MEMORANDUM FOR SGVT
ATTN: CAPT SHANE D. RIGGS

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Challenges in Diagnosis and Management of Serotonin Syndrome in A Patient With Schizophrenia Treated with A LAI Antipsychotic** presented at/published to **2017 American Psychiatric Association Annual Meeting, San Diego, CA, 20-24 May 2017** in accordance with MDWI 41-108, has been approved and assigned local file #17065.

2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are a 59 MDW staff member, we can forward your request for funds to the designated Wing POC at the Chief Scientist’s Office, Ms. Alice Houy, office phone: 210-292-8029; email address: alice.houy.civ@mail.mil.

4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

*Warrior Medics — Mission Ready — Patient Focused*
PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

INSTRUCTIONS

USE ONLY THE MOST CURRENT 59 MDW FORM 3039 LOCATED ON AF E-PUBLISHING

1. The author must complete page two of this form:
   a. In Section 2, add the funding source for your study [e.g., 59 MDW CRD Graduate Health Sciences Education (GHSE) (SG5 O&M); SG5 R&D; Tri-Service Nursing Research Program (TSNRP); Defense Medical Research & Development Program (DMRDP); NIH; Congressionally Directed Medical Research Program (CDMRP); Grants; etc.]
   b. In Section 2, there may be funding available for journal costs, if your department is not paying for figures, tables or photographs for your publication. Please state “YES” or “NO” in Section 2 of the form, if you need publication funding support.

2. Print your name, rank/grade, sign and date the form in the author's signature block or use an electronic signature.

3. Attach a copy of the 59 MDW IRB or IACUC approval letter for the research related study. If this is a technical publication/presentation, state the type (e.g. case report, QA/QI study, program evaluation study, informational report/briefing, etc.) in the "Protocol Title" box.

4. Attach a copy of your abstract, paper, poster and other supporting documentation.

5. Save and forward, via email, the processing form and all supporting documentation to your unit commander, program director or immediate supervisor for review/approval.

6. On page 2, have either your unit commander, program director or immediate supervisor:
   a. Print their name, rank/grade, title and sign and date the form in the approving authority's signature block or use an electronic signature.

7. Submit your completed form and all supporting documentation to the CRD for processing (59crdpubsres@us.af.mil). This should be accomplished no later than 30 days before final clearance is required to publish/present your materials. If you have any questions or concerns, please contact the 59 CRD/Publications and Presentations Section at 292-7141 for assistance.

8. The 59 CRD/Publications and Presentations Section will route the request form to clinical investigations, 502 ISG/JAC (Ethics Review) and Public Affairs (59 MDWPA) for review and then forward you a final letter of approval or disapproval.

9. Once your manuscript, poster or presentation has been approved for a one-time public release, you may proceed with your publication or presentation submission activities, as stated on this form. Note: For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.

10. If your manuscript is accepted for scientific publication, please contact the 59 CRD/Publications and Presentations Section at 292-7141. This information is reported to the 59 MDWICC. All medical research or technical information publications/presentations must be reported to the Defense Technical Information Center (DTIC). See 59 MDW 41-108, Presentation and Publication of Medical and Technical Papers, for additional information.

11. The Joint Ethics Regulation (JER) DoD 5500.07-R, Standards of Conduct, provides standards of ethical conduct for all DoD personnel and their interactions with other non-DoD entities, organizations, societies, conferences, etc. Part of the Form 3039 review and approval process includes a legal ethics review to address any potential conflicts related to DoD personnel participating in non-DoD sponsored conferences, professional meetings, publication/presentation disclosures to domestic and foreign audiences, DoD personnel accepting non-DoD contributions, awards, honoraria, gifts, etc. The specific circumstances for your presentation will determine whether a legal review is necessary. If you (as the author) or your supervisor check “NO” in block 17 of the Form 3039, your research or technical documents will not be forwarded to the 502 ISG/JAC legal office for an ethics review. To assist you in making this decision about whether to request a legal review, the following examples are provided as a guideline:

   For presentations before professional societies and like organizations, the 59 MDW Public Affairs Office (PAO) will provide the needed review to ensure proper disclaimers are included and the subject matter of the presentation does not create any cause for DoD concern.

   If the sponsor of a conference or meeting is a DoD entity, an ethics review of your presentation is not required, since the DoD entity is responsible to obtain all approvals for the event.

   If the sponsor of a conference or meeting is a non-DoD commercial entity or an entity seeking to do business with the government, then your presentation should have an ethics review.

   If your travel is being paid for (in whole or in part) by a non-Federal entity (someone other than the government), a legal ethics review is needed. These requests for legal review should come through the 59 MDW Gifts and Grants Office to 502 ISG/JAC.

   If you are receiving an honorarium or payment for speaking, a legal ethics review is required.

   If you (as the author) or your supervisor check “YES” in block 17 of the Form 3039, your research or technical documents will be forwarded simultaneously to the 502 ISG/JAC legal office and PAO for review to help reduce turn-around time. If you have any questions regarding legal reviews, please contact the legal office at (210) 671-5795/3955, DSN 473.

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement:

   "The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement for research involving humans:

   "The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402."

NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement for research involving animals, as required by AFMAN 40-401 IP:

   "The experiments reported herein were conducted according to the principles set forth in the National Institute of Health Publication No. 80-23, Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966, as amended."
1. TO: CLINICAL RESEARCH
Shane D. Riggs, D.O., Capt, O3, SGVT

5. PROTOCOL TITLE: (NOTE: For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:
Challenges in Diagnosis and Management of Serotonin Syndrome in a Patient With Schizophrenia Treated With a LAI Antipsychotic

7. FUNDING RECEIVED FOR THIS STUDY? \( \square \) Yes \( \square \) No

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES? \( \square \) Yes \( \square \) No

9. IS THIS MATERIAL CLASSIFIED? \( \square \) Yes \( \square \) No

10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.? \( \square \) Yes \( \square \) No

11. MATERIAL IS FOR: \( \square \) Domestic Release \( \square \) Foreign Release

12. HAVE YOUR ATTACHED RESEARCH/TECHNICAL MATERIALS BEEN PREVIOUSLY APPROVED TO BE PUBLISHED/PRESENTED? \( \square \) Yes \( \square \) No

13. EXPECTED DATE WHEN YOU WILL NEED THE CRD TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC

14. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email)
Shane D. Riggs, D.O., shane.d.riggs.mil@mail.mil

16. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.

17. IS A 502 ISG/JAC ETHICS REVIEW REQUIRED (JER DOD 5500.07-R)? \( \square \) Yes \( \square \) No

I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401 IP, AND 59 MDW 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.
The proper disclaimer has been added to the presentation. The presentation is approved.
Midline electroconvulsive therapy following left fronto-temporo-parietal craniectomy and cranioplasty:

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Abstract
We report on an interesting case of necessity using an innovative electrode placement in a 20-year-old female with major depressive disorder (MDD) who received two series of ECT treatments in 2014 and 2015. In 2013, following a suicide attempt by jumping out of a moving vehicle and sustaining severe cranial fractures, she underwent left fronto-temporo-parietal craniectomy and reconstruction cranioplasty with titanium mesh-plating. She was treated with midline electrode placement for ECT, as the mesh-plating barrier would affect traditional techniques. We found improvement in the patient following treatment with quality average EEG results over the course of treatment. We hypothesize that the cortical midline structures (CMS) could play an important role as targets of ECT treatment and improvement in this patient.

Case Presentation
This is a 20-year-old female with history of MDD and THI in 2013 status post left fronto-temporo-parietal craniectomy and reconstruction cranioplasty with titanium mesh-plating. The patient has an extensive history of depression with multiple suicide attempts including cutting her wrists. She has had multiple admissions for acute depressive episodes with suicidal ideations and/or suicidal behavior. She has been treated with multiple pharmacological interventions over the years. Her most recent and critical suicide attempt was jumping out of a moving vehicle in February 2013, during which she suffered multiple cranial injuries.
Following this incident the patient underwent several neuropsychological procedures including a right ventriculoperitoneal shunt placement, left fronto-temporo-parietal craniectomy and left fronto-temporo-parietal reconstruction cranioplasty with titanium mesh-plating over the course of 6 months. CT imaging in figure 2 shows the extent of the cranioplasty performed.
The patient was admitted in January and March of 2014 for worsening depression and suicide attempts by cutting her wrists. She sustained multiple lacerations each time requiring sutures on bilateral wrists. She did not receive ECT treatments during those admissions and was managed medically. The patient presented to the inpatient admission in July 2014 for major depressive episode with suicidal ideations. She remained inpatient for 12 days and we history ECT treatment with midline electrode placement as shown in figure 1. This was clinical decision based on the patient's surgical history.
The patient was discharged and continued to receive 4 more treatments as an outpatient for a total of 15 sessions. We achieved good EEG readings based on the rhythm strip with average stimulus of 33%, average seizure duration of 90 seconds, average postictal suppression index (PSI) of 48%, average seizure energy index (ASEI) of 746.6 V2 and an average maximum sustained coherence (MSC) of 83%. The patient started treatment with a quick inventory of depressive symptomatology (QIDS) of 21 and throughout treatment, her improvement on the QIDS to a lowest score of 3. Self-reported memory difficulties were reported on a scale on 1-10, with 1 being minimal and 10 being significant difficulty. The patient's average score throughout treatment was 3.5. Self-reported score of ECT helping the patient's depressive symptoms was also scored on a scale of 1-10, with 1 being minimal help and 10 being significant improvement. The patient's average score throughout treatment was 8.5.

The patient was in remission and remained functional for the next year, until she admitted again for a depressive episode with suicidal ideations in June 2015 for 10 days in which she received 4 ECT treatments with midline placement and 3 more treatments post-discharge. We achieved excellent EEG readings based on rhythm strip with average stimulus of 40%, average seizure duration of 106.3 seconds, average PSI of 41%, ASEI of 7606 V2 and an average MSC of 93%. The patient started treatment with a QIDS score of 15 and throughout treatment, she improved on the QIDS to a lowest score of 4. Self-reported memory difficulties were reported on a scale of 1-10, with 1 being minimal and 10 being significant difficulty. The patient's average score throughout treatment was 4.5. Self-reported score of ECT helping the patient's depressive symptoms was also scored on a scale of 1-10, with 1 being minimal help and 10 being significant improvement. The patient's average score throughout treatment was 5.7.

The patient continued with self-reported improvement in each round of treatment.

The patient continued to be in remission since that time. She is currently living with her grandmother, is planning to go back to school to complete a general education degree and is following her medication regimen with good outpatient follow up. She reported less irritability, improved self-worth, good sleep, good family relations and growing interest in daily activities to help her move on with her life.

Discussion
Ongoing efforts continue to elucidate optimal electrical stimulus parameters and electrode placement for ECT. Currently used stimuli with right unilateral placement are improving (6, 7).
Our experience suggests that using a novel electrode placement may result in seizures with characteristic comparable to traditional ECT.
Because of the traumatic brain injury and subsequent neurosurgery our patient's skull and brain architecture were considerably altered. The extent of the titanium mesh over most of the left side of her skull precluded using a bilateral electrode placement. We also considered the right unilateral electrode position however, opting for using a midline electrode position because of concerns about the residual brain damage and our belief that a midline network of brain loci is highly germane to the manifestation and alleviation of depressive symptoms. Reports have shown that cortical midline structures as well as self-referential processing do play an important role in the course and treatment of MDD (3).

Functional MRI studies have shown the neural network involved in manifesting depression extends from the inferior frontal midline structures including the subgenual cingulate region 25 to the prefrontal. It also includes structures such as medial prefrontal, anterior cingulate cortex, dorsal lateral prefrontal cortex and the posterior cingulate gyrus in the posterior parietal area (3, 4). Initial MRI studies have shown midline networks to be affected by ECT. However these studies have not found a strong relationship between the fMRI changes and patient outcomes (4, 5).
We believe that targeting these networks might be a strategy in treating MDD with ECT. It may be possible to position ECT electrode to have the stimulus pass through the presumed midline network of relevance yet bypass direct effects on the hippocampus and other structures mostly involved in memory processes. What continues to be unclear is to what extent a generalized seizure, in and of itself, is a necessary and sufficient basis for ECT response. The seminal report by Sackheim et al. in 1993 strongly suggested that all seizures are not equally efficacious given the inferior response of seizures induced by how close unilateral stimulus (2). Induced seizures are regarded as a necessary but not sufficient phenomenon for ECT to effectively treat depression. Extreme divergent opinions range from proposing that seizure induction by any means is effective to the passage of non-convulsive amounts of electric current being efficacious (6, 7).

We are aware of two prior reports using a similar electrode position referred to as frontomedial (8, 9). These reports posit electrodes over the mid-frontal area and the vertex. We opted for a more posterior positioning of the latter in order for the stimulus to pass through the affective and default mode networks to a fuller extent. Animal studies and computer simulations have explored the path of the current stimulus and suggested that it may be possible to largely avoid memory relevant areas while affecting areas linked to depression (8).
In conclusion, we have presented a unique case of a patient that forced us to use our medical knowledge, expertise and literature reference to determine the course of treatment. We opted for midline electrode placement and did achieve good results. The basis for using a midline electrode position was highly speculative but we find it is worthwhile to introduce it for further consideration and discussion.

References