



DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS



30 MAY 2017

MEMORANDUM FOR ST
ATTN: SANDRA VALTIER

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Impact of Juvenile Cannabinoid Receptor Targeting on Adult Restrictive-Repetitive Behaviors and Cytokine Expression** presented at/published to **Society of Neuroscience, Washington, DC, 11-15 November 2017** in accordance with MDWI 41-108, has been approved and assigned local file #**17240**.
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

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

INSTRUCTIONS

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

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

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"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."

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Impact of juvenile cannabinoid receptor targeting on adult restrictive-repetitive behaviors and cytokine expression

AUTHOR BLOCK: M. LEONARD¹, L. FERREIRA², N. A. WITT², C. AMAYA¹, H. XIA³, S. T. SCHULTZ², *G. G. GOULD²;

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Abstract:

Restrictive-repetitive behaviors are a core autism symptom that can be modeled in mice for behavioral pharmacology studies. Marble burying is an index of repetitive behavior that is sensitive to sedatives. In prior studies, administration of WIN55,212-2 (0.1 mg/kg), a cannabinoid receptor (CB1 and CB2) agonist, attenuated burying. Yet marble burying captures only "lower order" repetition, paralleling stereotypies like repetitive movements or manipulation of objects. To examine higher order restrictive "perseverative" behaviors such as insistence on sameness (narrow interests), cognitive flexibility or "reversal learning" tests provide more insight. The water T-maze for mice is modified approach to measure potential efficacy of therapeutics to this end. The test is for a position habit reinforced by successfully locating a platform to escape from water. Following acquisition, the platform position is changed to assess reversal learning. Since the CB₁ agonist WIN 55,212-2 acutely suppressed burying, we hypothesized targeting CB₁ and/or CB₂ receptors in adolescence might persistently alter burying and reversal learning. We compared effects of juvenile sub-chronic exposures to cannabinoid agonists, inverse agonists, and endocannabinoid clearance (FAAH) inhibitors in water T-maze and marble burying in adulthood. We found the cannabinoid agonist WIN 55,212-2 delayed habit acquisition. Mice administered FAAH inhibitors such as URB597 or acetaminophen exhibited delays in reversal learning, with no reduction in marble burying. Treatment with the CB₁ inverse-agonist AM251 accelerated reversal. In a pilot study, serum collected after behavior was used for cytokine and chemokine measures using a Biorad Bio-plex mouse cytokine 23-plex panel. Eotxain levels, which inhibit neurogenesis, were high in C57BL6 treated as juveniles with >100 mg/kg acetaminophen. These mice also had elevated

TNFalpha and G-CSF, which act as granulocyte stimulation factors. By contrast eotaxin levels were low and along with G-CSF unaffected by acetaminophen, while TNFalpha expression was reduced in acetaminophen treated BTBR mice relative to controls. Studies to determine if these effects can be diminished by adipose derived mesenchymal stem cell treatments are ongoing.

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. 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 1966m as amended.
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Support: Yes

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