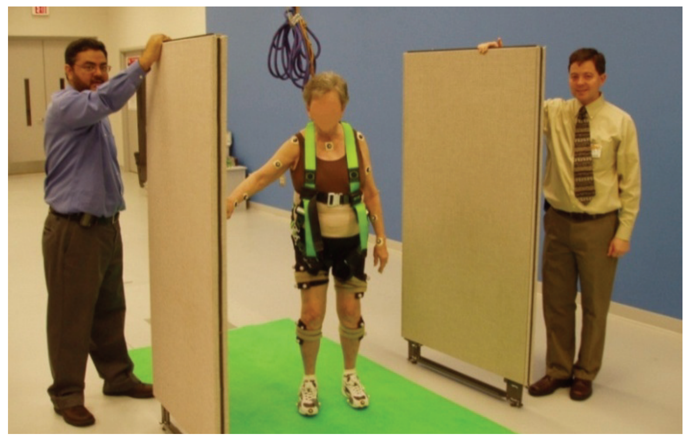

Figure 1. Parkinson's patient (center) walking between obstacles in the Human Performance and Biodynamics Laboratory.

STUDY DESIGN

Human beings are complex organisms with many system and subsystems working together synergistically. Thus, from an engineering perspective they are highly coupled. As a result, a multitude of parameters often contributes to the outcome of clinical interest. Furthermore, there are often multiple treatment options from which to choose.

Parkinson's disease is a progressive neurodegenerative condition characterized by bradykinesia, rigidity, tremors, and gait and postural instability. While bradykiensia, rigidity, and tremors respond well to medications and surgery, gait and postural instability have an unpredictable or negligible response to the available medical and surgical treatments. Falls, as a result of gait and postural instability, remain as the most debilitating risk for people with PD.

DBS has proven its role as a very effective and relatively safe surgical treatment for PD patients with medically refractory symptoms. In USA, it is considered as a surgical

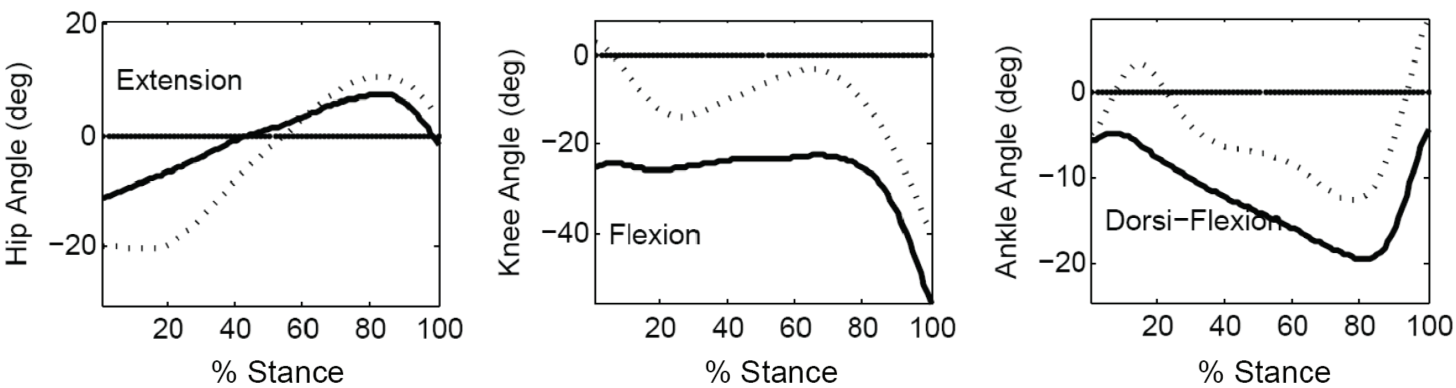

Figure 2. Kinematic data for Parkinson's patient (solid) differs from the normal gait (dashed).

treatment of choice for PD. DBS has the advantage over other surgical options to be a reversible treatment and its stimulation parameters can be adjusted and customized to the individual needs of the patient. Voltage, pulse width, frequency and location of the electrical impulse can be adjusted with resultant influence on the outcome. However, some of these parameters are coupled further adding to complexity of testing these measures. If we were to design a study to evaluate all four parameters at three levels each, it would require 243 (3^5) different testing conditions, each needing multiple tests subjects. Since this is not practical, for our study we selected one parameter to study first and tried to minimize the variability of the other parameters.

SELECTION OF TESTING METHODS AND OUTCOME PARAMETERS

Generally, the clinically relevant motor outcomes in terms of gait and postural instability in PD patients are difficult or not practical to measure. For PD patients, the most important clinical parameter is the risk of falling. Since it is an impractical and unsafe approach to experiment with different treatments by simply following the patient and counting the number and severity of falls, an indicator of fall risk is needed. This measurable parameter must be sensitive to differences in treatments and specific enough to avoid being strongly affected by changes in parameters that are not being testing.

The selection of tasks to perform should generally match the activity of clinical interest. The patients in the DBS study are elderly, so we chose to analyze normal walking. If we were assessing the effectiveness of a training program for athletes, a more physically challenging task would be required.

In order to aid in selecting an appropriate measureable parameter, a typical patient was tested in the laboratory and preliminary data was collected (Figure 1). Based on the preliminary data, we selected lower extremity joint kinematics (Figure 2) as the measureable parameters for the study because they were observed to be dramatically different than normal gait. In addition, they are traditional outcome parameter that may be easily compared to those of other researchers.

One of the reasons that new outcome parameters are developed is to improve sensitivity. Some of these may be original ideas while others may be borrowed from more established fields. It is often fruitful for engineers to meet with clinicians to determine if an existing technique can be applied or adapted which can improve analysis sensitivity. This interdisciplinary approach is used extensively in industry.

CHALLENGES IN TESTING HUMANS

Human subject testing has additional challenges beyond those encountered when testing engineered products. Mental and physical fatigue often limits the amount of testing that can be performed by a person. Motivation can vary among subjects leading to inaccurate or inconsistent results. Disclosure of the test protocol is required, but it is generally best not to tell the participant too much about the study details because they may try to "help" you achieve the desired outcome, either consciously or unconsciously. This will distort the results. In addition, Testing must be approved by the Institutional Review Board (IRB) to ensure ethical treatment of participants and to verify that the benefits outweigh the risks. One must also take into account that each person is different and affected differently by the disease adding to study variability. Co-morbidities are also common among elderly patients sometimes making it difficult to find patients with *only* the condition that you are trying to study. If planning a multisession study, retaining participants through the end of the study is sometimes difficult. Finally, it should be noted that it is easier to recruit volunteers for fun experiments.

INTEGRATED APPROACH

Human subject testing can provide an accurate assessment of efficacy of a treatment, but it is often time consuming and costly. In contrast, mathematical modeling may be used to quickly assess the effect of changes to important parameters. However, when applying these conclusions to complex systems like a human, the results should be verified experimentally. By performing both real experiments and simulated experiments through mathematical models, the advantages of both approaches can be realized while minimizing the negative aspects of each.

CONCLUSIONS

A general approach for applying dynamic system analysis methods to medical problems was presented. We showed how to design a study to evaluate clinically relevant outcomes for different DBS treatments, but the approach may be generalized to a variety of different applications. Our overall goal is to encourage an interdisciplinary approach to solve real clinical problems using advanced engineering techniques.