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Revised Date:

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Application Number: **1 F99 NS120412-01A1**
Formerly: **1F99NS120412-01**

Review Group:	**ZNS1 SRB-B (80)**
	National Institute of Neurological Disorders and Stroke Special Emphasis Panel
	Review of Applications for DSPAN F99/K00 Awards
Meeting Date:	**02/08/2021**
Council:	**MAY 2021** *PCC:* **JONESMWD**
Requested Start:	**07/01/2021**
	Dual IC(s): **NB**

Project Title:	**Dopaminergic neuromodulation of social decision making**
	Requested:
Sponsor:	
Department:	**Psychology and Neuroscience**
Organization:	**DUKE UNIVERSITY**
City, State:	**DURHAM NORTH CAROLINA**
SRG Action:	**Impact Score:11**
Next Steps:	**Visit https://grants.nih.gov/grants/next_steps.htm**
Human Subjects:	**X4-Human subjects involved - Exemption #4 designated**
Animal Subjects:	**10-No live vertebrate animals involved for competing appl.**

1F99NS120412-01A1 Castrellon, Jaime

RESUME AND SUMMARY OF DISCUSSION: This is a resubmitted DSPAN F99/K00 application from Jaime Castrellon, who is a 4th year graduate student in the lab of Dr. Gregory Samanez-Larkin at Duke University. Reviewers indicated that Mr. Castrellon is an outstanding candidate for this grant mechanism. They noted Mr. Castrellon has extensive prior research experience as an undergraduate at USC, a post-bac at Vanderbilt and now at Duke as a graduate student. All of Mr. Castrellon's research experience and interests have centered around neuroimaging in humans in the context of learning, reward and social decision making. Mr. Castrellon has excellent letters of reference, an impressive list of honors and has 14 publications, of which 3 are as first author. The application, including the research strategy, training plan, career goals and sponsorship plan, is well-written and the K00 phase is well-phrased as well. The sponsor, Dr. Samanez-Larkin, is a leader in the field of social neuroscience. Reviewers indicated that Dr. Samanez-Larkin has a strong track record of training graduate student and postdoctoral fellows. While the prior submission of this application was considered quite strong, it lacked a clear stating of hypotheses and had some other minor concerns. All prior concerns are now well-addressed. As such, the revisions have substantially improved the quality of application. Overall, this is an outstanding application from a stellar candidate.

DESCRIPTION (provided by applicant): The ability to socially navigate the world has been strongly linked to health and well-being in humans and across a wide range of human psychological disorders and depends on prosocial choices in affiliative environments and strategic learning in competitive ones. These kinds of social decisions involve balancing tradeoffs between maximizing rewards for oneself versus others and learning from others' reward preferences. Neuroimaging studies have shown that human decisions in interpersonal economic games recruit neural structures associated with social cognition and reward valuation. While previous studies have shown that dopamine function is paramount to decisions involving rewards for oneself, it's role in social decisions is much less well understood. Since disruptions to social decision making span multiple psychopathologies linked to dopamine dysfunction (like ADHD and schizophrenia), it is critical to understand the mechanism by which dopamine influences social decisions about rewards. To address this, the F99 phase of this proposal will investigate the relationship between dopamine function and social decision making in humans. Specifically, this work will combine positron emission tomography (PET), pharmacology, computational modeling, and behavioral experiments to address how individual differences in dopamine relates to personal reward processing and decision making as well as prosocial and strategic social decisions. Results from these studies will provide critical information about the role of dopaminergic modulation of multiple forms of social decisions and may eventually shed light on disruptions to prosocial behavior and social learning across psychopathologies. Completion of the F99 phase sets a strong intellectual, technical, and professional foundation for the postdoctoral (K00) phase of this award. During the K00 phase, training will include: learning new methods to study dynamic social interactions, understanding how dopamine and other neuromodulators support social decisions, and testing whether differences in affiliative or competitive decisions contribute to observed differences in psychopathology. These goals will support the development of knowledge, expertise, and skills essential to becoming an independent investigator.

PUBLIC HEALTH RELEVANCE: This research will investigate dopamine's role in human social decision making by combining multiple behavioral, computational, and neuroimaging methods. Results from these studies will identify how dopamine is related to multiple forms of social decisions for rewards and may identify disruptions to prosocial behavior and social learning across psychopathologies, given that dopamine is implicated in disruptions to reward- related decisions in schizophrenia, ADHD, and substance use disorder. Completion of the proposed work will provide the ideal transition to an independent academic research career.

CRITIQUES: *Please note that the evaluations and criterion scores from individual reviewers are provided below in an essentially unedited form. These were prepared prior to the review meeting and may not have been updated or revised after the discussion at the meeting. Therefore, they may not fully reflect the final opinions of the individual reviewers at the close of group discussion or the final majority opinion of the group. The Resume and Summary of Discussion above summarizes the outcome of the group discussion.*

CRITIQUE 1
Fellowship Applicant: 2
Sponsors, Collaborators, and Consultants: 1
Research Training Plan: 2
Training Potential/Development Plan: 2
Institutional Environment & Commitment to Training: 1

Overall Impact: This is a resubmission from an outstanding fourth year grad student from Duke, mentored by an outstanding team led by Prof. Samanez-Larkin. There are numerous strengths in the application including the applicant's academic record and research experience. The applicant has multiple authorships and has completed a large part of his training in PET imaging in the context of social neuroscience. The training potential is very high, as the applicant will learn about the design and analysis of complex paradigms of social decision making, with profound implications in our understanding of human social interactions. Enthusiasm is very high.

1. Applicant:
Strengths
- Extensive research experience at USC (Undergrad), Vanderbilt (post-Bac) and Duke (graduate), all around fMRI in the context of learning and reward.
- Excellent letters
- Impressive list of honors
- Multiple first authorships

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

2. Sponsors, Collaborators and Consultants:
Strengths
- Dr. Samanez-Larkin, the primary mentor, is a world-class researcher in the field of social neuroscience. He will provide mentorship in human neuroimaging methods and statistical analysis, overall project management, access to the research population and data, career advisement, etc.
- Dr. Samanez Larkin has a solid track record of training graduate student and postdocs. He organizes courses and conferences on social neuroscience and decision making
- Dr. Hsu will complement the primary mentor. Evidence for successful remote collaboration has been included.
- Makeba Wilbourn & Sarah Gaither will consult on professional development

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

3. Research Training Plan:

Strengths

- The overall training is based on the study of the role of Dopamine in the decision for social rewards
- PET for D2R is used to measure individual differences in stable measures of dopamine in the context of reward discounting in clinical groups
- Hypotheses in aim 2 are clearly delineated and tested with appropriate combination of methodologies
- Impressive progress report in aim 1 with multiple new publications.
- Aim 2 will incorporate PET imaging with the dictator game. This approach may lead to interesting interpretations of social interactions with potential consequences in organizational behavior theory

Weaknesses

- *Reviewer did not provide any comments regarding weaknesses*

4. Training Potential/Development Plan:

Strengths

- The candidate has already acquired significant expertise in PET imaging analysis with multiple first authorships in the F99 period.
- The PI has recruited multiple consultants that will help him develop the details of his career plan.
- The candidate has identified several potential postdoctoral labs and arranged interviews in the next few months.
- Additional training in decision making paradigms will place the candidate in a unique position to study neuronal mechanisms of social interaction.

Weaknesses

- *Reviewer did not provide any comments regarding weaknesses*

5. Institutional Environment & Commitment to Training:

Strengths

- The Duke program has an outstanding team of faculty and offers an ideal environment for professional development.

Weaknesses

- *Reviewer did not provide any comments regarding weaknesses*

Training in the Responsible Conduct of Research: Acceptable

Comments on Format (Required):

- Adequate

Comments on Subject Matter (Required):

- Adequate

Comments on Faculty Participation (Required):

- Adequate

Comments on Duration (Required):

- Adequate

Comments on Frequency (Required):
  • Adequate

Protections for Human Subjects: Acceptable Risks and Adequate Protections
  •   This Human Subjects Research falls under Exemption 4. Involves secondary data analysis
      of anonymized behavioral and neuroimaging data that were previously collected as part of 3
      completed studies
Vertebrate Animals: Not applicable (No Vertebrate Animals)
Budget and Period of Support: Acceptable

CRITIQUE 2
Fellowship Applicant: 1
Sponsors, Collaborators, and Consultants: 1
Research Training Plan: 2
Training Potential/Development Plan: 1
Institutional Environment & Commitment to Training: 1

Overall Impact: This is a strong re-submission application from an outstanding graduate student at
Duke University. The application satisfactorily addresses the concerns from the previous round of
reviews. The applicant's work focuses on understanding the mechanism(s) underlying social decision
making about rewards and how it is regulated by the neurotransmitter dopamine in humans. This area
of research has overarching implications for several psychopathologies believed to be
modulated/mediated by dopamine dysfunction. The PI has a long/strong trajectory of training in human
brain imaging, thus demonstrating a commitment to neuroscience and the goal of becoming an
independent scientist and leader in the field. His primary mentor, Dr. Samanez-Larkin, is world-
renowned in the field of decision-making neuroscience and has a strong record of mentoring. The
letters of recommendation are outstanding and reflect the commitment to the field demonstrated by the
applicant. The research plan is solid and aligns well with the short- and long-term academic and
professional goals of the applicant. This is a strong application from a promising future scientist.

1. Applicant:
Strengths
  • Solid track record of research involvement prior to joining Duke University.
  • Several merit fellowships at both undergraduate and graduate levels.
  • National Science Foundation Graduate Fellowship.
  • Five research publications, with three as first author.
  • Applicant has advanced to PhD candidacy.
  • Quality research training and mentoring experiences at the graduate level preparing the
    applicant to be competitive at the postdoctoral level.
  • Outstanding letters of support.
Weaknesses
  • *Reviewer did not provide any comments regarding weaknesses*

2. Sponsors, Collaborators and Consultants:
Strengths
  • Dr. Samanez-Larkin is an outstanding scientist and mentor.

- Mentor has the expertise necessary to guide the application through the various professional stages to achieve independence.
- Excellent funding and publication records.
- Excellent mentoring track.
- Laboratory currently funded through 2023.
- Dr. Ming Hsu, a leader in the study of decision making, and collaborator, will also serve as an advisor for the applicant.

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

3. Research Training Plan:
Strengths
- This project will assess the role of dopamine on decision-making for social reward in human subjects and further determine the influence of dopamine on dysregulated decision-making for personal rewards underlying certain psychopathologies.
- Aim 2 characterizes individual differences in dopamine and receptor availability of dopamine D1/D2 receptors in supporting prosocial and strategies that balance cooperation and self-interest.
- Timeline proposed is well delineated and shows feasible.
- Letters from potential postdoctoral advisors from Yale and U Penn.

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

4. Training Potential/Development Plan:
Strengths
- The applicant has strong research experience and will acquire cutting-edge additional training to answer the questions posed in the research plan.
- Will gain further expertise in fMRI and PET imaging data, new statistical methodology such as meta-analysis and a series of professional skills.
- Plan for transitioning to the K00, which will also have opportunities to mentor undergraduate and graduate students.
- The sponsor's laboratory has the expertise necessary to provide training experience.
- Detailed timeline provided.
- Training plan provided by mentor is tailored to applicant.

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

5. Institutional Environment & Commitment to Training:
Strengths
- The laboratory of Dr. Samanez-Larkin is well-established and has the necessary expertise, equipment/resources to complete the proposed studies and guide the applicant in achieving goals.
- The environment at Duke University is excellent and provides many opportunities for interactions with like-minded colleagues focused on related research on whom the applicant can rely for productive consultation, and guidance.

Weaknesses

- *Reviewer did not provide any comments regarding weaknesses*

Training in the Responsible Conduct of Research:

Comments on Format (Required):

- Appropriate. Candidate has completed CITI online course series, which satisfies NIH's requirements.

Comments on Subject Matter (Required):

- Appropriate: history and ethics, scientific integrity, peer review, data sharing, plagiarism, conflict of interest, informed consent, privacy/confidentiality

Comments on Faculty Participation (Required):

- Ongoing.

Comments on Duration (Required):

- Appropriate

Comments on Frequency (Required):

- Appropriate

Protections for Human Subjects: Acceptable Risks and Adequate Protections
- Data has been collected and masked.

Vertebrate Animals: Not applicable (No Vertebrate Animals)

Biohazards: Not applicable (No Biohazards)

Resubmission: Acceptable

Select Agents:

Resource Sharing Plans: Acceptable

Budget and Period of Support: Recommend as Requested

CRITIQUE 3

Fellowship Applicant: 1

Sponsors, Collaborators, and Consultants: 1

Research Training Plan: 2

Training Potential/Development Plan: 2

Institutional Environment & Commitment to Training: 1

Overall Impact: This is a revised application from an outstanding applicant. The revisions have substantially improved the quality of application. The major concerns have been addressed.

1. Applicant:

Strengths

- The applicant has an impressive resume, and strong training in a variety of imaging methods. The applicant has improved his CV by securing an internal grant, publishing two papers (one of these article as the first author), among other accolades. The candidate has a very bright future ahead.

Weaknesses

- None

2. Sponsors, Collaborators and Consultants:
Strengths
- The primary and secondary sponsors are experts in imaging and computational field relating to social decision making, respectively.
- The sponsors have excellent training records
- The concern with the location difference between co-sponsor Hsu and the applicant has been resolved.

Weaknesses
- None

3. Research Training Plan:
Strengths
- All data have been collected.
- Clever experimental designs.
- Previous major concerns have been addressed

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

4. Training Potential/Development Plan:
Strengths
- The applicant has received great training in different imaging modalities
- The applicant has already begun to identify potential postdoc mentors for the K00 phase
- Previous major concerns have been addressed

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

5. Institutional Environment & Commitment to Training:
Strengths
- Duke has an impressive faculty roster and state-of-the-art facilities for the applicant to successfully achieve his goals in the F99 phase.

Weaknesses
- None

Training in the Responsible Conduct of Research: Acceptable
    Comments on Format (Required):
- Acceptable

    Comments on Subject Matter (Required):
- Acceptable

    Comments on Faculty Participation (Required):
- Acceptable

    Comments on Duration (Required):
- Acceptable

    Comments on Frequency (Required):
- Acceptable

Protections for Human Subjects: Acceptable Risks and Adequate Protections
Vertebrate Animals: Not applicable (No Vertebrate Animals)
Biohazards: Acceptable
Resubmission: Acceptable
Select Agents: Not applicable (No Select Agents)
Resource Sharing Plans: Not applicable (No Relevant Resources)
Budget and Period of Support: Recommend as Requested

Additional Comments to Applicant (Optional)
- Some of the references don't seem to align with the text (e.g., 27 and 28)
- There seems to be a lot of synergy between the research interest of the applicant and those from the Michael Frank's lab at Brown University. I would recommend that the applicant consider his lab as potential postdoc mentor for the K00 phase
- Fallypride has a high affinity for both D2 and D3 receptors. This point should be made clearer in the grant. I assume the applicant means the D2 family, which typically includes D2, D3, and D4 receptors..

CRITIQUE 4
Fellowship Applicant: 1
Sponsors, Collaborators, and Consultants: 1
Research Training Plan: 2
Training Potential/Development Plan: 2
Institutional Environment & Commitment to Training: 2

Overall Impact: This is a revised application from a very productive applicant with a clear career goal who has already taken sustained steps towards the overall stated professional pursuit. The applicant has been very responsive to the comments from the previous panel, which were mostly focused on clarifying the scope of the various statements made in the body of the prior application as well as the role of one of the sponsors. These concerns have been addressed in the current application. The applicant is technically very proficient at carrying out many of the experimental analyses described in the application. The hypotheses are now well-laid out and focus on the relationship between dopamine receptor function and social decision making, an area of inquiry often targeted in the neuroscience literature. The training plan is clear, the sponsors very supportive of the applicant and the institutional resources excellent. Overall, this revised application is outstanding. The enthusiasm from this reviewer is very high.

1. Applicant:
Strengths
- High quality technical skills and a strong track record of participation in cognitive neuroscience research with different roles and levels of contributions to various publications. Commitment to Neuroscience is abundantly clear.
- Good handle on technical aspects of the proposed research and a continuing growth on the conceptual implications of the proposed experiments and available literature are clear in this application.
- Interaction with sponsors and peer lab members also appears to be excellent, which indicates high potential for undertaking role as a mentor upon successfully securing a faculty position.

- Existing and developing experience will place applicant in a good position to take advantage of K00 phase of the proposal.

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

2. Sponsors, Collaborators and Consultants:
Strengths
- Excellent laboratory environment and expertise are provided by the sponsors. They have a well-documented record of scientific engagement with the applicant, which in many cases have led to publication in reputable neuroscience journals.
- Expertise of the sponsors is highly complementary.
- Expertise and scientific interests of sponsors are clearly in-line with the research plan proposed by the applicant.

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

3. Research Training Plan:
Strengths
- Clearly stated and well laid out focusing on secondary analysis of already available neuroimaging data.
- Easily achievable in the proposed time frame as technical skills are already available to the applicant.
- K00 phase is focused on establishing secondary analyses of available data (different, more challenging factor analyses, for example).

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

4. Training Potential/Development Plan:
Strengths
- Good alignment between career plan and activities described in the proposal.
- Most of the training appears to be focused on professional development activities as the technical neuroimaging analysis skills of the applicant are already well developed.

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

5. Institutional Environment & Commitment to Training:
Strengths
- Excellent intellectual and technical resources are available to the applicant.
- Prior record of accomplishment support commitment towards the transition to the K00 phase of the proposal.

Weaknesses
- *Reviewer did not provide any comments regarding weaknesses*

Training in the Responsible Conduct of Research:
    Comments on Format (Required):

- Online (e.g., CITI) as well as in person.

Comments on Subject Matter (Required):

- Includes the standard curricula used by most institutions, but in addition there are courses addressing accuracy of digital media reports, reproducibility and predatory journal practices. Overall, a bit more comprehensive than average.

Comments on Faculty Participation (Required):

- There are also in person, lab-wide, fora with participation from sponsoring faculty

Comments on Duration (Required):

- In person courses are, on average, two hours long.

Comments on Frequency (Required):

- Courses are available at different times during the year, every year.

Protections for Human Subjects: Acceptable Risks and Adequate Protections

- Data has already been collected as part of prior studies
- Exemption 4

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only): Not applicable (No Clinical Trials)

Inclusion of Women, Minorities, and Ages Across the Lifespan:

- **Sex/Gender:** G4A: Sex representation unknown, Acceptable
- **Race/Ethnicity:** M4A: Minority representation unknown, Acceptable
- **For NIH-Defined Phase III trials, Plans for valid design and analysis**: Not applicable
- **Inclusion/Exclusion Across the Lifespan:** C4A: Child Representation Unknown; Scientifically Acceptable

Vertebrate Animals: Not applicable (No Vertebrate Animals)

Biohazards: Not applicable (No Biohazards)

Resubmission: Acceptable

from the previous scientific review group and changes made to the project.

- The applicant has been very responsive to the comments from the previous panel

Select Agents: Not applicable (No Select Agents)

Resource Sharing Plans: Not applicable (No Relevant Resources)

Budget and Period of Support: Recommend as Requested

THE FOLLOWING SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE, OR REVIEWERS' WRITTEN CRITIQUES, ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS (Resume): ACCEPTABLE

- Exemption E4: uses anonymized behavioral and neuroimaging data that was collected previously as part of other studies.

VERTEBRATE ANIMAL (Resume): NOT APPLICABLE.

BIOHAZARD COMMENT: NOT APPLICABLE

MODEL ORGANISM SHARING PLAN: NOT APPLICABLE.

DATA/RESOURCE SHARING: ACCEPTABLE.

TRAINING IN THE RESPONSIBLE CONDUCT OF RESEARCH: ACCEPTABLE

AUTHENTICATION OF KEY BIOLOGICAL AND/OR CHEMICAL RESOURCES: NOT APPLICABLE

COMMITTEE BUDGET RECOMMENDATIONS: RECOMMENDED AS REQUESTED.

Footnotes for 1 F99 NS120412-01A1; PI Name: Castrellon, Jaime Jorge Fernando

NIH has modified its policy regarding the receipt of resubmissions (amended applications).See Guide Notice NOT-OD-18-197 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-197.html. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.

MEETING ROSTER

National Institute of Neurological Disorders and Stroke Special Emphasis Panel
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
Review of Applications for DSPAN F99/K00 Awards
ZNS1 SRB-B (80)
02/08/2021 - 02/09/2021

Notice of NIH Policy to All Applicants: Meeting rosters are provided for information purposes only. Applicant investigators and institutional officials must not communicate directly with study section members about an application before or after the review. Failure to observe this policy will create a serious breach of integrity in the peer review process, and may lead to actions outlined in NOT-OD-14-073 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-073.html and NOT-OD-15-106 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-106.html, including removal of the application from immediate review.

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Consultants are required to absent themselves from the room
during the review of any application if their presence would
constitute or appear to constitute a conflict of interest.