Brain-Behavior Quantification and Synchronization

RFA-DA-23-030
Transformative and Integrative Models of Behavior at the Organismal Level (R34 Clinical Trial Not Allowed)

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On behalf of BRAIN Initiative BBQS Team

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Talk Outline

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

- Background
  - BRAIN Initiative's Brain-Behavior Quantification and Synchronization (BBQS)
  - BBQS Emphasis Area: Behavior at the Organismal Level

- Goals of RFA-DA-23-030

- R34 Planning Grant Mechanism

- Topics considered responsive

- Topics considered non-responsive

- Key elements

- FOA-specific Review Criteria

- Peer Review Process

- Program Evaluation

- Key Dates and Contact Info

- Questions

(copies of slides will be available)

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Brain-Behavior Quantification and Synchronization (BBQS)

- **The BRAIN Initiative 2.0: From Cells to Circuits, Toward Cures**

  - Call for "more sophisticated methods of quantifying behavioral, environmental, and internal state influences on individuals."

  - Call for "tools to analyze naturalistic (untrained) and trained behaviors" and "to assimilate and link brain recordings with behavior."

- **BBQS: Understanding the full complexity of behavior in the context of complex environments**

  - High-resolution capture of multiple 'dimensions' of behavior, including correlated physiological function at the organismal level

  - Simultaneous capture of data from organism's complex, dynamic physical and/or social environment

  - Computational models that capture dynamic behavior-environment relationships across multiple timescales and designed to integrate correlated neural activity

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BBQS - Behavior at the Organismal Level

➢ Behavior is …

- how an individual responds to and/or interacts with his/her/their environment

- critical determinant of health and a major mediator of morbidity for nearly all diseases

➢ Validity/rigor in modeling neurobehavioral function research can increase with …

- Consideration of functional and adaptive significance

  - development of the individual

  - evolution of the relevant population/species

  - conservation of brain-body-behavior relationships across species

- Development of quantitative models that can be tested across model organisms

https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-23-030.html

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Limitation: Tradeoffs between resolution, multi-dimensionality and environmental complexity
High resolution tracking and/or simultaneous capture of neural activity and other physiological data require unnatural environments

Video camera

2.45 m   2.75 m

2.45 m

a

EEG cap

Treadmill

IMUs

Laser line

EEG amplifiers
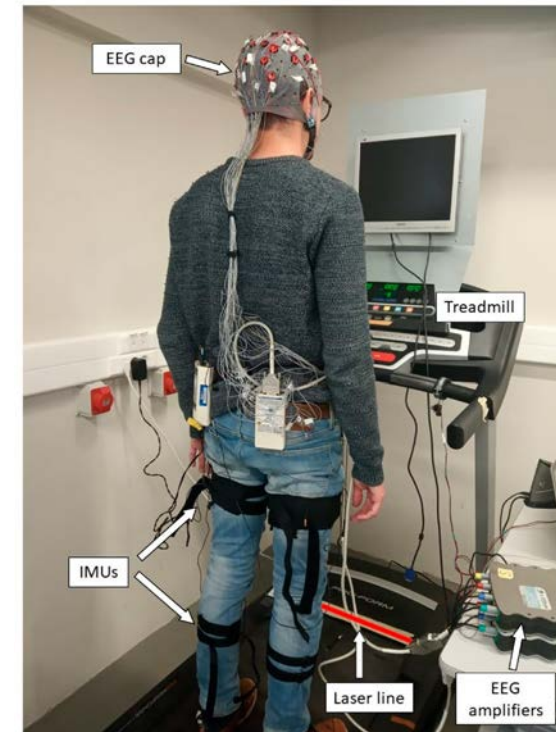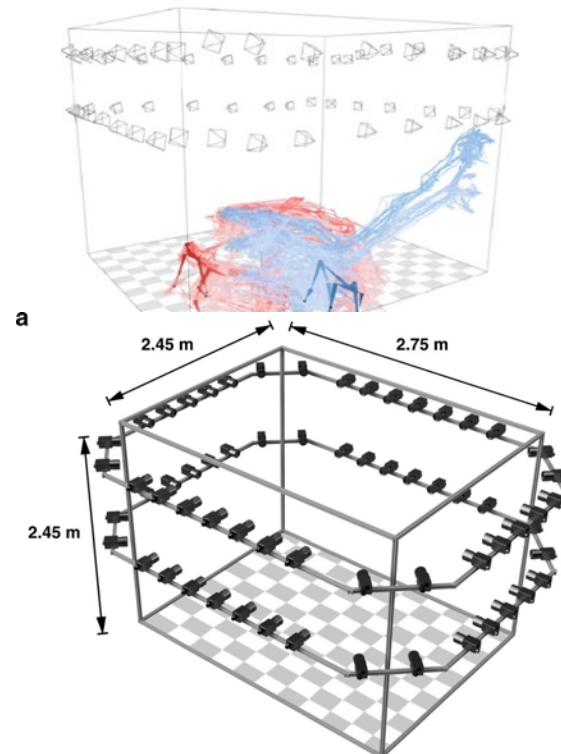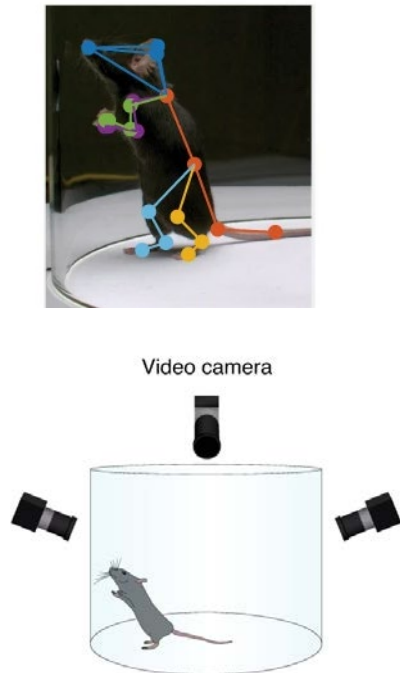
Dunn TW, et al. *Nature Methods,* 2021.
doi: 10.1038/s41592-021-01106-6

Bala, P.C. *et al.,* *Nature Commun*, 2020.
doi: 10.1038/s41467-020-18441-5

Elvira M, et al., *Sensors,* 2019. doi:10.3390/s19245444

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Current State of the Science: Deep learning-enabled behavioral tracking

Limitation: Laboratory conditions limit our understanding of the functional and adaptive value of the behavior in the animal's natural environmental

Meerkat sentinel behavior

- Would meerkat sentinel behavior be the same under highly controlled conditions?

- Would the neural mechanisms mediating sentinel-like behavior be the same in these two environments?

2.75 m

2.45 m
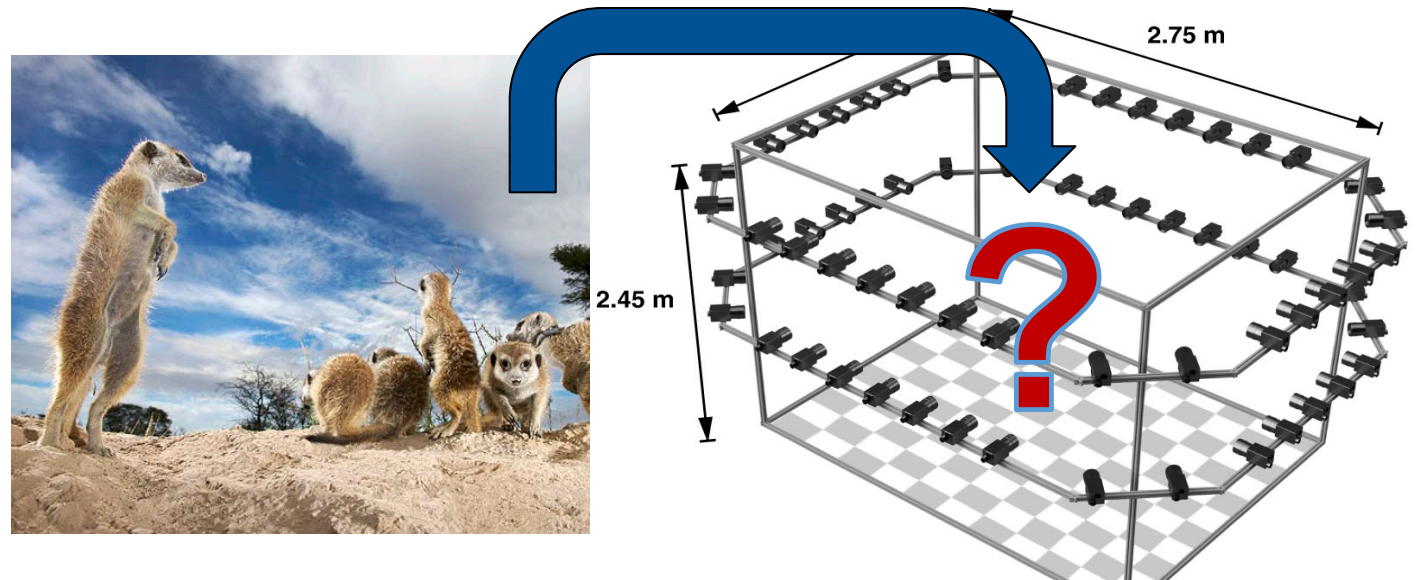
How do we incorporate functional and adaptive significance into our models of neurobehavioral function?

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RFA-DA-23-030

BRAIN Initiative: Brain-Behavior Quantification and Synchronization - Transformative and Integrative Models of Behavior at the Organismal Level (R34 Clinical Trial Not Allowed)

Goals - To support planning of a project aimed at   Part 2, Section I

1) Integration of theoretical frameworks guiding the study of behavior, its underlying mechanisms, and adaptive value

2) Acceleration of the development of technologies and methods for objective, high-resolution measurement of behavior at the level of the organism and its environment

3) Development of sharable standards and archives for high dimensional data sets from the organism and its environment

4) Development of new computational models that capture the behavior-environment interface as a complex dynamic system

https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-23-030.html

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R34 Mechanism

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

R34 mechanism - *planning* grant designed to

- permit early peer review of the rationale and concept for the proposed research project

- support development of essential elements of the research

- lead to a proposal for a full-scale project award (e.g. R01, U01), based on elements developed with the R34

R34 DA-23-030 aims to support planning activities including

- Coordination of multi-disciplinary team that may not have worked together previously

- Integration of theoretical perspectives to achieve new research design in behavioral science

- Designing/testing complex, dynamic testing environments

- Planning approaches to integrate sensing methods and/or adapting sensing method to new species

- Early development of new approaches for data analysis and archiving, including data standards

- Early development of new computational approaches for multiple heterogeneous data streams

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Responsive Research Topics

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Section I

New approaches/tools to advance synchronous high-resolution capture of multidimensional behavioral and environmental data

- multiple dimensions of behavior and correlated physiology

  - e.g. ambulation, limb, head, facial and/or eye movements, sniffing, vocalizations, glandular secretion, and peripheral physiology

  - can include reducing the burden of or constraint related to sensing method, increasing dimensionality of measurements, improving the temporal resolution, sampling duration, data storage capacity, and/or quality of data analysis

- synchronous measurement and integration of environmental with behavioral data

  - e.g. stimuli or signals presented to and/or detectable by the organism

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Responsive Research Topics

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Section I

Data informatic and computational approaches for integrating multidimensional, dynamic behavioral and environmental data into a model

- Data science approaches to integrate multiple data modalities and/or data streams
  - behavioral measures from different domains including peripheral biophysiological correlates of complex behaviors
  - Integration of data captured from the organism with data capture from the environment

- Analytic tools and statistical and/or computational approaches (e.g., ML/AI methods) to incorporate multiple data arrays
  - representing the organism's response to environmental change,
  - relationships across multiple timescales

- Use of existing data and/or synthetic data to help validate or assess feasibility of sensor methodology and/or computational models

- Approaches that integrate multidimensional behavioral and/or environmental data with synchronous measures of neural activity

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Responsive Research Topics

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Section I

Cross-cutting themes

- Simultaneous capture of multiple behavioral and environmental variables
- Unconstrained behavior in a complex and/or dynamic environment
- Overall design informed by multiple disciplines with consideration of ecologic validity
- Planning for quantitative model that integrates multi-dimensional data sets, including neural data
- Toward ultimate goal of integrating environmental and organismal (behavior+brain) data into a model of behavior as complex dynamic system

Inclusion of neural data is not required, but responsive if

- behavior and environment are sufficiently complex
- behavior is NOT significantly constrained by the method used to capture neural data

Human subj research allowed; planning activities may not qualify as an NIH Clinical trial

To learn more about NIH Clinical trials, see https://grants.nih.gov/policy/clinical-trials/definition.htm#

https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-23-030.html

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"Not Responsive" Criteria

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Section I

Applications considered to be <u>not responsive</u> to this FOA and not reviewed:

- Measuring behavior solely as a proxy for an internal cognitive or affective process

- Exclusive focus on neural activity/behavior measured solely as a function of neural activity

- Research in which behavior is highly constrained (e.g., head-fixed or chair-restrained preps) or consists of highly trained or stereotyped responses (e.g., isolated arm , eye movement)

- Lacking proposed activities that work toward a conceptual or computational model of behavior and the organism's environment as an interactive system

- Primary focus on the modeling of a neurobehavioral disorder or psychopathology

- Proposing activities that qualify as an NIH Clinical Trial

- Lacking the required one-page Plan for Enhancing Diverse Perspectives

https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-23-030.html

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Key Elements

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Section IV

1. Team-building - multi-disciplinary, functionally diverse, team

   - e.g. from fields such as neuroethology, evolutionary biology, behavioral ecology, anthropology, the social sciences, cognitive neuroscience, neurocognitive development, biokinetics, computational sciences (incl AI), bioengineering and ethics

   - must include substantial expertise in neuroscience and computational science

   - members bringing diverse perspectives and expertise to inform observing, measuring, and modeling of behavior

   - [for human subjects research] - must include an ethicist

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Key Elements

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Section IV

2. <u>Data Capture</u> - establishing feasibility of the development, adaptation and/or validation of approach to simultaneously capture multiple data streams from the organism and its dynamic social and/or physical environment

- Synchronous, high-temporal-resolution measurement of multiple modalities of behavior and correlated physiology from the freely-moving organism

- Simultaneous capture of dynamic environmental data

3. <u>Species considerations</u>

- how the selected species offer the best conditions for revealing general principles about the behavioral domain of interest or offer optimal conditions for development of approaches for capturing multiple dimensions of behavior and peripheral physiology at the level of the organism

- [For human subjects research] analytic and ethical challenges of collecting subject-level data

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Key Elements

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Section IV

4. <u>Data Analysis and Model-building</u> – establishing feasibility of approach for modeling multidimensional, dynamic behavior of the organism interacting with its social/physical environment

   - framework for a conceptual and computational integrating multidimensional behavioral and environmental data across multiple temporospatial scales

   - informed by multiple behavioral science frameworks or approaches

   - designed to ultimately integrate neural data, anticipating advances in methods for capturing neural data from freely moving animals in ecologically relevant conditions

   - [for human data] analytic and ethical challenges of archiving and analysis of subject-level data

5. <u>Data quality and harmonization</u>

   - quality assurance processes for data collection, annotation, open source/open sharing, and dissemination

   - potential for harmonization of the data generated by the planned project with existing neural data archives, including data collected by BRAIN Initiative-supported projects

6. <u>Milestones</u> - toward development of a project and basis of a competitive application for a Team U01/R01 or similar award

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Key Elements

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Sections I and IV

7. <u>Plan for Enhancing Diverse Perspectives (PEDP)</u> - required

- Through the PEDP, the BRAIN Initiative encourages the research community to consider how diverse perspectives advance the proposed specific aims and are integral to equity and inclusion in the science they perform.

- Now a required component of most BRAIN Initiative funding opportunities.

- Evaluation of the PEDP will be done during scientific review and programmatic review.

- More information, including examples, can be found at https://braininitiative.nih.gov/about/plan-enhancing-diverse-perspectives-pedp

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Key Elements

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Sections I and IV

8. Planning for Resource and Data Management and Sharing - required

- plan to address the NIH Data Management and Sharing Policy (https://sharing.nih.gov/data-management-and-sharing-policy/planning-and-budgeting-DMS/writing-a-data-management-and-sharing-plan)

- plan to address BRAIN Initiative expectations for data sharing (see NOT-MH-19-010) and include participation in post-award activities (e.g., BRAIN Initiative investigator meetings) designed to increase sharing of resources, data, protocols, and other information for BRAIN Initiative awardees

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RFA-DA-23-030 Part 2, Section V

Core Review Criteria

- Significance
- Investigators
- Innovation
- Approach
- Environment

RFA-DA-23-030
FOA-specific Review Criteria

https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-23-030.html

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RFA-DA-23-030 Part 2, Section V

Significance – how well do the planned activities ...

- lay the groundwork for a project that will address the major objectives of BBQS Transformative and Integrative Models of Behavior at the Organismal Level, specifically:

  - Building an interdisciplinary and functionally diverse team with the goal of integrating conceptual and methodological approaches to measuring and modeling behavior

  - Establishing the feasibility of the development, adaptation and/or validation of sensing technology that allows synchronous measurement of multiple variables that capture the multidimensional and dynamic nature of behavior of an organism interacting with its social or physical environment

  - Establishing the framework for a conceptual and/or statistical/computational model (including machine learning/AI methods) that integrates multimodal behavioral and environmental data across multiple temporospatial scales.

- support the rationale to be the basis for a R01/U01 or similarly scaled project that advances the overarching goal of the BRAIN Initiative?

https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-23-030.html

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Investigators

RFA-DA-23-030 Part 2, Section V

- To what extent does the proposed research include a multi-disciplinary team of researchers including complementary expertise in neuroscience, behavioral science, computer/data science and/or engineering?

  - How is the overall quality of the proposed planning project impacted by the diversity among team members with respect to racial, ethnic, cultural, gender and other biological or social dimensions of background and identity; philosophical perspective; educational background, professional experiences and career stage; general and specific scientific expertise; and other competencies relevant to the proposed project?

  - Is expertise in the areas of neuroscience and computational modeling represented on the team?

- If human subjects or data will be included in the planned project, does the team include a member whose primary area of expertise is neuroethics or related field within ethics?

https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-23-030.html

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FOA-specific review criteria

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Section V

Innovation - how well do planned activities ...

- draw from multiple disciplines and perspectives to create or advance a process for team science project development?

- increase the potential for innovation in the planned project with respect to

  - development or adaptation of sensing technology, software tools and/or computational modelling approaches to advance the study of behavior in the context of a dynamic social or physical environment?

  - development of innovative tools and/or methods to advance conceptual and/or computational modeling of behavior to integrate multiple types of environmental and behavioral data and/or integrates theories on behavioral function?

https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-23-030.html

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FOA-specific review criteria

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Section V

Approach - How well do the planning activities...

- create and support a team structure and process that assure that different perspectives of the team members will inform the project?

- lay the groundwork for the development of hardware and/or software tools to simultaneously capture and quantify

  - multiple observable dimensions of behavior and correlated physiology

  - the organism's environment

  in the context of minimally constrained behavior in a complex dynamic, ecologically-relevant environment

- lay the groundwork for a future Team R01/U01 (or project of similar scale) relevant to the goals of the BRAIN Initiative?

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RFA-DA-23-030 Part 2, Section V

Approach – How well do the planning activities...

- address the potential impact of the proposed approaches on the organism's behavior?

  - Do the planning activities increase the likelihood that the planned project will lead to less intrusive methods for capturing behavior than are currently widely available?

- address data storage and analysis appropriate for the data to be collected in the planned project? Are quality assurance processes for data collection, annotation, open source/open sharing, and dissemination addressed as part of the planning process supported by this R34?

- lay the groundwork for a conceptual or computational model that will integrate multidimensional behavioral data and environmental data, and the potential to integrate neural data and/or harmonize with existing neural data sets or models of brain function?

- if validation is proposed – the rigor of the proposed criteria for validation?

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FOA-specific review criteria

RFA-DA-23-030 - Transformative and Integrative Models of Behavior at the Organismal Level (Clinical Trial Not Allowed)

RFA-DA-23-030 Part 2, Section V

Approach – human subjects

- consider potential bias, privacy and other considerations and principles foundational to ethical conduct of research involving human subjects or human data

Reminder – activities that meet criteria as an NIH Clinical Trial are not allowed

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RFA-DA-23-030 Part 2, Section V

Environment –

- How well is the environment and proposed planning process are suited to designing and executing successful Team Science, i.e., project planning and execution by and for a multi-disciplinary, functionally diverse research team?

    - How well do the planning activities address potential barriers to team science, including logistical or other barriers associated with multi-institutional and/or private-public collaborations?

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Plan for Enhancing Diverse Perspectives (PEDP)

Plan for Enhancing Diverse Perspectives (PEDP)

- <u>Significance</u>: To what extent do the efforts described in the PEDP further the significance of the project?

- <u>Investigators</u>: To what extent will the efforts described in the PEDP strengthen and enhance the expertise required for the project?

- <u>Innovation</u>: To what extent will the efforts described in the PEDP meaningfully contribute to innovation?

- <u>Approach</u>: Are the timeline and milestones associated with the PEDP well-developed and feasible?

- <u>Environment</u>: To what extent will features of the environment described in the PEDP (e.g., collaborative arrangements, geographic diversity, institutional support) contribute to the success of the project?

https://braininitiative.nih.gov/about/plan-enhancing-diverse-perspectives-pedp

Application Review

Core Review Criteria
- Significance
- Investigators
- Innovation
- Approach
- Environment

Additional Review Criteria
- Protection of Human Subjects
- Inclusion of Women, Minorities, and Individuals Across the Lifespan
- Vertebrate Animals
- Biohazards

Overall Impact
Likelihood for the project to exert a sustained, powerful influence on the research field(s) involved

Additional Review Considerations
Foreign Institution, Select Agents, Resource Sharing Plan, Authentication, Budget

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Application Review Process

- Administrative review carried out by NIH Staff

- Submissions evaluated by NIH staff for
  - Completeness and compliance (See NOT-OD-17-105)
  - Adherence to NIH formatting guidelines
  - Biosketch and Other Support Format page requirements (See NOT-OD-21-073)

- Include **only** allowable appendix materials as per the application instructions.

Incomplete applications or applications not adhering to the FOA requirements may be returned without review

https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-23-030.html

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Peer Review Process: Pre-Review

- Peer review of applications conducted at NIDA

- Special Emphasis Panel created by the SRO based on the areas of science described in the applications

- Conflicts of interest are managed for all panel members

- At least three reviewers assigned to evaluate each application

- Panel receives guidance from NIH staff on how to evaluate the application

- Panel members have at least 30 days to evaluate the application

- Meeting roster is publicly available 30 days before the meeting

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- As part of the scientific peer review, all applications will receive a written critique (*summary statement*)

- Applications may undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score

- Summary statement will be available within 4-6 weeks after the peer review meeting

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BRAIN Initiative: Post-review Program Evaluation

- PO and BRAIN Initiative Program Team members review applications and summary statements; based on Impact Score and other factors, identify a subset for further consideration

- PIs of applications to be considered for funding invited to submit a response to the critiques (typically, 1-week turnaround)

- BRAIN Initiative Program Team evaluates the applications, summary statements and response to the SS to make funding recommendations to BRAIN Initiative Leadership

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RFA-DA-23-030 - Key Dates

- Letter of intent on/around Jan 14, 2023
  - Program evaluates potential responsiveness
  - Informs Review of potential expertise needed for special emphasis panel
- Application Deadline: Feb 14, 2023
- Scientific Merit Review: July 2023
- Program and Advisory Council Review: October 2023
- Earliest Start Date: December 2023

Contact: BRAINBBQS@od.nih.gov (Holly Moore, POC)

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Learn more about this FOA and BBQS

- Contact: BRAINBBQS@od.nih.gov

- 2022 BBQS Workshop videos, slides, and resources: https://event.roseliassociates.com/bbqs-workshop/
- NIH BRAIN Initiative Multi-Council Working Group Concept Clearance: https://videocast.nih.gov/watch=42301
- BBQS Transformative and Integrative Research at the Level of the Organism
  - Organismal Behavior Concept Clearance: https://nida.nih.gov/about-nida/advisory-boards-groups/national-advisory-council-drug-abuse-nacda/national-advisory-council-drug-abuse-nacda-approved-concepts#222_nih_brain
  - RFA-DA-23-030: https://grants.nih.gov/grants/guide/rfa-files/RFA-DA-23-030.html
- BBQS Human Neuroscience
  - Human Neuroscience Concept Clearance: https://www.nimh.nih.gov/funding/grant-writing-and-application-process/concept-clearances/2021/brain-research-through-advancing-innovative-neurotechnologiesr-brain-initiative-brain-behavior-quantification-and-synchronization
  - RFA RFA-MH-22-240: https://grants.nih.gov/grants/guide/rfa-files/RFA-MH-22-240.html

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