Supplementary Material 2 for Vanugopal S (2023) Teaching Scientific Literature Analysis: A Systematic Adoption of Skill-Building Methods to Enrich Research Training for Undergraduate Students. J Undergrad Neurosci Educ 22(1):A74-A81.

THE C.R.E.A.T.E AND C.S.S METHODS FOR SCIENTIFIC SKILL DEVELOPMENT & KNOWLEDGE INTEGRATION

C.R.E.A.T.E: **C**onsider, **R**ead, **E**lucidate hypotheses, **A**nalyze and interpret data, and **T**hink of the next **E**xperiment

C.S.S: **C**urate **S**cientific **S**ummaries

Author: Sharmila Venugopal, Ph.D.
University of California Los Angeles

Cite: S Venugopal, Journal of Undergrad Neurosci Edu, 2023

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PROMPT (CLASS DISCUSSION)

Reading a research article is __________

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TYPES OF SCIENTIFIC PUBLICATIONS

- **Primary Research Articles (PRAs)**
- **Reviews**
- Methods and Protocols
- Resources: Databases and Repositories
- Others
  - Letters and Short Reports
  - Commentaries
  - Perspectives
  - Clinical Case Study
  - Book Review etc.

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WHAT TO LOOK FOR IN A SCIENTIFIC PRA?

- Look for comprehensive studies in journals such as NEURON, Journal of Neuroscience, Journal of Neurophysiology, Cell Reports etc.
- Look for articles which follow best practices in scientific writing with
  - Detailed figures showing the data points and rigorous statistics based on the data distributions.
  - Multiple figure panels with one or more approaches to support their findings (e.g., gene expression change validated with functional protein expression).
  - Validated methodology on standard assays.
  - Provides code, data repositories etc. as needed to justify the results.

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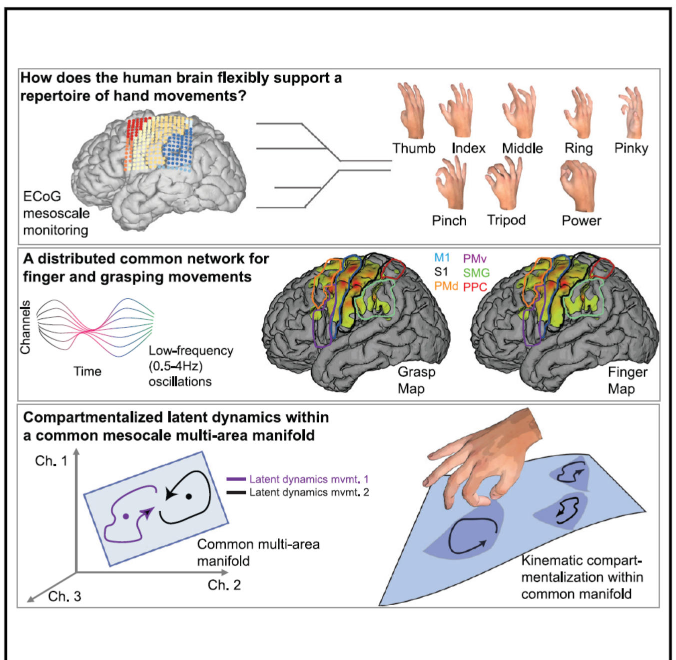
WHAT'S IN A GOOD PRA?

Neuron

Article

Compartmentalized dynamics within a common multi-area mesoscale manifold represent a repertoire of human hand movements

Graphical abstract



Authors

Nikhilesh Natraj, Daniel B. Silversmith, Edward F. Chang, Karunesh Ganguly

Correspondence

nikhilesh.natraj@ucsf.edu (N.N.), karunesh.ganguly@ucsf.edu (K.G.)

In brief

How does the human brain flexibly support a remarkably diverse repertoire of hand movements? Natraj et al. show that mesoscale activity, for movements ranging from grasps to finger individuation, lie within a common multi-area manifold spanning the "grasp network." However, latent dynamics within this manifold were movement specific and compartmentalized into distinct behaviorally relevant submanifolds.

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STUDY HYPOTHESIS IS CLEARLY STATED AND/OR DEMONSTRATED IN A GRAPHICAL FORMAT

Neuron
Article
CellPress

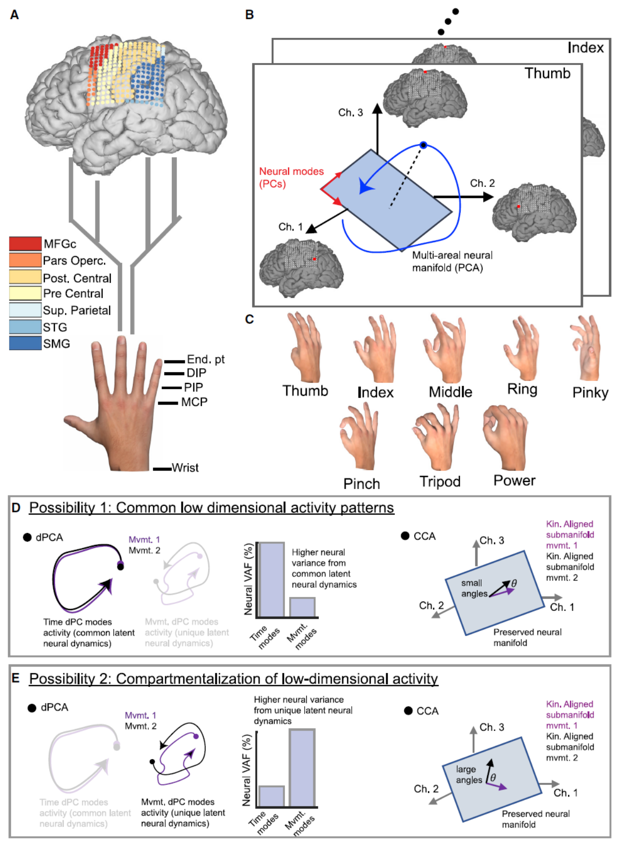

Figure 1. Latent dynamics and neural manifolds for hand-movement repertoire
(A) Multi-area ECoG grid coverage in grasp network colored by anatomical region (MFGc, caudal medial frontal gryus along the dorsal premotor cortex; Pars Operc., pars opercularis along the ventral premotor cortex; Post. Central, post central gyrus or primary S1; Pre Central, pre central gyrus or primary M1; Sup. Parietal, superior parietal gyrus along the posterior parietal cortex; STG, superior temporal gyrus along temporal cortex; SMG, supramarginal gyrus along inferior

(legend continued on next page)

CLEAR, MULTI-PANEL FIGURES SHOWING DATA POINTS IN GRAPHS AND REPRESENTATIVE IMAGES OF RAW DATA

Neuron
Article
CellPress

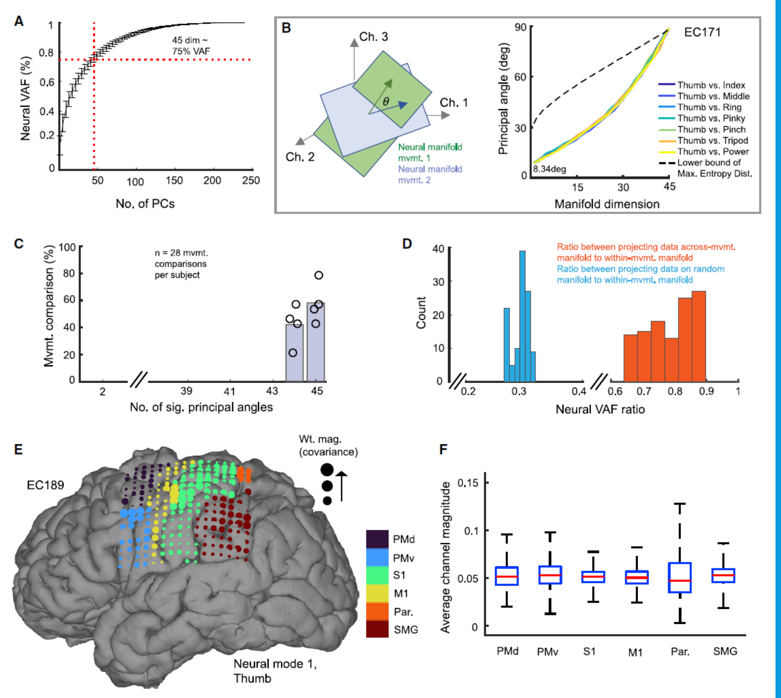

Figure 3. Common multi-areal manifold represents the movement repertoire

(A) PCA was used identify a manifold for each movement from LFOs. Average neural variance accounted for (VAF) by the PCs or neural modes is shown in the figure.

(B) (left) Similarity in the orientation between movements' 45D manifolds was evaluated in pairwise manner using the method of principal angles; smaller angles imply highly overlapping manifolds. (right) Principal angles between thumb manifold and the other seven movements in the repertoire is shown for an example subject. The black dotted line represents the lower bound of the null distribution of principal angles (2.5^{th} percentile for $\alpha = 0.05$), and the average first principal angle is highlighted (8.34 degrees).

(C) Average normalized histogram of number of significant principal angles between movements' 45D manifolds (angles computed pairwise), where each open circle represents a single subject.

(D) Ratios of across-movement VAF to within-movement VAF in real (orange) and control data (light blue) depicted as histograms.

(E) Cortical channel representation of an exemplar neural mode (1^{st} neural PC weights, EC189 thumb). Increasing sizes of electrode represent increasing spatial covariance.

(F) Boxplots of the average channel weight magnitudes within each node of the grasp network for all 45 neural modes (across movements and subjects). Edge of blue box correspond to 25^{th} and 75^{th} percentile of data; red horizontal line corresponds to the median and the whiskers extend to the entire data spread not considered outliers.

METHODS ARE WELL-DOCUMENTED AND VALIDATED IN THE STUDY

Neuron
Article

CellPress

It should also be noted that notwithstanding the differences between local population spiking activity and multi-areal mesoscale recordings, it might also be the case that the complexity of hand movements might elicit mesoscale dynamics that are fundamentally different from M1 population spiking data during well-learned and stereotyped upper-arm movements. For instance, recent studies have shown that the latent dynamics of even local population activity in M1 can be highly variable from movement to movement during grasping actions (Suresh et al., 2020; Rouse and Schieber, 2018). Although participants in our study performed pantomimed movements, it may be that multi-area neural dynamics might differ if the hand were to actually interact with objects during both grasping and finger movements (e.g., using the index finger to flip a switch). Interaction with an object can further alter the compartmentalization of neural dynamics in the grasp network (Michaels et al., 2020; Russo et al., 2020), and the resultant extrinsic inputs can result in more tangling of the latent mesoscale neural dynamics (Russo et al., 2018).

Summary

In conclusion, we present here a neural framework highlighting how distinct manifolds of mesoscale ECoG dynamics within the grasp network represent a repertoire of human hand movements; this might be a mechanism through which humans can rapidly switch among a repertoire of complex hand movements that are kinematically similar. Extending our framework to clinical populations and to naturalistic hand interactions with daily objects can aid in further understanding the function of large-scale neural manifolds for dexterous human hand control.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

- KEY RESOURCES TABLE
- RESOURCE AVAILABILITY
  - Lead contact
  - Materials Availability
  - Data and code availability
- EXPERIMENTAL MODEL AND SUBJECT DETAILS
  - Participants
- METHOD DETAILS
  - Experimental design and data acquisition
  - Sample size estimation
  - ECoG signal processing
  - Movement related information in grasp-network LFO amplitudes
  - Phase-coupling of ECoG LFOs to kinematics
  - Neural manifold analyses
  - demixed Principal Component Analysis to evaluate latent dynamics
  - Relationship between LFOs and γ_H
  - Shared variance between the manifolds of LFOs and γ_H^{LFO}
  - Kinematic recordings of the repertoire of human hand movements
  - Kinematically aligned submanifold analyses
  - Distinctiveness of aligned submanifolds
  - Compartmentalization of behaviorally relevant neural dynamics by the submanifolds
  - Multiplexing of synergies
  - Spatial map of the CCA neural modes
- QUANTIFICATION AND STATISTICAL ANALYSIS

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.neuron.2021.10.002.

ACKNOWLEDGMENTS

We thank Kate Derosier, Reza Abiri, and Preeya Khanna for valuable feedback and Sarah Seko for help with kinematic data, specifically for nonlinear inverse kinematic analyses. This work was supported by grant 2013101 from the Doris Duke Charitable Foundation, the National Institutes of Health through the NIH Director's New Innovator Award (1 DP2 HD087955), the Weill Neurohub, and the National Institute of Neurological Disorders and Stroke (K02NS093014).

AUTHOR CONTRIBUTIONS

Conceptualization, N.N., D.B.S., E.F.C., and K.G.; hypothesis, N.N. and K.G.; kinematic data acquisition code, D.B.S.; data collection, N.N. and D.B.S.; data analysis, methodology, and software, N.N.; patient care, brain surgery, and ECoG data management, E.F.C.; article draft, N.N.; article revision, N.N., D.B.S., and K.G.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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Published: October 21, 2021

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Benabid, A.L., Costecalde, T., Eliseyev, A., Charvet, G., Verney, A., Karakas, S., Foerster, M., Lambert, A., Morinière, B., Abroug, N., et al. (2019). An exoskeleton controlled by an epidural wireless brain-machine interface in a tetraplegic patient: a proof-of-concept demonstration. Lancet Neurol. 18, 1112–1122.

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UNDERSTANDING A PRA:

In this course, you will learn two approaches:

- **The C.R.E.A.T.E. approach** ✓
- **The C.S.S. approach**

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LEARNING OBJECTIVES

EACH STUDENT MUST:

- Demonstrate comprehension of scientific literature through systematic development of pedagogical outcomes using the C.R.E.A.T.E approach.
- Demonstrate longitudinal improvement in the C.R.E.A.T.E outcomes such as concept maps, figures analysis etc.
- Demonstrate enhancement in critical analysis skills by application of a novel C.S.S. approach for a research theme.
- Build confidence and peer collaboration skills.
- Demonstrate improvements in their scientific communication skills.

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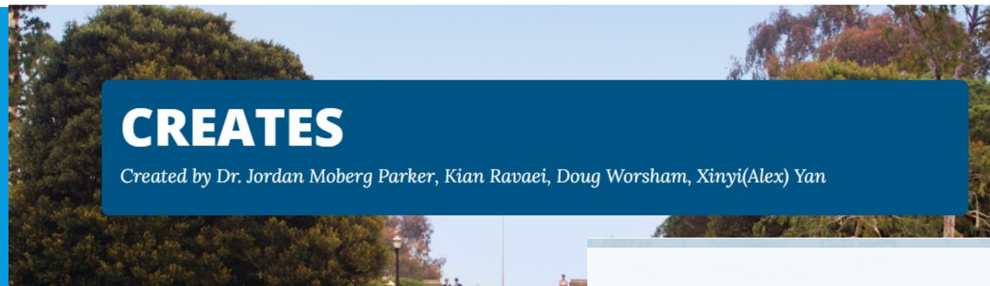
C.R.E.A.T.E. RESOURCE TO GUIDE YOU

WI+RE

ABOUT · WORKSHOPS · TUTORIALS · HANDOUTS · CONTACT



CREATES is a set of 6 steps to help you read, analyze, and fully understand the narrative of scientific papers!

AN INNOVATIVE METHOD FOR UNDERSTANDING SCIENTIFIC ARTICLES

C.R.E.A.T.E.S.

The CREATES website guides you through all six steps of the CREATES process, providing helpful examples and tips from both teachers and students along the way. You'll find detailed annotations of authentic student work to help you get the most out of the CREATES process!

INSTRUCTIONS

HOW TO USE THE C.R.E.A.T.E.S. SITE

- **C**oncept map the introduction
- **R**ead & annotate the methods and results
- **E**lucidate the hypothesis for each experiment
- **A**nalyze & interpret the data
- **T**hink of the next...
- **E**xperiment
- **S**ynthesize the entire paper to illustrate the scientific narrative

1. Choose any primary scientific journal article.
2. Start at C and go in order (or, choose one letter to focus on).
3. Read the entire webpage.
   - **Steps**: Specific, concrete steps to follow for each letter.
   - **Examples**: Real student examples with real instructor feedback.
   - **Tips**: Additional tips, strategies, and quotes, plus a checklist to track your progress.
4. Give it a try!
5. Advance to the next letter!

Get started!

https://uclalibrary.github.io/creates/

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C.R.E.A.T.E. ARTICLES TO GUIDE YOU

CBE—Life Sciences Education
Vol. 12, 59–72, Spring 2013

Article

CREATE Cornerstone: Introduction to Scientific Thinking, a New Course for STEM-Interested Freshmen, Demystifies Scientific Thinking through Analysis of Scientific Literature

Alan J. Gottesman and Sally G. Hoskins

City College and the Graduate Center, City University of New York, New York, NY 10031

Submitted November 21, 2012; Revised December 15, 2012; Accepted December 15, 2012
Monitoring Editor: Jose Vazquez

The Journal of Undergraduate Neuroscience Education (JUNE), Spring 2008, 6(2):A40-A52

ARTICLE

Using a Paradigm Shift to Teach Neurobiology and the Nature of Science—a C.R.E.A.T.E.-based Approach

Sally G. Hoskins
Biology Department, City College and the Graduate Center, City University of New York, New York, NY 10031

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EXPECTED OUTPUTS OF C.R.E.A.T.E. BASED PRA ANALYSIS

1. A **Concept Map** for Introduction
2. A **Methods Diagram** for illustrating the Approaches
3. **Annotations of Results Figures** consisting of: the experimental hypothesis, data and statistics to elucidate the hypothesis.
4. Think of the **Next Experiment**
5. A **Synthesis Map** of the whole study

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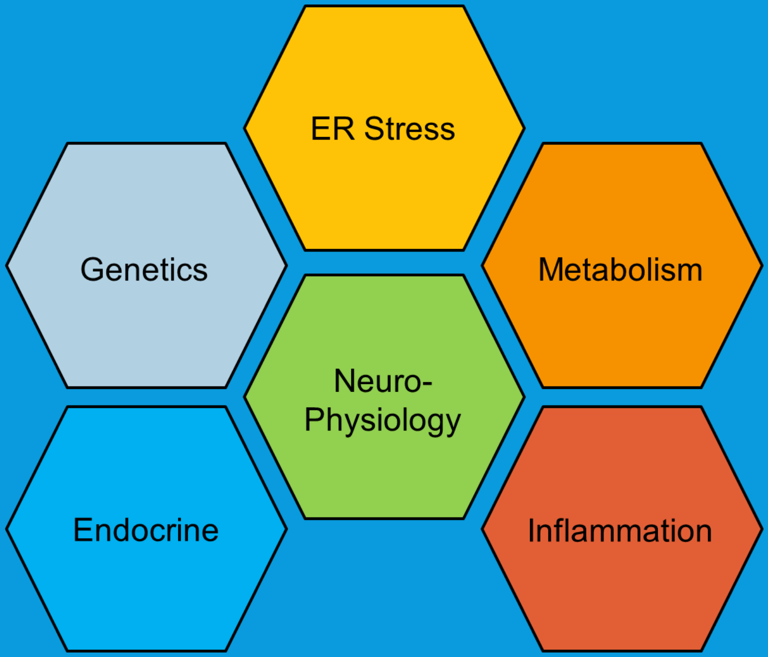
C.S.S.: Curate Scientific Summaries

- The novel C.S.S. approach leverages published work curated in the National Center for Biotechnology Information (NCBI) databases.
- Peer Learning PODs (PLPs) curate published evidence for causal interactions between proteins and other biomolecules mediating various functional crosstalks in the nervous system (e.g., interactions between neural excitability, neuroinflammation, and neuroendocrine functions).



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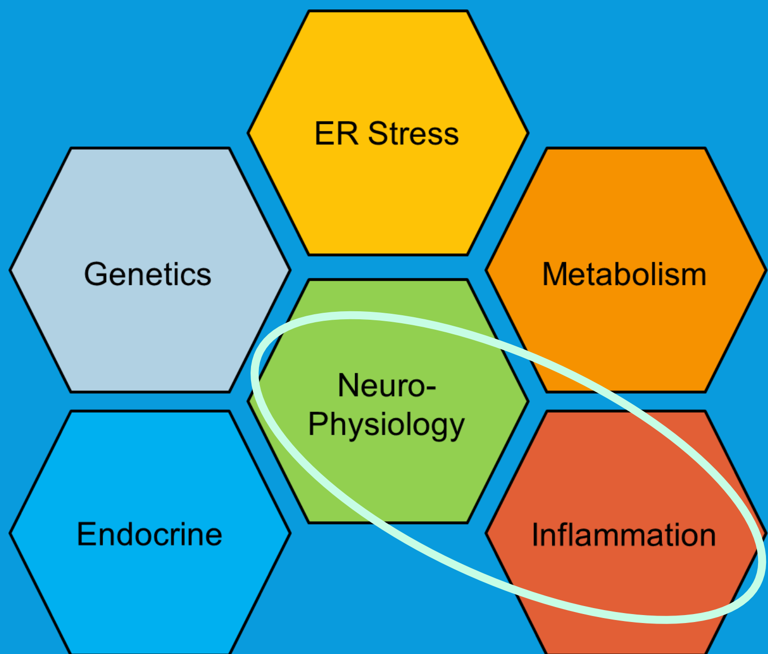
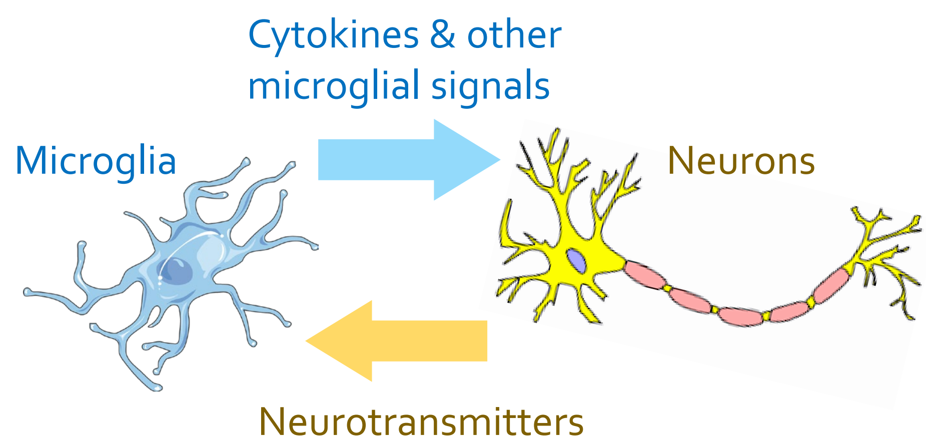
RESEARCH THEME

What cellular and molecular signaling mechanisms mediate the crosstalk between neurophysiology and neuroinflammation?



* **Microglia** are the resident immune cells of the nervous system

Focus on the molecular mediators of Neuron-Microglia* interactions



Effects on Neurophysiology

- Intrinsic plasticity
- Synaptic plasticity
- Structural plasticity
- • Neurotoxicity
  • Neuroprotection

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C.S.S. SUMMARY EXAMPLE

STEP-1: PRA pre-evaluation

– Is there experimental evidence for causal effect from A → E → T?

Front Neurol. 2016 Mar 30;7:44. doi: 10.3389/fneur.2016.00044. eCollection 2016.

Changes in Neuronal Excitability by Activated Microglia: Differential Na(+) Current Upregulation in Pyramid-Shaped and Bipolar Neurons by TNF-α and IL-18

Lars Klapal [1], Birte A Igelhorst [1], Irmgard D Dietzel-Meyer [1]

Affiliations + expand

PMID: 27065940 PMCID: PMC4812774 DOI: 10.3389/fneur.2016.00044

Free PMC article

Activator(s) A	Effector(s) E	Target(s) T	Functional Effect
TGF-b	-	Nav current	Intrinsic
TNF-a	TNF-a1, TNF-a2	Nav current	Intrinsic
IL-18	-	Nav current	Intrinsic

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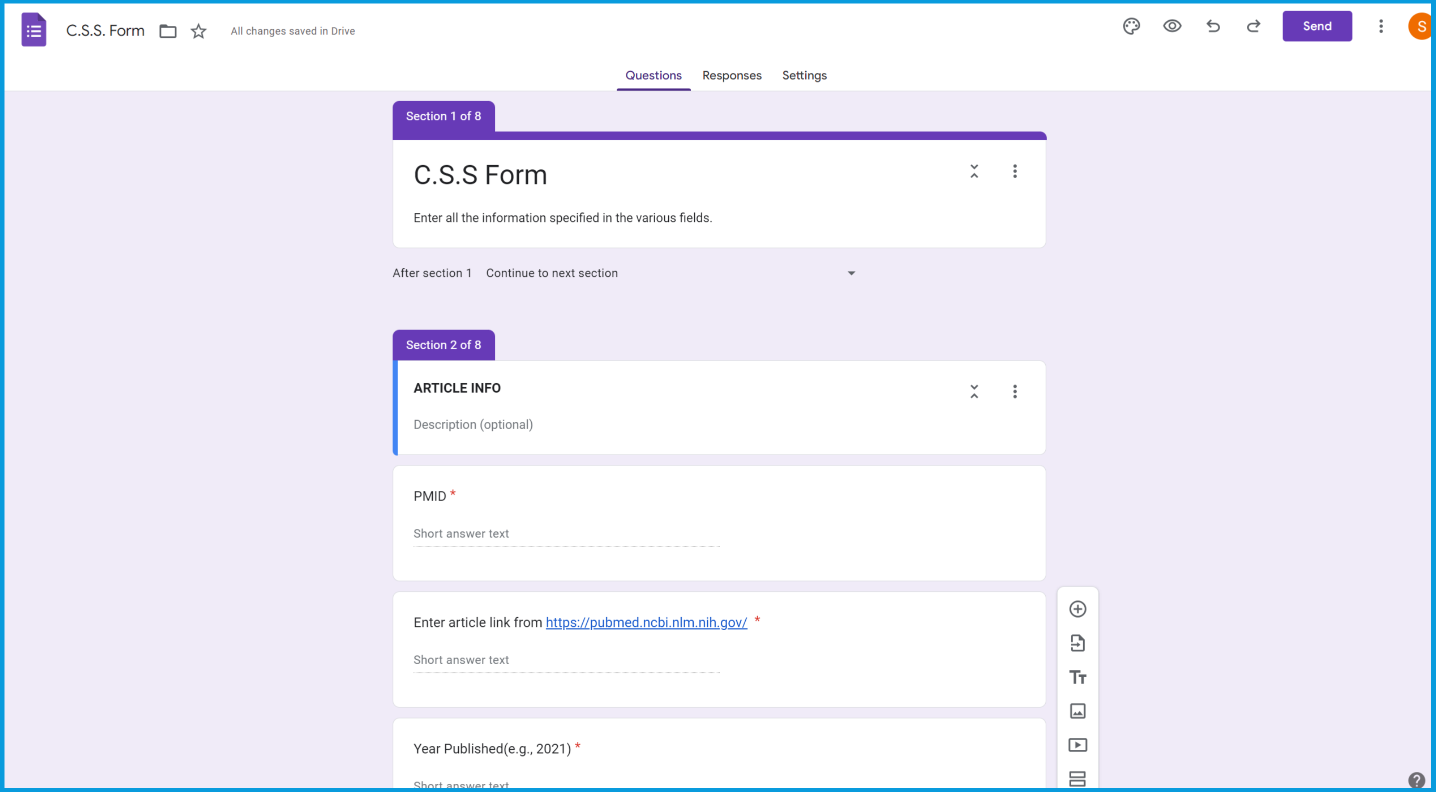
C.S.S. SUMMARY EXAMPLE

STEP-2: PRA curation

– Complete the C.S.S. Form to consolidate evidence of causal molecular and cellular crosstalk in the nervous system.



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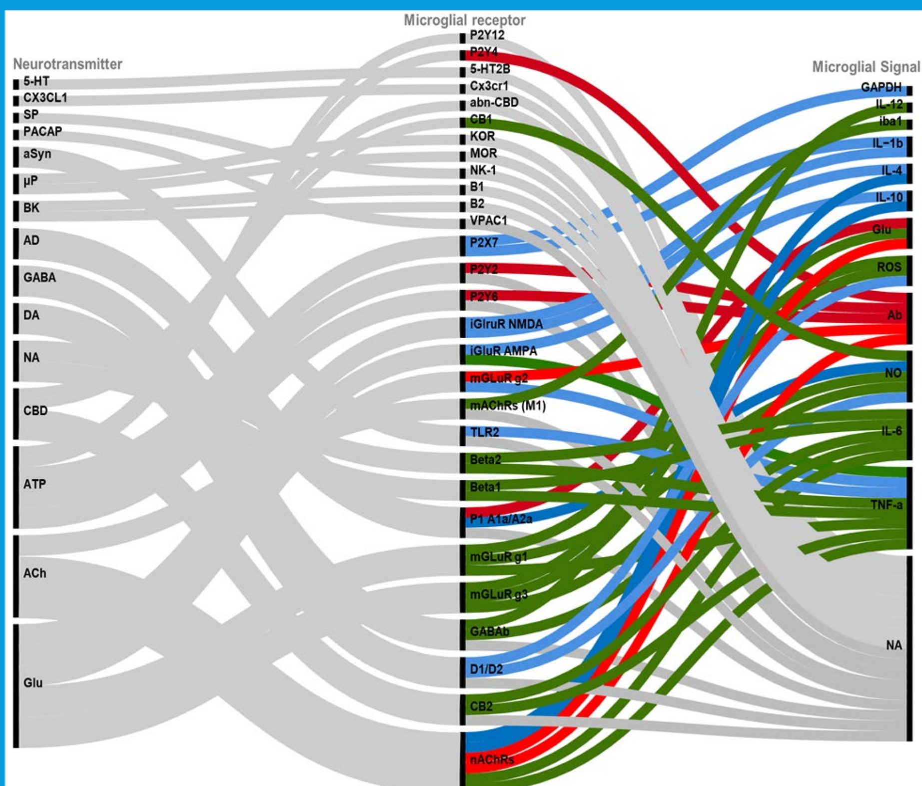
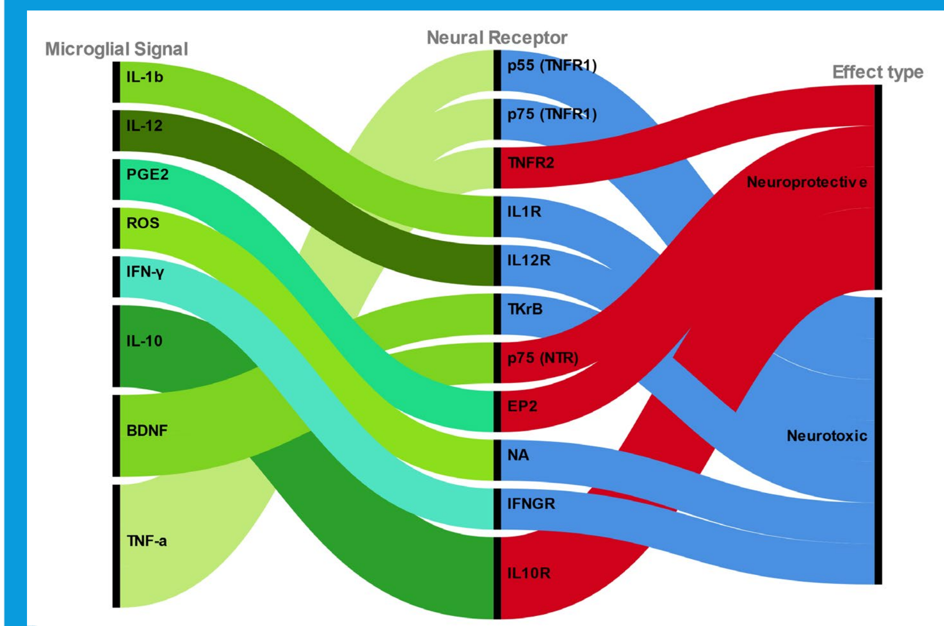
RESULTS OF AN EXAMPLE CASE STUDY USING THE C.S.S APPROACH

A → E → T



A → E → T



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GUIDELINES FOR WEEKLY CLASS ACTIVITIES

- Week-1: Review class lecture and notes on the C.R.E.A.T.E. and C.S.S. approaches.
- Week-2:
  - Each PLP reads and presents 1 of the 3 assigned review articles.
  - All PLPs must present.
  - PLPs select PRAs (4 per PLP) and enter article PMIDs and NCBI article link in the collective Google Sheet! (make sure that there are no duplicates).
- Weeks 3-6:
  - Conduct C.R.E.A.T.E-based analysis of each PRA with your PLP. Each POD makes a 15 mins slide presentation of the C.R.E.A.T.E outcomes during class discussion each week.
  - Concurrently, each week, fill out the Google Form to complete the C.S.S. step for each PRA analyzed using the C.R.E.A.T.E approach.

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LEARNING ASSESSMENTS

DOES EACH STUDENT…

- Demonstrate comprehension of scientific literature through systematic development of pedagogical outcomes using the C.R.E.A.T.E approach?
  - Assessed based on the clarity and presentation of concept maps, synthesis maps etc.
- Demonstrate longitudinal improvements in the C.R.E.A.T.E outcomes such as concept maps, figures analysis etc?
  - Assessed based on improved clarity and presentation of scientific theories, hypothesis and results analysis in the concept maps etc.
- Demonstrate enhancement in critical analysis skills by application of a novel C.S.S. approach for a research theme?
  - Assessed based on students' ability to unravel cause-effect analysis in the PRAs.
- Build confidence and peer collaboration skills?
  - Assessed based on self-evaluation survey, individual and group presentations.
- Demonstrate improvements in their scientific communication skills?
  - Assessed based on class presentations, ability to answer peer and instructor's questions.