Albert Einstein Healthcare Network

Annual Progress Report: 2014 Formula Grant

Reporting Period

January 1, 2015 – June 30, 2015

Formula Grant Overview

The Albert Einstein Healthcare Network received $68,170 in formula funds for the grant award period January 1, 2015 through June 30, 2016. Accomplishments for the reporting period are described below.

Research Project 1: Project Title and Purpose

Therapeutic Tablet Application for Post-Stroke Motor Rehabilitation – One of the most devastating long-term post-stroke disabilities is impairment in movement production. Recent innovations in computer tablet application-based therapies ("therapeutic apps") are notable because they offer expanded rehabilitation opportunities due to their low cost, ease of dissemination, and widespread availability. The project will first complete a single-session analysis of usability of a previously-developed tablet-based motor app, and then test the app in the home setting with a chronic stroke population to collect pilot data on efficacy. If effective, app therapy would be a novel and significant advance in the cost-effectiveness of stroke rehabilitation.

Anticipated Duration of Project

1/1/2015 – 6/30/2016

Project Overview

Survivors of stroke often live the remainder of their lives with significant disability. One of the most common and devastating long-term post-stroke disabilities is impairment in movement production ("hemiparesis"). Treatment of hemiparesis is expensive and labor intensive. As a consequence, many patients receive insufficient treatment, which in turn results in incomplete recovery. This is especially true for chronic stroke patients, many of whom fail to receive any treatment multiple months post-stroke because of limited insurance coverage. Recent innovations in computer tablet technology and application-based therapies ("therapeutic apps") are notable because they offer expanded rehabilitation opportunities due to their low cost, ease of dissemination, and widespread availability. To date, reports of therapeutic apps' benefits have been largely anecdotal, or made by companies producing the apps for profit with little empirical

support. The research aim of the project will be to pilot test the feasibility and efficacy of a tablet-based motor rehabilitation app modeled after the popular "Fruit Ninja" game, but programmable for the motor capacities of stroke survivors. The PI and his colleagues have developed a prototype tablet game that requires bisection of moving targets of varying sizes and speeds. The app uses an adaptive approach to keep the game difficulty close to the user's skill level, and gamification schemes including point system, levels, and varying visual scenes and auditory responses were included to maintain user interest. Specific aim: We propose to test the feasibility and efficacy of a tablet-based motor rehabilitation app in the home setting with a chronic stroke population to collect pilot data on app use.

Principal Investigator

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Other Participating Researchers

Andrew Packel, PT; Genevieve Curtis, BA – employed by Albert Einstein Healthcare Network

Expected Research Outcomes and Benefits

Upon completion, there will be three outcomes/benefits of the project. First, 10 stroke survivors will have completed a month of app therapy in Phase II of the study, and thus each could potentially experience improved arm functioning following participation. Second, if evidence for efficacy is observed, the data will significantly improve the PI's chances of obtaining further funding to test the app therapy in a larger number of stroke survivors. Third, the PI and colleagues will publish the results of the study in a peer reviewed rehabilitation journal, which will improve the chances of other investigators pursuing similar forms of rehabilitation.

Summary of Research Completed

Although the original anticipated start date for the project was 1/1/2015, this date was changed to 6/1/2015 due to the PI's family experiencing a premature birth (requiring an extended stay in the Neonatal Intensive Care Unit) and his subsequent partial paternity leave. During the month of June 2015, the team completed extensive Beta testing of the app before beginning Phase 1 (usability testing in stroke survivors). During this testing, the team identified several changes to make to the app to improve the chances of Phase 1 success. These changes including (1) adding a greater variety of speeds of the to-be-intercepted objects, (2) varying the trajectories of the to-be-intercepted object, (3) simplifying the on-screen score feedback, and (4) improving the experimenter interface to speed any changes needed during the testing session. The PI then worked with the app programmer to implement these changes. It is anticipated these changes

should be completed by the end of August 2015, with Phase 1 being completed during the following 2 months. The team has also identified likely participants from the local research registry who will meet the inclusion criteria. Given the delayed start of the project, we have modified the anticipate project end date to 6/30/2016. Thus, we anticipate the project will be completed in the original project timeframe.

Research Project 2: Project Title and Purpose

Thromboelastography (TEG) Validation in Liver Disease Patients – The purpose of this project is (1) to establish intra-subject variability of TEG with platelet mapping and functional fibrinogen in liver disease without cirrhosis, cirrhotic patients, and stable post-orthotropic liver transplant (OLT) patients and (2) to evaluate complex coagulation in liver disease patients, cirrhotic patients, and stable post-OLT patients utilizing TEG with platelet mapping and functional fibrinogen.

Anticipated Duration of Project

1/1/2015 – 1/31/2016

Project Overview

Primary objectives:

1. To establish intra-subject variability of TEG with platelet mapping and functional fibrinogen in liver disease without cirrhosis.
2. To establish intra-subject variability of TEG with platelet mapping and functional fibrinogen in cirrhotic patients.
3. To establish intra-subject variability of TEG with platelet mapping and functional fibrinogen in stable post OLT patients.

Secondary objectives:

1. To establish TEG parameters with platelet mapping and functional fibrinogen in liver disease patients, cirrhotic patients, and stable post OLT patients.
2. To compare TEG parameters with platelet mapping and functional fibrinogen between, liver disease patients, cirrhotic patients, and stable post OLT patients.
3. To compare the difference in TEG parameters with platelet mapping and functional fibrinogen between Child-Pugh classification and etiology of liver disease.
4. To compare TEG parameters along with platelet mapping and functional fibrinogen with conventional coagulation tests in liver disease patients, cirrhotic patients, and stable post OLT patients.

Methods: Adult patients with liver diseases, cirrhosis, and stable 1-year post-OLT in both inpatient and outpatient settings will be reviewed for eligibility. Patients who are enrolled into the study will receive blood draws at separate 2 occasions, 1 hour apart. The first blood draw will be analyzed using conventional coagulation tests and TEG with platelet mapping and functional fibrinogen. The second blood draw will be analyzed only for TEG with platelet mapping and

functional fibrinogen. The results of TEG with platelet mapping and functional fibrinogen on 2 occasions will be compared, and coefficient of variation of TEG parameters with platelet mapping and functional fibrinogen of liver disease patients, cirrhotic patients, and post-OLT patients will be calculated to evaluate intra-subject variability in each group.

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Other Participating Researchers

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Expected Research Outcomes and Benefits

1) TEG with platelet mapping and functional fibrinogen has acceptable intra-subject variability in liver disease patients, cirrhotic patients, and post-OLT patients.
2) TEG with platelet mapping and functional fibrinogen reflects coagulation in liver disease patients, cirrhotic patients, and post-OLT patients more accurately than conventional tests.

Benefits: Given TEG with platelet mapping and functional fibrinogen can simultaneously evaluate overall coagulation along with platelet function, coagulation factors, and fibrinogen, TEG may provide better prediction of bleeding or thrombosis risk in liver disease, cirrhotic patients, and post-OLT patients. TEG also can be used to guide the type of blood product or antifibrionlytic agent required to correct coagulation disorders. For example, if bleeding is caused by hyperfibrinolysis, anti-fibrinolytic agent such as epsilon aminocaproic acid or tranexamic acid can be given instead of transfusion. As a result, TEG may reduce unnecessary transfusion based on conventional coagulation tests as shown studies of patients undergoing liver transplantation. Finally, TEG offers the opportunity for point of care approach to coagulation management, which would improve expediency of care, and thus safety, and acceptability on the part of the patient.

Summary of Research Completed

In the early phase of the award year, we focused on assembling the equipment and materials needed to perform the TEG and platelet mapping (PM). This required securing reagents and training the research staff in the TEG machine operation by the manufacturer, as well as establishing quality control procedures. Thereafter, recruitment of study subjects began.

Prior to a scheduled office visit in the outpatient Hepatology office, the clinical records of all adult cirrhotic patients were evaluated for eligibility. Those found to be eligible were contacted by phone and the study procedures were explained; patients willing to participate were asked to come to their appointment 30 minutes early for consent procedures, and to remain in the unit during the period of study activities (two phlebotomies). Exclusion criteria included 1) pregnancy, 2) patients who were on antiplatelet, anticoagulation, NSAIDs, or aspirin, 3) patients with acute decompensation (e.g. hepatorenal syndrome, acute infection, or unstable vital signs), 4) history of thrombotic or recent bleeding events, 5) primary or secondary hemostatic disorders, and 6) patients who were unable to give informed consent. Two blood draws were performed 1 hour apart after the patient signed the informed consent. TEG with PM and FF from two blood draws were performed by one operator. Reliability coefficient of each TEG parameters were calculated from the first and second blood draw using Cronbach's alpha.

To date, over 30 patients were offered participation and twenty patients were included in the study, 13 male and 7 female. The mean age was 60 ± 8 years. The etiology of cirrhosis included hepatitis C (63%), alcohol (41%), hepatitis B (5%), autoimmune hepatitis (5%), and primary biliary cirrhosis (5%). The mean MELD score was 11 ± 5. Reliability coefficient of several TEG parameters, including R time, LY-30, % ADP inhibition, and % AA inhibition were low whereas reliability coefficient of others, namely MA-ADP and MA-AA were acceptable. Furthermore, the reliabilities of K time, Alpha angle, MA, MA-FF, and FLEV were high. In addition, Ly-30, % ADP inhibition, and % AA inhibition had the highest variation both in the first and second blood draw.

Preliminarily, our study is demonstrating that R time, LY-30 and PM have low reliability while other conventional TEG parameters and FF are reliable in cirrhotic patients. Therefore, the result of R time, LY-30, and PM should be interpreted with caution. In order to fully assess the clinical utility of TEG with PM, the reliability of the process in the cirrhotic population must be established. This will form the foundation of the next step, which is to establish the clinical utility of TEG with PM.