

PROTOCOL

Study Title: Prospective treatment study of Catatonia patients with RUL ECT and BL ECT treatment regimens

Principal Investigator, Co-investigator(s):

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Sponsor or funding source: None needed specifically for the study. ECT is standard of care for catatonia and patients' insurance covers ECT treatments as a result.

Background, Rationale and Context

Catatonia was first described in 1873 by a German psychiatrist, Karl Ludwig Kahlbaum in his monograph titled "Die Katatonie oder Das Spannungsirresein" (Catatonia or tension insanity) (Kahlbaum, 1873). He conceptualized catatonia as a motor syndrome characterized by lack of motion, speech, alternating with periods of excessive purposeful motor activity, rigidity, negativism, verbigeration, automatic imbalance, posturing, grimacing and stereotypes. He also described that the syndrome generally had a periodic course and lethal outcome in a few. Despite a long history, "katatonia" was associated with different illnesses and was given as diagnostic specifier. DSM- V made a change and added catatonia as an independent diagnostic symptom.

According to DSM-V, catatonia is characterized by the following:

A. the clinical picture is dominated by 3 or more of the following symptoms
(1) Stupor (2) Catalepsy (3) Waxy flexibility (4) Mutism (5) Negativism (6) Posturing (7) Mannerism
(8) Stereotypy (9) Agitation (10) Grimacing (11) Echolalia (12) Echopraxia

B. There is evidence from the history, physical examination or laboratory findings that the disturbance is in the direct patho-physiological consequence of another medical condition.

C. The disturbance is not better explained by another mental disorder

D. the disturbance does not occur exclusively during the course of a delirium

E. The disturbance causes clinically significant distress or impairment in social, occupational or other important areas of functioning

Electroconvulsive therapy or ECT has a very good track record in treatment of catatonia (World J Psychiatr. 2015 June 22; 5(2): 182-192), but current literature does not shed light on the speed and degree of response of catatonia to ECT. This study aims to analyze and describe the change of clinical signs and symptoms as a response parameter to judge ECT treatment series efficacy.

This treatment study, will be able to compare response rate of catatonia to RUL ECT and BL ECT. Also having a control group of catatonia patients, which will not be treated with ECT will provide additional information on early ECT treatment of Katatonia.

Objectives

- Study the response rate of catatonia to right unilateral (RUL) ECT and bilateral (BL) ECT.
- Compare response rate of catatonia to RUL ECT and BL ECT
- Analyze and describe the change of clinical signs and symptoms after ECT treatment series

Methods and Measures

Design

This study is a case control study. Currently ECT is considered standard of treatment for catatonia in addition to alternative medication options.

Study participants meeting inclusion and exclusion criteria will be and providing informed consent will be randomly assigned to receive either bilateral electroconvulsive treatment (BLECT) or right unilateral electroconvulsive treatment (RULECT)

- Patients who are otherwise eligible and consent to participate in our study, but refuse ECT (or ones who are unable to consent but their court appointed legal guardian or health care power of attorney refuse ECT) will be enrolled as a control group. The control group will undergo all the same laboratory investigations and Bush Francis measurements for evaluation of their catatonia but will not receive ECT.
- Informed consent will be obtained from the study participant or their legally authorized representative by the principal investigator or sub-investigator.
- Prior to treatment each patient will be examined by a clinician (psychiatrist and psychiatric resident) in which the following information will be obtained:

- **Psychiatric interview** with uniformed questioner

- **HPI** with onset, course of presenting symptoms, comorbidities, *precipitating illness or life events – emphasis upon psychological stress*

- **Substance abuse screening**

- **Psychiatric history** – Psychiatric diagnoses with age/date of diagnoses

- **Medical history**, with focus on comorbid developments and chronic medical disease states – especially if recent worsening or change in therapy

- **Previous episodes of catatonia** – dates and pertinent developments to social history (as noted above with HPI) with time course and treatment response/failure to ECT or medications

- **Recent medication changes**, with specific focus on timing of symptoms if possible – regimen prior to symptom/sign development, medication changes, and current medication

- **Neurological conditions** – including TBI, seizure history, neurodevelopmental disorders, delirium, dementia

- The Montreal Cognitive Assessment (MOCA) will be administered the day prior to each ECT treatment and the day after each ECT treatment for pre and post procedure cognitive monitoring.

- **Incontinence**

- medical, metabolic, and/or psychiatric comorbidities are recorded but intentionally NOT excluded, with limited exceptions: CVA

- Questionnaires and rating scales: The following instruments will be administered by a trained clinician (psychiatric resident, medical student)

1) Bush- Francis Scale (BFCRS): The BFCRS is a rating scale consisting of 23 catatonia items (Bush et al., 1996a). The first 14 items on this scale are the most common, classical signs of catatonia & are also known as Catatonia Screening Instrument (BFCSI). If two or more of the BFCSI signs are present, for 24 hours or longer, catatonia is a possibility (Sienaert et al, 2011). For the purpose of this study, a score of 4 or more on the 23-item BFCRS will be considered for

inclusion in this study.

- 2) **Hamilton depression scale**
- 3) **Montreal Cognitive Assessment (MoCA)**

The administration of the BFCRS, Hamilton depression scale and MoCA will be completed before and after each ECT treatment.

- Labs and testing (to rule out organic causes of catatonia)

EEG electroencephalogram
EKG – electrocardiogram
CT scan of the head w/o contrast
CMP complete metabolic panel,
CBC diff complete blood count with differential
Thyroid studies TSH T3 T4
Metabolic/Inflammatory laboratory tests (in specific conditions)
Urine Analysis with Urine Drug Screen within 48 hours of admission)
Fe serum level
Fibrin D-dimer
–Magnesium (Mg)

- Pre-anesthesia work-up performed by the department of anesthesia to determine fitness for ECT. Anesthesia faculty will administer anesthesia to participants during the ECT procedure. They will monitor patient in the OR before, during and after the ECT procedure for at least 30 minutes for any adverse effects.
- ECT treatments will begin after initial evaluation as described above. ECT treatments will be administered three times a week.
- Participants will not be required to try and fail a challenge of IV or IM Lorazepam prior to being assigned to receive ECT treatments.

Setting

Study participants' medical histories, examinations, administration of rating scales (Bush Francis scale, MoCA and Hamilton Depression scale) will be done in the respective patient's room on the adult inpatient psychiatry unit at Wake Forest Baptist Health.

ECT treatments will be administered in OR at Wake Forest Baptist Health.

Subjects selection criteria

- **Inclusion Criteria**
- Adult patients admitted to WFBMC Inpatient Psychiatry unit with catatonia who are clinically eligible for ECT.
- Clinical catatonia as evidenced by a Bush-Francis Catatonia Rating Scale (BFCRS) score of 4 or more

- **Exclusion Criteria**

Pregnant women

Patients with any of the following medical conditions which are contraindications for ECT:

- Pheochromocytoma
- History of stroke within the past 3 months
- Cardiac conduction defects
- Cerebral or aortic aneurysms

- **Sample Size**

This study will require 30 or more to answer the questions stated in the study objectives. We will enroll 15 ECT subjects and 15 control group subjects (total sample size 30).

Interventions and Interactions

- Participants will be administered the Bush Francis Scale (BFCRS) by the principal investigator or the study coordinator the day before each ECT procedure and the day after each ECT procedure.
- Participants will receive up to 10 ECT treatments. These ECT treatments can be terminated earlier if study participants show objective clinical improvement defined as a reduction of 50% or more in the Bush Francis scale score

Outcome Measure(s)

Reduction of 50% or more in the Bush- Francis Scale (BFCRS) score.

Analytical Plan

Results will be analyzed initially using descriptive statistics. Comparison between groups will be done using chi square tests for proportions, t-tests, ANOVA procedures or other appropriate statistical analytical procedures. Regression analysis may be performed to identify independent outcome predictors. Other inferential statistical analysis will be conducted as appropriate.

Human Subjects Protection

Subject Recruitment Methods

Patients who are suffering from catatonia and hospitalized to the adult inpatient psychiatry unit will be recruited for the study. Informed consent will be obtained from patients who have capacity to make their own medical decisions and are their own legal guardians. Patients who are unable to understand the nature of their illness, the risks or benefits of accepting or refusing treatment or are unable to understand their treatment options will be determined not to have capacity to provide informed consent. In that situation, their legally appointed representative (healthcare power of attorney) or court appointment emergency legal guardian will be approached for informed consent. Informed consent will be obtained from a court appointment legal guardian for patients who have already been deemed incompetent by the court.

A trained psychiatry physician (attending psychiatrist or resident psychiatrist) will do the recruiting. Privacy will be protected by interviewing patients in the privacy of their patient room.

Informed Consent

Signed informed consent will be obtained from each subject, their legal guardian if they are deemed incompetent by a judge or their legally authorized representative if the subject is unable to provide informed consent. Informed consent will be obtained by the principal investigator or study coordinator. Informed consent will be obtained from patient or patient's legally authorized representative in

the patient's hospital room when the patient is hospitalized to the adult inpatient psychiatry unit at least a day prior to the first ECT procedure to protect patient privacy. Patient or their legally authorized representatives can rescind the consent for ECT at any time by simply verbally informing the principal investigator or study coordinator. Principal investigator will evaluate subject for capacity to consent to ECT procedure. If principal investigator determines that subject does not have capacity to consent and does not understand the risks or benefits of the ECT procedure, subject's legally authorized representative (either court appointed legal guardian or designated health care power of attorney) will be contacted for informed consent. A subject who does not have capacity and does not have a legally authorized representative or a court appointed guardian will not be enrolled in the study.

Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a linkage file, stored separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Following data collection subject identifying information will be destroyed. Identifying data will be destroyed three years after closure of the study. Data stored on paper will be shredded and videos will be deleted. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. All study procedures will take place in the participant's hospital room with study personnel. No one other than the participant and study personnel will be allowed in the participant's hospital room when any study procedure is underway. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate. Adverse Events will be collected and assessed for relationship for ECT treatments on ECT subjects only.

References

1. Kahlbaum KL. Die Katatonie: oder das Spannungsirresein, eine klinische Form psychischer Krankheit. 1973
2. World J Psychiatr. 2015 June 22; 5(2): 182-192.
3. Bush, G., Fink, M., Petrides, G., Dowling, F., Francis, A., 1996a. Catatonia. I. Rating scale and standardized examination. Acta Psychiatr. Scand. 93, 129–136.
4. Sienaert, P., Rooseleer, J., De Fruyt, J., 2011. [Measuring catatonia: a systematic review of rating scales. J. Affect. Disord. 135 \(1–3\), 1–9.](#)

