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TITLE: Repair of the Traumatically Injured Central Visual System by Interneuron Transplantation

PRINCIPAL INVESTIGATOR: Robert Hunt, PhD

CONTRACTING ORGANIZATION: University of California, Irvine, CA

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6. AUTHOR(S)

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5d. PROJECT NUMBER

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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Irvine, CA 92697-7600

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

In the second year of the award, we performed a comprehensive analysis of the anatomical and electrophysiological incorporation of MGE cells into brain injured V1 circuits. These studies will be presented as an abstract at SfN this year (Hou, et al., 2023) and show encouraging results for the further development of this cell therapy for central visual system injury. We completed an anatomical analysis of the grafted cells. We discovered deficits in synaptic inhibition following TBI to V1, and inhibitory drive to V1 neurons was restored by MGE cell grafts. We performed initial behavioral and in vivo electrophysiological analysis of V1 in control and brain injured animal with and without MGE cell grafts. During the next year, we plan to complete the proposed anaomical, electrophysiological and behavioral studies testing the therapeutic efficacy of interneuron cell transplantation for V1 TBI. This work will provide new information about the plasticity of the injured visual system and advance our long-term goal of developing an interneuron cell therapy for TBI.

15. SUBJECT TERMS

Traumatic brain injury, vision, central visual system, interneuron, cell therapy, transplantation, circuit plasticity

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	14	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. INTRODUCTION: *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Traumatic injuries, such as those that occur on the battlefield, can result in permanent visual impairment, because neurons that die from brain injury cannot be regenerated. We propose studies to restore vision following traumatic brain injury (TBI) using a cell therapy approach. Based on findings from our lab and others that inhibitory interneurons are particularly vulnerable to TBI and play critical roles in visual circuit function, the planned cell therapy product is a progenitor population that develops into physiologically mature inhibitory neurons. This approach is builds off our recent work demonstrating that progenitors of inhibitory interneurons derived from the embryonic medial ganglionic eminence (MGE) migrate, integrate and restore inhibition in the injured adult brain. This is a robust property of MGE cells that makes them an ideal candidate for use in cell therapy. The proposed research will address the Vision Research Program Investigator-Initiated Research Award Focus Area of "Restoration of visual function after trauma-related vision loss or severe visual impairment." We will test the hypothesis that MGE cell transplantation results in widespread synaptic incorporation of functionally mature GABAergic interneurons that reconstruct visually-relevant circuits and restore long-lasting impairments in vision after visual cortex injury. Our aims are to (1) examine the integration of MGE cells into brain injured visual cortex and (2) assess the therapeutic potential of MGE cells in a mouse model of visual cortex TBI. We will transplant MGE progenitors into a mouse model of visual cortex injury at acute and chronic stages post-injury. In Aim 1, we will determine precisely where these cells integrate within brain injured visual circuits. Our approach includes (1) immunostaining to evaluate the survival, migration and cell types generated by cell grafts into V1; (2) viral tracing, iDISCO tissue clearing and whole brain light-sheet imaging to visualize the pre- and post-synaptic targets of grafted neurons and (3) a combination of whole-cell patch-clamp recordings and optogenetics in acute brain slices to determine input-output patterns of these cells within recipient brain circuits. In Aim 2, we will test whether MGE transplantation can correct long-lasting impairments in visual acuity or the responses of visual cortex neurons to a range of visual stimuli *in vivo*. Comparisons will be made between adult control and brain injured mice receiving cell grafts or media injections. Our work has the potential to allow injured soldiers to return to active service or return to normal civilian life.

2. KEYWORDS: *Provide a brief list of keywords (limit to 20 words).*

Traumatic brain injury, vision, central visual system, interneuron, cell therapy, transplantation, circuit plasticity

3. ACCOMPLISHMENTS: *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Major Task 1: Immunohistochemical analysis of transplanted MGE cells	Months	% complete
Subtask 1: ACRURO and IACUC approvals	1	100%
Subtask 2: Immunostaining to evaluate MGE cell survival / migration in brain injured V1 - up to 1 year after transplantation	1-24	75%
Subtask 3: Immunostaining to evaluate markers expressed by transplanted MGE cells	1-24	100%
Major Task 2: Visualization of local and long-distance connections	6-24	
Subtask 1: Immunostaining to evaluate post-synaptic targets of transplanted interneurons in control and brain injured V1	6-24	0%
Subtask 2: Viral tracing to evaluate pre-synaptic targets of transplanted interneurons in control and brain injured V1	6-24	15%
Major Task 3: Electrophysiological analysis	9-24	
Subtask 1: Current-clamp recordings from transplanted interneurons	9-24	50%
Subtask 2: Voltage-clamp recordings from host neurons	9-24	75%
Subtask 3: Current-clamp recordings from transplanted interneurons; Voltage-clamp recordings from host neurons	9-24	25%

Major Task 4: Behavioral assessment of visual acuity **Hypothesis:** MGE-derived interneurons correct long-term visual deficits in adult mice following CCI injury	12-36	
Subtask 1: Behavioral assessment of visual acuity in MGE-grafted mice	12-36	70%
Subtask 2: Confirm the presence of GFP cells in MGE-grafted mice.	18-36	70%
Major Task 5: In vivo electrophysiology	12-36	
Subtask 1: Use *in vivo* electrophysiology to test if MGE transplantation restores responses to visual stimuli	12-36	70%
Subtask 2: Use *in vivo* electrophysiology to test effect of MGE transplantation on center-surround responses	12-36	25%
Subtask 3: Confirm the presence of GFP cells in MGE-grafted mice.	18-36	25%

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

1) Major activities completed during year 1:

1. We performed transgenic animal croses and established breeding colonies for the proposed viral tracing studies.

2. We completed immunostaining experiments to test survival, migration and cell phenotype of MGE grafted cells in brain injured mice (outlined in Aim 1 of the proposal). Cohorts for transplants made at 1wk and 15wk after TBI were completed.

3. We completed patch-clamp electrophysiology studies (outlined in Aim 1 of the proposal) to test electrophysiologyical phenotype of the transplanted cells (e.g., firing properties) and to test whether MGE transplantation increases inhibition after V1 TBI.

4. We optimized the visual acuity behavior assay to test vision after TBI and after MGE transplantation. We examined three cohorts (n=15 mice each) of uninjured control, TBI+media and TBI+MGE mice.

5. We initiated in vivo electrophysiological recordings in V1, ensuring reproducibility in vivo repsonses of V1 to mild TBI. We then examined three cohorts (n=15 mice each) of uninjured control, TBI+media and TBI+MGE mice.

6. We submitted an abstract to Society for Neuroscience describing our initial results on MGE transplantation after TBI to visual cortex (Hou et al, 2022).

2) Specific objectives

1. Determine if MGE cells survive, migrate and mature into inhibitory interneurons
    a. This objective was accomplished for acute and chronic transplants, and these data were analyzed.
2. Evaluate the electrophyiological integration of MGE transplanted cells
    a. This objective has been completed. Experiments have been initiated and are expected to take two years to complete.
3. Behavioral of visual acuity
    a. This objective has not been completed. Experiments have been initiated and are expected to take two years to complete.

4. Evaluate in vivo electrophysiological responses after MGE transplantation
    a. This objective has not been completed. Experiments have been initiated and are expected to take two years to complete.

3) Significant results or key outcomes

1. During the current reporting period, we performed studies to evaluate MGE progenitors transplanted into the traumatically injured visual cortex of mice. Our results show that MGE progentiors survive, migrate up to 1.5mm in visual cortex and differentiate into subtypes of MGE-GABAergic neurons (e.g., they express GAD67, PV and SST, but not VIP which derives from CGE). This phenotyping of the grafted cells is consistent with what we expect.
2. Using slice electrophysiology, we obtained patch-clamp recordings from host and grafted neurons 45-60 DAT. Grafted cells display functional properties of physiological mature GABAergic neurons, with intrinsice membrane and firing properties consisted with mature MGE-derived interneurons. All grafted neurons received excitatory synaptic input, indicating functional integration into injured V1 circuits.
3. We also obtained voltage-clamp recordings from layer 2/3 pyramidal neurons in V1. After TBI there was a significant loss of both spontaneous (network-driven) and miniature (action potential independent) inhibitory drive onto V1 neurons. IPSC frequencies were reduced by ~60%; no significant difference in event amplitude or kinetics was observed. At 45-60 DAT, both spontaneous and miniature IPSC frequencies were restored to control levels.
4. We performed behavior assessment of uninjured controls, brain injured mice receiving media injections and brain injured mice receiving MGE grafts. Experiments were performed ~60 DAT, and animals were trained to reach a platform in a water-based task and then tested for visual acuity. Three cohorts of animals have been completed, but these experiments are still underway. Initial results suggest a deficit in visual acuity after TBI (i.e., brain injured mice make fewer correct choices for a hidden platform at increasing spatial frequencies), and MGE-grafted animals perform similar to controls. This is an encouraging result, but preliminary. Animals are examined post-hoc to confirm presence of GFP cells in grafted mice.
5. Following behavior analysis, we performed in vivo electrophysiological recordings to quantify neuron responses to visual stimuli. In these experiments, we confirmed deficits reported in our prior publication (Frankowski, Foik, Communications Biology, 2021). In MGE-grafted mice, some aspects of V1 neuron tuning is improved while other aspects still show deficits. These experiments are incomplete and we are still analyzing the single unit activity in these animals. We also plan to record from additional cohorts in the upcoming year.

4) Other achievements

1. Results from this award will be presented at the following conferences:
    a. Hou B, Eom J, Lyon DC, Hunt RF (2021) Loss of inhibition following mild traumatic brain injury to primary visual cortex. **Society for Neuroscience Abstracts**

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

1. **Structured one-on-one training with collaborators at UCI:** Lab members recieved joint mentorship and training in the Hunt and Lyon labs through one-on-one mentorship, joint lab meetings, etc. These on-going interactions have been extremely valuable as they provide a forum for lab members to discuss project progress and exchange technical knowledge within our collaborative group at UCI.

2. **Seminars at UCI:** Our laboratories actively participate in the UCI Center for Translational Vision Research, Epilepsy Research Center as well as the Stem Cell Research Center. Each center hosts a seminar series featuring outside speakers. As a faculty member in each of these programs, I strongly encourage lab participation and attendance at these meetings. The Department of Anatomy & Neurobiology also hosts a seminar series and a monthly Progress in Neuroscience series in which lab members presented the funded research. In these meetings, postdocs and graduate students in the department present their unpublished research in a journal club format. These events have been an excellent opportunity to interact with other faculty / laboratories, present original data and discuss shared research interests.

3. **Responsible Conduct of Research Lecture:** All lab members attended our research ethics course sponsored by the UCI School of Medicine in the Spring Quarter. I participated as a faculty instructor in this lecture series (and every year).

4. **Conferences:** Bowen Hou will present our initial MGE transplantation results at the Society for Neuroscience annual meeting in Nov 2023.

5. **Individual Development Plans (IDPs):** All trainees in my laboratory (postdocs, graduate students, undergraduates and technicians) are required to complete an IDP based on the AAAS myIDP (http://myidp.sciencecareers.org/). I meet one-on-one with each member of the lab (from undergraduate to postdoc) in Septameber every year to discuss career/research progress and future goals. Graduate students also complete an annual IDP as part of their training in the Neuroscience Graduate Program.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

We presented our research to the broader neuroscience community through scientific publication (e.g., Frankowski, Foik, 2021) and national conferences (e.g., SfN). We also presented our research locally to neuroscientists, clinicians and the public through lectures (e.g., Bench-to-Bedside symposium, departmental talks, etc.)

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

In the next year, I think we can fully complete the following:
1. Major Task 2 – circuit tracing. The mouse colonies have been established, but the analysis is complex. This will take at least a year to complete.
2. Major Task 3, Subtask 3 – optogenetics
3. Major Tasks 4 and 5 – in vivo analysis of MGE grafted animals. This is Aim 2 of the proposal. We have made good progress on these experiments over the past year, but the analysis is complex and will take another year to complete these studies.

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

This proposal directly addresses circuit plasticity of the central visual system after TBI. Our initial results from this work were recently published (Frankowski, Foik, Communications Biology, 2021). This is the first comprehensive report of acute and long-term deficits that emerge after brain injury to V1. As we are essentially the only group studying central visual system TBI and repair, we consider this work foundational to our understanding of how V1 neurotrauma affects visual function. To our knowledge, our work is the only cell therapy for brain injury to the central visual system. This work will be important in the field of neurotrauma, but results from our studies could be applied to other neurological disorders involving visual dysfunction or maladaptive plasticity of visual circuits.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Long-term, our studies will directly test important hypotheses about the role of inhibition in visual system plasticity that have been proposed in the literature, but have not yet been tested. For example, one hypothesis suggests inhibitory interneuron transplantation works via activating plasticizer molecules in the host brain whereas other studies (including our own prior work) demonstrate electrophysiological integration of the new neurons into injured brain circuits is important.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:
- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:
- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*

- *improving social, economic, civic, or environmental conditions.*

Nothing to report

5. **CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to report

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Nothing to report

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects
NA

Significant changes in use or care of vertebrate animals
None

Significant changes in use of biohazards and/or select agents
None

6. **PRODUCTS:***List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

None

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like.Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

None

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Hou B, Eom J, Lyon DC, Hunt RF (2021) Loss of inhibition following mild traumatic brain injury to primary visual cortex. **Society for Neuroscience Abstracts**

Yes – acknowledgement of federal support

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

  NA

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

  NA

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

  NA

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

NA

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Name: *Robert Hunt, PhD*
Project Role: *PI*
Researcher Identifier (e.g. ORCID ID): *0000-0003-4490-8718*
Nearest person month worked: *1.3*

Contribution to Project: *Dr. Hunt has performed work in the area of MGE cell transplants, anatomy and electrophysiology.*

Name: *David Lyon, PhD*
Project Role: *Co-PI*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *1.2*

Contribution to Project: *Dr. Lyon has performed work in the area of electrophysiology and data analysis.*

Name: *Jisu Eom*
Project Role: *Technician*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *4.4*

Contribution to Project: *Ms Eom has performed work in the area of TBI surgeries, anatomical evaluation of injured and grafted tissues.*

Name: *Bowen Hou, PhD*
Project Role: *Postdoc*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *7.58*

Contribution to Project: *Dr. Hou has performed work in the area of MGE cell transplantation surgeries, anatomy and slice electrophysiology analyses.*

Name: *Amir Alizadeh, PhD*
Project Role: *Postdoc*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *9.5*

Contribution to Project: *Dr. Alizadeh has performed work in the area of in vivo electrophysiology, animal behavior and data analysis.*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

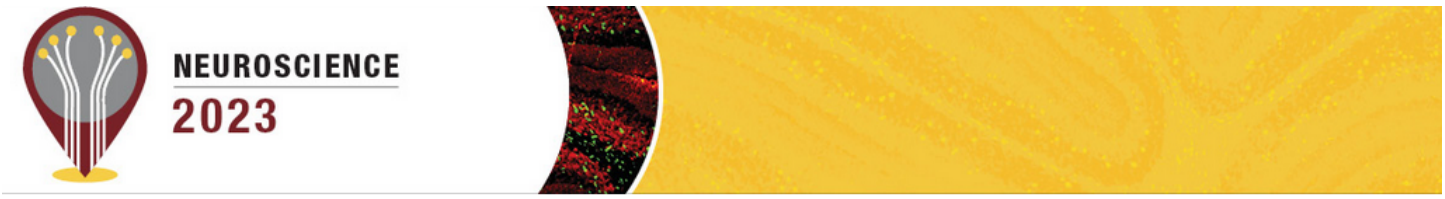
COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ebrap.org/eBRAP/public/index.htm*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil/Pages/Resources.aspx)should be updated and submitted with attachments.*

Nothing to report

9. APPENDICES:

Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.



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Add to Itinerary

Session PSTR471 - Brain Injury: Cellular Mechanisms

PSTR471.05 / X9 - Loss of inhibition following mild traumatic brain injury to primary visual cortex

November 15, 2023, 8:00 AM - 12:00 PM | WCC Halls A-C

Presenter at Poster
Wed. Nov. 15, 2023 8:00 AM - 9:00 AM

Session Type
Poster

Grant Support
DoD CDMRP W81XWH-21-1-0884

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CRIM Research Scholar Award EDUC4-12822

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Authors
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Univ. of California, Irvine, Irvine, CA

Disclosures
B. Hou: None. J. Eom: None. D. Lyon: None. R. Hunt: None.

Abstract
Visual impairments are among the most common health related challenges for individuals with traumatic brain injury (TBI). In addition to cognitive, motor and neuropsychiatric changes, as many as 75% of military veterans' self-report visual symptoms as a result of TBI. Here we performed a series of slice electrophysiology studies in a mouse model of central visual system TBI. Approximately 2 months after TBI, whole-cell voltage-clamp recordings of layer II/III neurons revealed ~50% reduction in the frequency of spontaneous (s) and miniature (m) inhibitory post-synaptic currents (IPSCs) in brain-injured V1 neurons versus uninjured controls. No concurrent change in event amplitude was found, but preliminary results indicate a potential change in event kinetics. These slice electrophysiology results suggest mild TBI to V1 produces a long-lasting reduction of GABA-mediated inhibition to principal neurons and are consistent with our prior studies describing interneuron loss throughout brain-injured V1. Ongoing experiments are testing the effect of transplanting interneuron progenitors, derived from mouse embryonic medial ganglionic eminence (MGE), on inhibition and *in vivo* electrophysiological responses to visual stimuli in V1 neurons. To date, our results suggest MGE cells survive, migrate and integrate into adult brain-injured V1 circuits.

Link to abstract: https://www.abstractsonline.com/pp8/#!/10892/presentation/42249