MEMORANDUM FOR SGVT
ATTN: CAPT KELSEY A CACIC

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled Concentrations of Serum Inflammatory Markers after Hypobaric Exposure in Aircrew Trainees presented at/published to MHSRS, Kissimee, FL, 27-30 Aug 2017 in accordance with MDWI 41-108, has been approved and assigned local file #17264.

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
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, 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 (59crdpubspres@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 ISGJAC (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 MDWCC. 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 ISGJAC 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 ISGJAC.

   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 ISGJAC 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) 671-5795/3365, DSN 473.

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

"The views expressed are those of the [author(s)] [presenters(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."

59 MDW FORM 3039, 20160628
Prescribed by 59 MDW 41-108
PREVIOUS EDITIONS ARE OBSOLETE
1. TO: CLINICAL RESEARCH
   Kelsey A. Cacic, 03, SGVT

2. FROM: (Author's Name, Rank, Grade, Office Symbol)
   Kelsey A. Cacic, 03, SGVT

3. GME/GHSE STUDENT: ☐ NO □ YES
   □ YES ☐ NO

4. PROTOCOL NUMBER: FWH20140087H

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.)
   MRI Following Single Exposure to Hypobaria and/or Hypoxia Protocol

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:
   Concentrations of Serum Inflammatory Markers after Hypobaric Exposure in Aircrew Trainees

7. FUNDING RECEIVED FOR THIS STUDY? ☒ YES ☐ NO
   FUNDING SOURCE: AFMS RDT&E

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES? ☐ YES ☒ NO

9. IS THIS MATERIAL CLASSIFIED? ☒ YES ☐ 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.? ☒ YES ☐ NO
    NOTE: If the answer is YES then attach a copy of the Agreement to the Publications/Presentations Request Form.

11a. MATERIAL IS FOR: ☒ DOMESTIC RELEASE ☐ FOREIGN RELEASE
    CHECK APPROPRIATE BOX OR BOXES FOR APPROVAL WITH THIS REQUEST, ATTACH COPY OF MATERIAL TO BE PUBLISHED/PRESENTED
    ☐ 11a. PUBLICATION/JOURNAL (List intended publication/journal.)

11b. PUBLISHED ABSTRACT (List intended journal.)

☒ 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.)
    MHSRS, Kissimee, FL 27-30 Aug

☐ 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meeting)

☐ 11e. OTHER (Describe: name of meeting, city, state, and date of meeting)

12. HAVE YOUR ATTACHED RESEARCH/TECHNICAL MATERIALS BEEN PREVIOUSLY APPROVED TO BE PUBLISHED/PRESENTED?
    ☐ YES ☒ NO
    ASSIGNED FILE # ____________________________
    DATE ____________________________________________________________________________

13. EXPECTED DATE WHEN YOU WILL NEED THE CRD TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC
    NOTE: All publications/presentations are required to be placed in the Defense Technical Information Center (DTIC).
    DATE ____________________________________________________________________________

14. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email)
    Cacic, Kelsey A.
    220-0847

15. DUTY PHONE/PAGER NUMBER

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

   LAST NAME, FIRST NAME AND M.I. | GRADE/RANK | SQUADRON/GROUP/OFFICE SYMBOL | INSTITUTION (If not 59 MDW)
   -------------------------------|------------|-----------------------------|--------------------------
   a. Cacic, Kelsey A            | 03         | 959 CSPS/SGVT               | SAMMC                    |
   b. Sladky, John H             | 06         | 959 MDOS/SGOT               | SAMMC                    |
   c. Sherman, Paul              | 06         | USAF School of Aerospace Medicine | Wright-Patterson    |
   d. McGuire, Steven            |            | 59 MDW & USAFSAM            |                          |

17. IS A 502 ISG/JAC ETHICS REVIEW REQUIRED (JEB DOD 5500.07-R)? ☐ YES ☒ NO

18. AUTHOR'S PRINTED NAME, RANK, GRADE
    Kelsey A Cacic, 03

19. AUTHOR'S SIGNATURE
    ____________________________

20. DATE
    08Jun2017

21. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE
    JEFFREY C. McCLEAN, Lt Col, Neurology Program Director

22. APPROVING AUTHORITY'S SIGNATURE
    ____________________________

23. DATE
    12Jun2017
The author added the human research disclaimer statement to the poster presentation and provided the IRB approval letter for the research study. The poster presentation is approved.
Concentrations of Serum Inflammatory Markers after Hypobaric Exposure in Aircrew Trainees

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2Department of Neurology, 5th Medical Wing, Joint Base San Antonio - Lackland, TX.
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BACKGROUND

Recurrent non-hypoxic hypobaric exposure in Air Force U-2 pilots is associated with acquired decrements in neurocognitive performance with parallel diffuse axonal injury demonstrated on magnetic resonance imaging (MRI). The pathophysiology of this brain injury is not well understood but may be related to quantitative changes in inflammatory serum markers.1-3 The aim of this study is to assess whether protein and cytokine concentrations change after non-hypoxic hypobaric exposure. We hypothesize that inflammatory markers, which elevate in decompression sickness, traumatic brain injury (TBI), and various neurological conditions associated with decreased neurocognitive performance, would change in response to hypobaric exposure.

RESULTS

**Concentrations of serum markers**

α-IFN: Biomarker of neuro-inflammatory response

TNF: Higher levels after TBI have been correlated with more severe injuries4

IL-6: Cytokine, seen elevated after severe TBI and subarachnoid hemorrhage5

SB-100: S-100 calcium binding protein B, elevate with hypoxic inflammatory injury, increase with greater injury severity and decreased survival6

### METHODS

**Subjects:** 75 aircrew trainees (AF) and 50 controls (NON) matched for age, health, and physical activity levels

**Exposure:** Aircrew chamber training: 100% O2 @ 25,000 ft at 4.5 psi; approximately 30 min hypobaric, 2-5 min hypoxic

**Data Collection:** Serum was collected 30 min before, 30 min after, 24 h, 72 h in relation to exposure.

**Analysis:** Within-group two-tailed paired t-test between time points

Within-group two-tailed paired t-test analysis demonstrated a decrease in SB-100 in the exposure group from pre-hypobaric exposure to post-hypobaric exposure without significant change 24 h or 72 h after exposure. There were no statistically significant differences in α-IFN, TNF, or IL-6 concentrations compared to baseline at any other time points.

CONCLUSION

This study provides evidence of inflammatory marker changes in serum SB-100 concentrations without clinical symptoms, demonstrating possible secondary response to hypobaric exposure. Prior research has demonstrated SB-100 involvement with blood-brain barrier regulation, an etiology that is thought to be involved in hypobaric-induced pathophysiology. SB-100 has also received recent attention as a biomarker for TBI associated with cell division, apoptosis, and inflammation.7 Changes in SB-100 after hypobaric exposure may help explain the pathophysiology for the pattern of damage seen on imaging. Limitations of this study include clinical lab analysis; further analyses will be conducted in a research lab. Further research is needed to elucidate involvement of other inflammatory cytokines and effects of repeated non-hypoxic hypobaric exposure.

FUTURE DIRECTIONS

Phase 3 Single Exposure Human Consider additional biomarkers

Phase 3 Recurrent Exposure (Swine) CSF and serum biomarkers

U-2 pilot occupational MRI

BIBLIOGRAPHY