Pl: Castrellon, Jaime Jorge Fernando	Title: Dopaminergic neuromodulation of social decision making		
Received: 12/14/2020	FOA: NS19-011 Council: 05/2021		
Competition ID: FORMS-F	FOA Title: NIH Blueprint Diversity Specialized Predoctoral to Postdoctoral Advancement in Neuroscience (D-SPAN) Award (F99/K00)		
1 F99 NS120412-01A1	Dual: NB	Accession Number: 4528193	
IPF: 2221101	Organization: DUKE UNIVERSITY		
Former Number: 1F99NS120412-01	Department: Psychology and Neuroscience		
IRG/SRG: ZNS1 SRB-B (80)	AIDS: N Expedited: N		
Subtotal Direct Costs (excludes consortium F&A) Year 1: 0	Animals: N Humans: Y Clinical Trial: N Current HS Code: X4 HESC: N HFT: N	New Investigator: Early Stage Investigator:	
Senior/Key Personnel:	Organization:	Role Category:	
Jaime J. Castrellon	Duke University PD/PI		
Gregory Samanez-Larkin	Duke University Other (Specify)-Sponsor		
Ming Hsu	University of California - Berkeley Other Professional-Co-Sponsor		

Reference Letters

David ZaldRutgers University12/14/2020Mara MatherUSC12/14/2020John PearsonDuke University12/14/2020

OMB Number: 4040-0010 Expiration Date: 12/31/2022

APPLICATION FOR I	FEDERAL ASS	SISTANCE			3. DAT	E RECEIV	/ED BY STATE	State	Applicat	ion Identifier
SF 424 (R&R)										
1. TYPE OF SUBMISSION*			4.a. Federal Identifier NS120412							
O Pre-application		ected	b. Agency Routing Number							
2. DATE SUBMITTE 2020-12-14	D	Application 263645	Identifier		c. Prev	ious Grar	nts.gov Trackin	g Numbe	•r	
5. APPLICANT INFO	ORMATION							Organi	zational	DUNS*: 044387793
Legal Name*:	Duke Unive	rsity						J		
Department:	DIBS P&N I	nvestigators								
Division:	Univ Admin	& Centers								
Street1*:	2200 West I	Main Street								
Street2:	Suite 710									
City*:	Durham									
County:										
State*:	NC: North C	Carolina								
Province:										
Country*:	USA: UNITE	ED STATES								
ZIP / Postal Code*:	27705-4010)								
Person to be contact	ed on matters	involving this	application							
	st Name*: Kei	-	Middle N	lame:			Last Name*: Hu	ırka-Owe	n	Suffix:
Position/Title:	Director, Of	c of Research	SPT							
Street1*:	2200 West I	Main Street								
Street2:	Suite 710									
City*:	Durham									
County:										
State*:	NC: North C	Carolina								
Province:										
Country*:	USA: UNITE	ED STATES								
ZIP / Postal Code*:	27705-4010)								
Phone Number*: (91	9) 681-8687	F	ax Number: (919) 684	-2418		Email: ors	-grant@d	luke.edu	
6. EMPLOYER IDE	NTIFICATION	NUMBER (Ell	N) or (TIN)*		56-05	532129				
7. TYPE OF APPLI	CANT*				O: Private Institution of Higher Education					
Other (Specify):	siness Organia	zation Type	O 10	/omen O	wood	\sim	Socially and Eco	nomically	v Dioodyr	ontaged
8. TYPE OF APPLIC									UISAUVA	aniageu
							ate box(es).	A	O 0 1-	Donation
		_	crease A	maia	O B. Decrease		O C. In	crease Duration		
	Continuation		Revision	l			O E. Other (spe	есіту) : ————		
Is this application b			jencies?*	OYes	●No		er Agencies?			
9. NAME OF FEDE National Institutes		*			10. CA	TALOG O	F FEDERAL DO	OMESTIC	ASSIST	ANCE NUMBER
11. DESCRIPTIVE T										
Dopaminergic neuro		ocial decision	making		140 00					
12. PROPOSED PR Start Date*		ding Date*					ONAL DISTRIC	IS OF A	PPLICAN	N I
07/01/2021		30/2026			NC-001	I				
	301				1					

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

Page 2

Prefix: First Name*: Jaime J. Middle Name: Last Name*: Castrellon Suffix:

Position/Title: Graduate Student
Organization Name*: Duke University

Department: Psychology and Neuroscience

Division: Arts and Sciences Street1*: 230 Erlwood Way

Street2: #22-202 City*: Durham

County:

State*: NC: North Carolina

Province:

Country*: USA: UNITED STATES

ZIP / Postal Code*: 27704-0000

Phone Number*: (661) 537-3546 Fax Number: Email*: jaime.castrellon@duke.edu

15. ESTIMATED PROJECT FUNDING		16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*		
a. Total Federal Funds Requested* b. Total Non-Federal Funds*	\$326,782.00 \$0.00	PROCESS FOR REVIEW ON:		
c. Total Federal & Non-Federal Funds*	\$326,782.00			
d. Estimated Program Income*	\$0.00	b. NO PROGRAM IS NOT COVERED BY E.O. 12372; OR		
		O PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW		

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

File Name:

I agree*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION

19. AUTHORIZED REPRESENTATIVE

Prefix: First Name*: Keith P. Middle Name: Last Name*: Hurka-Owen Suffix:

Position/Title*: Director, Ofc of Res Support

Organization Name*: Duke University

Department:

Division: Univ Admin & Centers
Street1*: 2200 West Main Street

Street2: Suite 710
City*: Durham

County:

State*: NC: North Carolina

Province:

Country*: USA: UNITED STATES

ZIP / Postal Code*: 27705-4010

Phone Number*: (919) 681-8687 Fax Number: (919) 684-2418 Email*: jennifer.bolognesi@duke.edu

Signature of Authorized Representative*

Keith P. Hurka-Owen 12/14/2020

20. PRE-APPLICATION File Name:

Tracking Number: GRANT13258952

21. COVER LETTER ATTACHMENT File Name:00_CoverLetter.pdf

Date Signed*

^{*} The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.

424 R&R and PHS-398 Specific Table Of Contents

SI	F 424 R&R Cover Page	. 1
	Table of Contents	3
Ρ	erformance Sites	. 4
R	esearch & Related Other Project Information	5
	Project Summary/Abstract(Description)	. 6
	Project Narrative	7
	Bibliography & References Cited	. 8
	Facilities & Other Resources	11
	Equipment	12
R	esearch & Related Senior/Key Person	13
ΡI	HS Fellowship Supplemental	29
	Introduction	32
	Applicant's Background and Goals for Fellowship Training	33
	Specific Aims	39
	Research Strategy	40
	Respective Contributions	46
	Selection of Sponsor and Institution	47
	Training in the Responsible Conduct of Research	48
	Sponsor and Co-Sponsor Statements	49
	Letters of Support from Collaborators, Contributors, and Consultants	55
	Description of Institutional Environment and Commitment to Training	61
	PHS Human Subjects and Clinical Trials Information	63
	Study 1: Dopaminergic neuromodulation of social decision making	66
	Inclusion Enrollment Reports	68
	Description of Candidate's Contribution to Program Goals	73
	Resource Sharing Plan	74
	Application for Concurrent Support	75

Table of Contents Page 3

Contact PD/PI: Castrellon, Jaime J.

OMB Number: 4040-0010 Expiration Date: 12/31/2022

Project/Performance Site Location(s)

Project/Performance Site Primary Location

O I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Duke University
Duns Number: 044387793

Street1*: LSRC

Street2: Box 90999
City*: Durham

County:

State*: NC: North Carolina

Province:

Country*: USA: UNITED STATES

Zip / Postal Code*: 27708-0000

Project/Performance Site Congressional District*: NC-001

Additional Location(s)

File Name:

OMB Number: 4040-0010 Expiration Date: 12/31/2022

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● Yes ○ No
1.a. If YES to Human Subjects
Is the Project Exempt from Federal regulations? ● Yes ○ No
If YES, check appropriate exemption number: _ 1 _ 2 _ 3 <u>✔</u> 4 _ 5 _ 6 _ 7 _ 8
If NO, is the IRB review Pending? ● Yes ○ No
IRB Approval Date:
Human Subject Assurance Number 00000265
2. Are Vertebrate Animals Used?* ○ Yes • No
2.a. If YES to Vertebrate Animals
Is the IACUC review Pending?
IACUC Approval Date:
Animal Welfare Assurance Number
3. Is proprietary/privileged information included in the application?* ○ Yes • No
4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ Yes • No
4.b. If yes, please explain:
4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an O Yes O No
environmental assessment (EA) or environmental impact statement (EIS) been performed?
4.d. If yes, please explain:
5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ Yes ● No
5.a. If yes, please explain:
6. Does this project involve activities outside the United States or partnership with international ○ Yes ● No
collaborators?*
6.a. If yes, identify countries:
6.b. Optional Explanation:
Filename
7. Project Summary/Abstract* Castrellon_Project_Abstract_12.8.20.pdf
8. Project Narrative* Castrellon_Project_Narrative_12.8.20.pdf
9. Bibliography & References Cited 01c_Bibliography.pdf
10.Facilities & Other Resources Castrellon_Facilities_11.17.20.pdf
11.Equipment Castrellon_Equipment_11.17.20.pdf

Project Summary/Project Abstract

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.

Contact PD/PI: Castrellon, Jaime J.

Project Narrative

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.

Project Narrative Page 7

REFERENCES

- 1. Ruff, C. C. & Fehr, E. The neurobiology of rewards and values in social decision making. *Nat. Rev. Neurosci.* **15**, 549–562 (2014).
- 2. Egerton, A. *et al.* The dopaminergic basis of human behaviors: A review of molecular imaging studies. *Neurosci. Biobehav. Rev.* **33**, 1109–1132 (2009).
- 3. Robson, S. E., Repetto, L., Gountouna, V.-E. & Nicodemus, K. K. A review of neuroeconomic gameplay in psychiatric disorders. *Mol. Psychiatry* **25**, 67–81 (2020).
- 4. Sáez, I., Zhu, L., Set, E., Kayser, A. & Hsu, M. Dopamine Modulates Egalitarian Behavior in Humans. *Curr. Biol.* **25**, 912–919 (2015).
- 5. Crockett, M. J. *et al.* Dissociable Effects of Serotonin and Dopamine on the Valuation of Harm in Moral Decision Making. *Curr. Biol.* **25**, 1852–1859 (2015).
- 6. Zhu, L., Mathewson, K. E. & Hsu, M. Dissociable neural representations of reinforcement and belief prediction errors underlie strategic learning. *Proc. Natl. Acad. Sci.* **109**, 1419–1424 (2012).
- 7. Zhu, L., Jiang, Y., Scabini, D., Knight, R. T. & Hsu, M. Patients with basal ganglia damage show preserved learning in an economic game. *Nat. Commun.* **10**, 802 (2019).
- 8. Björklund, A., Divac, I. & Lindvall, O. Regional distribution of catecholamines in monkey cerebral cortex, evidence for a dopaminergic innervation of the primate prefrontal cortex. *Neurosci. Lett.* **7**, 115–119 (1978).
- 9. Berger, B., Gaspar, P. & Verney, C. Dopaminergic innervation of the cerebral cortex: unexpected differences between rodents and primates. *Trends Neurosci.* **14**, 21–27 (1991).
- 10. Rilling, J. K. & Sanfey, A. G. The Neuroscience of Social Decision-Making. *Annu. Rev. Psychol.* **62**, 23–48 (2011).
- 11. Cutler, J. & Campbell-Meiklejohn, D. A comparative fMRI meta-analysis of altruistic and strategic decisions to give. *NeuroImage* **184**, 227–241 (2019).
- 12. Schultz, W. Neuronal Reward and Decision Signals: From Theories to Data. *Physiol. Rev.* **95**, 853–951 (2015).
- 13. Smith, C. T. *et al.* Modulation of impulsivity and reward sensitivity in intertemporal choice by striatal and midbrain dopamine synthesis in healthy adults. *J. Neurophysiol.* **115**, 1146–1156 (2016).
- 14. Weber, S. C. *et al.* Dopamine D2/3- and μ-opioid receptor antagonists reduce cue-induced responding and reward impulsivity in humans. *Transl. Psychiatry* **6**, e850–e850 (2016).
- 15. Pine, A., Shiner, T., Seymour, B. & Dolan, R. J. Dopamine, Time, and Impulsivity in Humans. *J. Neurosci.* **30**, 8888–8896 (2010).
- 16. Robertson, C. L. *et al.* Striatal D ₁ and D ₂ -type Dopamine Receptors Are Linked to Motor Response Inhibition in Human Subjects. *J. Neurosci.* **35**, 5990–5997 (2015).
- 17. Frank, M. J. Dynamic Dopamine Modulation in the Basal Ganglia: A Neurocomputational Account of Cognitive Deficits in Medicated and Nonmedicated Parkinsonism. *J. Cogn. Neurosci.* **17**, 51–72 (2005).
- 18. Ghahremani, D. G. *et al.* Striatal Dopamine D2/D3 Receptors Mediate Response Inhibition and Related Activity in Frontostriatal Neural Circuitry in Humans. *J. Neurosci.* **32**, 7316–7324 (2012).
- Oberlin, B. G. et al. Monetary discounting and ventral striatal dopamine receptor availability in nontreatment-seeking alcoholics and social drinkers. Psychopharmacology (Berl.) 232, 2207–2216 (2015).
- 20. Crunelle, C. L., van den Brink, W., Dom, G. & Booij, J. Dopamine transporter occupancy by methylphenidate and impulsivity in adult ADHD. *Br. J. Psychiatry* **204**, 486–487 (2014).
- 21. Mikolajczyk, K., Szabatin, M., Rudnicki, P., Grodzki, M. & Burger, C. A JAVA environment for medical image data analysis: Initial application for brain PET quantitation. *Med. Inform. (Lond.)* **23**, 207–214 (1998).
- 22. Castrellon, J. J. *et al.* Individual Differences in Dopamine Are Associated with Reward Discounting in Clinical Groups But Not in Healthy Adults. *J. Neurosci.* **39**, 321–332 (2019).
- 23. Volkow, N. D., Wang, G.-J., Fowler, J. S., Tomasi, D. & Telang, F. Addiction: Beyond dopamine reward circuitry. *Proc. Natl. Acad. Sci.* **108**, 15037–15042 (2011).
- 24. Cools, R. & D'Esposito, M. Inverted-U–Shaped Dopamine Actions on Human Working Memory and Cognitive Control. *Biol. Psychiatry* **69**, e113–e125 (2011).
- 25. Haber, S. N. & Knutson, B. The Reward Circuit: Linking Primate Anatomy and Human Imaging. *Neuropsychopharmacology* **35**, 4–26 (2010).
- 26. Smith, K. S., Tindell, A. J., Aldridge, J. W. & Berridge, K. C. Ventral pallidum roles in reward and motivation. *Behav. Brain Res.* **196**, 155–167 (2009).

References Cited Page 8

- 27. Castrellon, J. J. *et al.* Mesolimbic dopamine D2 receptors and neural representations of subjective value. *Sci. Rep.* **9**, 20229 (2019).
- 28. Hill, D. F., Parent, K. L., Atcherley, C. W., Cowen, S. L. & Heien, M. L. Differential release of dopamine in the nucleus accumbens evoked by low-versus high-frequency medial prefrontal cortex stimulation. *Brain Stimulat.* **11**, 426–434 (2018).
- 29. Soares-Cunha, C. *et al.* Nucleus Accumbens Microcircuit Underlying D2-MSN-Driven Increase in Motivation. *eneuro* **5**, ENEURO.0386-18.2018 (2018).
- 30. Beaulieu, J.-M. & Gainetdinov, R. R. The Physiology, Signaling, and Pharmacology of Dopamine Receptors. *Pharmacol. Rev.* **63**, 182–217 (2011).
- 31. Heal, D. J., Cheetham, S. C. & Smith, S. L. The neuropharmacology of ADHD drugs in vivo: Insights on efficacy and safety. *Neuropharmacology* **57**, 608–618 (2009).
- 32. Johnstone, E. C., Frith, C. D., Crow, T. J., Carney, M. W. P. & Price, J. S. Mechanism of the antipsychotic effect in the treatment of acute schizophrenia. *The Lancet* **311**, 848–851 (1978).
- 33. Castrellon, J. J., Meade, J., Greenwald, L., Hurst, K. & Samanez-Larkin, G. R. Dopaminergic modulation of reward discounting in healthy rats: a systematic review and meta-analysis. *Psychopharmacology (Berl.)* (2020) doi:10.1007/s00213-020-05723-5.
- 34. Berkman, E. T., Hutcherson, C. A., Livingston, J. L., Kahn, L. E. & Inzlicht, M. Self-Control as Value-Based Choice. *Curr. Dir. Psychol. Sci.* **26**, 422–428 (2017).
- 35. Hofmann, W., Baumeister, R. F., Förster, G. & Vohs, K. D. Everyday temptations: An experience sampling study of desire, conflict, and self-control. *J. Pers. Soc. Psychol.* **102**, 1318–1335 (2012).
- 36. Hofmann, W., Vohs, K. D. & Baumeister, R. F. What People Desire, Feel Conflicted About, and Try to Resist in Everyday Life. *Psychol. Sci.* **23**, 582–588 (2012).
- 37. Barrett, L. F. & Barrett, D. J. An Introduction to Computerized Experience Sampling in Psychology. *Soc. Sci. Comput. Rev.* **19**, 175–185 (2001).
- 38. Simon, H. A. Altruism and economics. Am. Econ. Rev. 83, 156–161 (1993).
- 39. Crockett, M. J., Kurth-Nelson, Z., Siegel, J. Z., Dayan, P. & Dolan, R. J. Harm to others outweighs harm to self in moral decision making. *Proc. Natl. Acad. Sci.* **111**, 17320–17325 (2014).
- 40. Wilson, E. O. Kin selection as the key to altruism: its rise and fall. Soc. Res. 159-166 (2005).
- 41. Fehr, E. & Schmidt, K. M. The Economics of Fairness, Reciprocity and Altruism Experimental Evidence and New Theories. in *Handbook of the Economics of Giving, Altruism and Reciprocity* vol. 1 615–691 (Elsevier, 2006).
- 42. Battigalli, P. & Dufwenberg, M. Guilt in Games. American Economic Review vol. 97 170–176 (2007).
- 43. Rapoport, A. & Amaldoss, W. Mixed strategies and iterative elimination of strongly dominated strategies: an experimental investigation of states of knowledge. *J. Econ. Behav. Organ.* **42**, 483–521 (2000).
- 44. Olsson, A., Knapska, E. & Lindström, B. The neural and computational systems of social learning. *Nat. Rev. Neurosci.* **21**, 197–212 (2020).
- 45. Joiner, J., Piva, M., Turrin, C. & Chang, S. W. C. Social learning through prediction error in the brain. *Npj Sci. Learn.* **2**, 8 (2017).
- 46. Takahashi, H. *et al.* When Your Gain Is My Pain and Your Pain Is My Gain: Neural Correlates of Envy and Schadenfreude. *Science* **323**. 937–939 (2009).
- 47. Dvash, J., Gilam, G., Ben-Ze'ev, A., Hendler, T. & Shamay-Tsoory, S. G. The envious brain: The neural basis of social comparison. *Hum. Brain Mapp.* NA-NA (2010) doi:10.1002/hbm.20972.
- 48. Gao, X. et al. Distinguishing neural correlates of context-dependent advantageous- and disadvantageous-inequity aversion. *Proc. Natl. Acad. Sci.* **115**, E7680–E7689 (2018).
- 49. Michl, P. *et al.* Neurobiological underpinnings of shame and guilt: a pilot fMRI study. *Soc. Cogn. Affect. Neurosci.* **9**, 150–157 (2014).
- 50. Krajbich, I., Adolphs, R., Tranel, D., Denburg, N. L. & Camerer, C. F. Economic Games Quantify Diminished Sense of Guilt in Patients with Damage to the Prefrontal Cortex. *J. Neurosci.* **29**, 2188–2192 (2009).
- 51. Güroğlu, B., Will, G.-J. & Crone, E. A. Neural Correlates of Advantageous and Disadvantageous Inequity in Sharing Decisions. *PLoS ONE* **9**, e107996 (2014).
- 52. Cox, J. C. & Sadiraj, V. On Modeling Voluntary Contributions to Public Goods. *Public Finance Rev.* **35**, 311–332 (2007).
- 53. Sul, S., Güroğlu, B., Crone, E. A. & Chang, L. J. Medial prefrontal cortical thinning mediates shifts in other-regarding preferences during adolescence. *Sci. Rep.* **7**, 8510 (2017).

References Cited Page 9

- 54. Fehr, E. & Schmidt, K. M. A Theory of Fairness, Competition, and Cooperation. *Q. J. Econ.* **114**, 817–868 (1999)
- 55. Forsythe, R., Horowitz, J. L., Savin, N. E. & Sefton, M. Fairness in Simple Bargaining Experiments. *Games Econ. Behav.* **6**, 347–369 (1994).
- 56. Homer, B. D. *et al.* Methamphetamine abuse and impairment of social functioning: A review of the underlying neurophysiological causes and behavioral implications. *Psychol. Bull.* **134**, 301–310 (2008).
- 57. Grabenhorst, F., Báez-Mendoza, R., Genest, W., Deco, G. & Schultz, W. Primate Amygdala Neurons Simulate Decision Processes of Social Partners. *Cell* **177**, 986-998.e15 (2019).
- 58. Rosenberger, L. A. *et al.* The Human Basolateral Amygdala Is Indispensable for Social Experiential Learning. *Curr. Biol.* **29**, 3532-3537.e3 (2019).
- 59. Lau, T., Gershman, S. J. & Cikara, M. Social structure learning in human anterior insula. *eLife* **9**, e53162 (2020).
- 60. Ashok, A. H., Mizuno, Y., Volkow, N. D. & Howes, O. D. Association of Stimulant Use With Dopaminergic Alterations in Users of Cocaine, Amphetamine, or Methamphetamine: A Systematic Review and Meta-analysis. *JAMA Psychiatry* **74**, 511 (2017).
- 61. Howes, O. D. *et al.* The Nature of Dopamine Dysfunction in Schizophrenia and What This Means for Treatment: Meta-analysis of Imaging Studies. *Arch. Gen. Psychiatry* **69**, (2012).
- 62. Fusar-Poli, P., Rubia, K., Rossi, G., Sartori, G. & Balottin, U. Striatal Dopamine Transporter Alterations in ADHD: Pathophysiology or Adaptation to Psychostimulants? A Meta-Analysis. *Am. J. Psychiatry* **169**, 264–272 (2012).
- 63. Pizzagalli, D. A. *et al.* Assessment of Striatal Dopamine Transporter Binding in Individuals With Major Depressive Disorder: In Vivo Positron Emission Tomography and Postmortem Evidence. *JAMA Psychiatry* **76**, 854 (2019).
- 64. Hamilton, J. P. *et al.* Striatal dopamine deficits predict reductions in striatal functional connectivity in major depression: a concurrent 11C-raclopride positron emission tomography and functional magnetic resonance imaging investigation. *Transl. Psychiatry* **8**, 264 (2018).
- 65. Schneier, F. R. *et al.* Dopamine transporters, D ₂ receptors, and dopamine release in generalized social anxiety disorder. *Depress. Anxiety* **26**, 411–418 (2009).
- 66. Plavén-Sigray, P. et al. Extrastriatal dopamine D2-receptor availability in social anxiety disorder. *Eur. Neuropsychopharmacol.* **27**, 462–469 (2017).

References Cited Page 10

FACILITIES

Behavioral testing and neuropsychological testing is performed in the Samanez-Larkin laboratory at the *Center for Cognitive Neuroscience*, MR imaging is conducted at the *Brain Imaging and Analysis Center (BIAC)*. All PET data to be analyzed in the proposed research were collected by the applicant at Vanderbilt University Medical Center (through a joint grant with the Samanez-Larkin lab) and Yale University Medical Center (where the Samanez-Larkin lab was previously).

Samanez-Larkin laboratory. The Samanez-Larkin laboratory (~700 sq. ft.) in the Center for Cognitive Neuroscience (CCN) is located in the Levine Science Research Center (LSRC building). Dr. Samanez-Larkin's laboratory is a custom-designed area with computer work spaces for 10 students and staff, and testing areas for behavioral studies. Dr. Samanez-Larkin has an office two floors above the laboratory.

Brain Imaging and Analysis Center (BIAC). BIAC is in Duke's North Hospital, a few hundred yards from the CCN (LSRC Building). BIAC serves investigators at Duke, the University of North Carolina, Chapel Hill, and the Durham VA Medical Center. The BIAC facility occupies 11,500 sq. ft. on the Duke University medical campus and houses research-dedicated, whole-body human scanners (details in Equipment). BIAC is a shared laboratory environment that provides access to facilities (e.g., scanners, behavioral testing suites, mock scanners, computer clusters) as well as offices and workstations for BIAC faculty and research staff. Under the leadership of BIAC's Director, Dr. Allen Song, the core faculty of the BIAC maintains ongoing research programs in the development of new MR and fMRI imaging methods and reconstruction techniques to improve the resolution, throughput, and quality of data collected.

Social Science Research Institute (SSRI). The Social Science Research Institute (https://ssri.duke.edu/) brings together researchers with interests that cross various social and behavioral sciences, with the goal of pioneering new social science research and methods. The Institute, which has locations on both East and West Campus, has various research resources. For instance, the Connection Bar provides both in-person and virtual one-on-one consultation on data access and management, as well as on qualitative and quantitative analysis methods. They provide subject screening and testing facilities off-campus in the community to facilitate recruitment of a broader diversity of participants.

Duke Institute for Brain Sciences (DIBS). The Duke Institute for Brain Science (https://dibs.duke.edu/) is an interactive community of scholars who advance interdisciplinary research in brain science, with the goal of transforming our understanding of brain function and translating research into innovative solutions for health and society. DIBS is organized into centers, which represent core areas of research and interest. These centers have significant faculty involvement in research, scholarship, and educational programs. Two of these centers, the Duke Center for Cognitive Neuroscience and the Duke Center for Interdisciplinary Decision Science, are described below.

Duke Center for Cognitive Neuroscience (CCN). The applicant's advisor and dissertation committee members are core faculty members in the CCN (https://dibs.duke.edu/centers/ccn). The Center focuses on interdisciplinary research, education, and training in the psychological, computational, and biological mechanisms of cognitive function. Research in the CCN focuses on various aspects of cognition, utilizing diverse methods ranging from single-cell recording to functional MRI. The center brings together faculty from multiple parts of campus, including Trinity College of Arts and Sciences, the Medical School, Pratt School of Engineering, and Fuqua School of Business – many of whom have interests in decision neuroscience.

Duke Center for Interdisciplinary Decision Science (D-CIDES). The applicant's advisor and dissertation committee members are faculty affiliates of D-CIDES (https://dibs.duke.edu/centers/d-cides). The Center brings researchers in decision sciences, including behavioral economics, judgment and decision making, marketing, neuroeconomics, medical decision making and addiction, together to promote and develop interdisciplinary scholarship. The center, which is jointly affiliated with the SSRI, is focused on facilitating new research partnerships, developing training programs for undergraduate, graduate, postdoc and faculty members, creating an intellectual community focused on decision making, and connecting Duke faculty and students with policy makers in industry and government.

EQUIPMENT

Brain Imaging and Analysis Center (BIAC)

The BIAC at Duke University houses two research-dedicated whole-body 3T human scanners (both operating on the newest GE MR750 platforms) and a 7 Tesla animal scanner. The scanners are equipped with high-dutycycle 50 mT/m gradients at 200 T/m/s slew rate. The RF systems include volume birdcage head coils, eightchannel head coils, 32-channel head coils, and receiver amplifier arrays of 128 channels. The eight- and thirtytwo- channel head coils are used for parallel imaging at high bandwidth up to 1MHz. To ensure high homogeneity critical for fMRI experiments at high field, the 3.0 T scanners are equipped with high-order roomtemperature resistive shimming coils in addition to the super-conducting shimming coils. In addition, both scanners use broadband transmission to enable multiple frequency excitation schemes important for multinuclei imaging and spectroscopy experiments. The scanners are controlled by Linux workstations, which are connected via a high-speed network interface. BIAC received a new 3T scanner in May 2018, a GE SIGNA Premier with cutting-edge multiband imaging capabilities. The SIGNA Premier has SuperG. which is GE's newest gradient coil. It features an 80 mT/m amplitude and 200T/m/s slew rate with an all-hollow construction to maximize duty cycle. The scanner has the industry's first 146-channel Total Digital Imaging (TDI) RF chain, which enhances SNR and improves parallel imaging and multi-slice excitation schemes. Each human scanner suite is equipped with Resonance Technology LCD goggles for visual stimulation which also have integrated eye tracking capability. MR-compatible auditory systems are also available in each suite. Additional sensory stimulation equipment includes a Mindware Technologies olfactometer, a Medoc thermode system, and a Grass Instrument's constant current nerve stimulator. Subject responses are obtained from button boxes and joysticks. Each suite is equipped with a pair of high performance PCs equipped with multi-function boards for timing, digital I/O, and A/D conversion that maintains experimental control in each scanner suite. A variety of software packages are available for experimental control including EPrime, Presentation, and Matlab Psych Toolbox. The CIGAL experimental control program developed by BIAC faculty member Dr. James Voyvodic is also available, and this program can be easily modified to allow for the integration of new devices. An MRIcompatible physiological monitoring system (In-Vivo Research) provides continuous measurement of ECG, end-tidal CO2, respiration, and non-invasive blood pressure. This system is used during clinical research studies involving sedation, or studies involving at-risk individuals. The BIAC has installed a Whisperroom sound-attenuating chamber, used for testing experimental paradigms and for behavioral studies, and it provides for eye-tracking. The Applied Science eye tracking system uses an infrared beam to track the position of the pupil and cornea over time in order to estimate position of gaze.

BIAC has extensive computational facilities. With funds from the NIH/NCRR Shared Instrument Grant, BIAC purchased a 456-CPU Linux High Performance Computing (HPC) cluster computer with 3.45 TB of total memory. The Linux cluster operates in concert with an ultra-high-speed BlueArc data server (which hosts the operating system for the cluster and contains all BIAC imaging data) via fiber channels. The total data storage capacity currently has 150 TB online, and is expandable to 4 PB. Automated processes move the image data directly from the scanners and organize the data into a hierarchy on the storage servers. The central computation and storage systems can be accessed from the campus network, or from two data analysis laboratories located within the BIAC, and are available to all BIAC users. These laboratories house an array of late-model workstations. The BIAC maintains a large library of commercial and custom software for functional and structural MRI analysis, for the analysis of MR spectroscopy data, and for fiber tractography from diffusion-weighted imaging data.

Samanez-Larkin laboratory

The laboratory of Dr. Samanez-Larkin includes 8 Mac desktops for data processing and analysis. All machines are connected to the BIAC HPC cluster and server on which the lab currently has 20TB of continuously backed-up storage space. The lab also has two Mac laptops primarily used for data collection in the CCN, community research centers, or at the BIAC. All computers are equipped with statistical and graphics software necessary for behavioral and brain imaging research. The lab also has a Wacom Cintiq tablet screen for manual tracing of brain structures.

Given that the data for the F99 phase are already collected, the primary equipment to be used will be access to the BIAC HPC for data processing and the applicant's own computer (for data processing, analysis, manuscript prep, talk prep, and dissertation writing).

Equipment Page 12

Contact PD/PI: Castrellon, Jaime J.

OMB Number: 4040-0010 Expiration Date: 12/31/2022

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: First Name*: Jaime J. Middle Name Last Name*: Castrellon Suffix:

Position/Title*: Graduate Student
Organization Name*: Duke University

Department: Psychology and Neuroscience

Division: Arts and Sciences Street1*: 230 Erlwood Way

Street2: #22-202 City*: Durham

County:

State*: NC: North Carolina

Province:

Country*: USA: UNITED STATES

Zip / Postal Code*: 27704-0000

Phone Number*: (661) 537-3546 Fax Number:

E-Mail*: jaime.castrellon@duke.edu

Credential, e.g., agency login: JCASTRELLON

Project Role*: PD/PI Other Project Role Category:

Degree Type: BA, MA Degree Year: 2013, 2019

Attach Biographical Sketch*: File Name: Biosketch_Castrellon_JJ_12.7.20.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Gregory Middle Name Last Name*: Samanez-Larkin

Position/Title*: Jack H. Neely Associate Profes

Organization Name*: Duke University

Department: Psychology and Neuroscience

Division: Arts and Sciences

Street1*: LSRC
Street2: Box 90999
City*: Durham

County:

State*: NC: North Carolina

Province:

Country*: USA: UNITED STATES

Zip / Postal Code*: 27708-0000

Phone Number*: (919) 660-5716 Fax Number:

E-Mail*: g.samanezlarkin@duke.edu

Credential, e.g., agency login: SAMANEZLARKIN.GREG

Project Role*: Other (Specify) Other Project Role Category: Sponsor

Degree Type: BA, MA, PhD Degree Year: 2002, 2008, 2010

Attach Biographical Sketch*: File Name: Biosketch_Samanez_Larkin_G_12.7.20.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Ming Middle Name Last Name*: Hsu Suffix:

Position/Title*: Associate Professor

Organization Name*: University of California - Berkeley

Department: Haas School of Business

Division:

Street1*: 2220 Piedmont Avenue

Street2:

City*: Berkeley

County:

State*: CA: California

Province:

Country*: USA: UNITED STATES

Zip / Postal Code*: 94720-1900

Phone Number*: (510) 643-2027 Fax Number:

E-Mail*: mhsu@haas.berkeley.edu

Credential, e.g., agency login: ming_hsu

Project Role*: Other Professional Other Project Role Category: Co-Sponsor

Degree Type: BA, PhD Degree Year: 2001, 2006

Attach Biographical Sketch*: File Name: Biosketch_Hsu_Ming_12.7.20.pdf

Attach Current & Pending Support: File Name:

Suffix:

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Castrellon, Jaime J.

eRA COMMONS USER NAME: JCASTRELLON

POSITION TITLE: Doctoral Candidate, Department of Psychology & Neuroscience, Duke University

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	START DATE	END DATE	FIELD OF STUDY
University of Southern California (USC), Los Angeles, CA	BA	08/2010	12/2013	Neuroscience/Political Science
Duke University, Durham, NC	MA	08/2017	12/2019	Psychology & Neuroscience
Duke University, Durham, NC	PHD	01/2020	In Progress	Psychology & Neuroscience

A. Personal Statement

My long-term research interests involve the development of a comprehensive understanding of the neural mechanisms of social decision making. My academic training and research experience to date have provided me with an excellent background in social neuroscience and neuroeconomics. As an undergraduate at the University of Southern California, I conducted research with Dr. Mara Mather on socially-shared memory. At USC, I received several competitive internal research grants and fellowships to support an independent project under the umbrella of social cognition. My contributions resulted in a co-authored publication, as well as an opportunity to present a poster at the Western Psychological Association annual meeting. Importantly, this research experience grounded my interest in social cognition and social decision making. As a postbaccalaureate research analyst in Dr. David Zald's lab at Vanderbilt University, I gained skills collecting and analyzing fMRI, PET, genetic, and behavioral data in the context of reward-related decision making.

During this time, I led analyses of fMRI data, PET measures of dopamine, genetics, social reward preferences, and impulsivity. I presented these findings with a poster at the Society for Neuroscience annual meeting and an oral presentation at the Interdisciplinary Symposium for Decision Neuroscience. This research experience allowed me to grow my technical knowledge and interest in applying molecular neuroimaging to study human decision making. Following this, I served as the inaugural lab manager for Dr. Katherine Karlsgodt's new group at UCLA where I helped build a team from the ground up while furthering my understanding of reward function in a clinical population. In particular, I contributed to a new line of research in the lab exploring neural mechanisms of social cognitive deficits in early-onset psychosis and schizophrenia. This experience helped me think critically about how basic social neuroscience research can translate into the clinic. For my graduate training at Duke University, I have applied my prior experiences to study dopaminergic mechanisms of reward- related decision making under the mentorship of Dr. Gregory Samanez-Larkin. Along with developing new conceptual and technical training, the proposed training plan outlines a set of career development activities and workshops – e.g. public speaking, literature analysis, project management, mentorship, and grant writing. For my initial projects I have investigated whether individual differences in dopamine D2 receptor availability support reward discounting and neural representations of subjective value. As a Latinx scientist, I am the first in my family to graduate from college. I am looking forward to becoming an independent scientist and inspiring future young Latinx trainees to pursue careers in cognitive

neuroscience. Overall, my choice of sponsor, research project, and the training I will get from this fellowship will provide a solid foundation for my long-term goal to become an academic researcher.

B. Positions and Honors

Positions and Employment

2012 - 2014	Undergraduate Research Assistant, Psychology Department, USC, Los Angeles, CA
2014 - 2016	Research Assistant, Department of Psychology, Vanderbilt University, Nashville, TN
2016 - 2017	Lab Manager, Department of Psychology, UCLA, Los Angeles, CA
2017 - Present	Graduate Student Research Assistant, Duke University, Durham, NC
2018 - Present	Teaching Assistant, Duke University, Durham, NC

Other Experience and Professional Memberships

Cognitive Neuroscience Society
Society for Neuroscience
Social Affective Neuroscience Society
Association for Psychological Science
Society for Neuroeconomics

<u>Honors</u>

2010 - 2013	Scholarship, Congressional Hispanic Caucus Institute
2010 - 2013	Scholarship, USC Latino Alumni Association
2011	Scholarship, Xerox Hispanic Association for Professional Advancement
2011 - 2013	Scholarship, Rose Hills Foundation
2011	Academic Achievement Award, University of Southern California
2012	Undergraduate Research Grant, University of Southern California
2012	Summer Undergraduate Research Fellowship, University of Southern California
2013	Summer Undergraduate Research Fellowship, University of Southern California
2013	Thematic Option Honors, University of Southern California
2013	University Honors, University of Southern California
2016	Summer Institute Fellowship, Sackler Institute for Developmental Psychobiology, Weil Cornell Medical College
2017	Fellowship, Summer School in Social Neuroscience & Neuroeconomics, Duke University
2017 - Present	National Science Foundation Graduate Research Fellowship
2018	Student Travel Award, Society for Neuroeconomics
2018	Best Poster Award, Society for Neuroeconomics
2019	Fellowship, Summer Institute for Cognitive Neuroscience, Kavli Foundation
2019	Charles Lafitte Foundation Travel Award, Duke University
2019	Best Poster Award, Society for Neuroeconomics
2020	Bass Connections Outstanding Mentor Award, Duke University

C. Contribution to Science

1. Undergraduate Research in Social Cognition: Under the mentorship of Dr. Mara Mather at USC, I coordinated a series of studies that investigated mechanisms by which recall memory is susceptible to social influence. In the lab, I recruited study participants and collected and analyzed data from dyadic interactions to evaluate how age modulates the effects of collaborative recall and retrieval-induced forgetting. I applied for and received Summer fellowships and a research grant to support this line of research by developing, collecting data for, and analyzing an independent project to assess memory conformity. My involvement in these projects resulted in a publication in 2017 that identified conditions under which collaboration disrupts recall of emotional pictures.

Selected Publications and Presentations:

- a. Barber, S.J., **Castrellon, J.J.**, Opitz, P., & Mather, M. (2017). Younger and older adults' collaborative recall of shared and unshared emotional pictures. *Memory & Cognition*. [PMC5500393]
- 2. Post-baccalaureate Research in Human Dopamine Function: As a full-time research analyst in Dr. David Zald's lab at Vanderbilt University, I was responsible for developing, collecting, and analyzing data from two large studies of dopamine function and decision making. For these studies, I recruited participants, collected and analyzed MRI, PET, genetic, and behavioral data. In addition to neuroimaging analysis skills, I gained experience in administering structured clinical interviews and coordinating interdisciplinary research across multiple departments (e.g., Psychology, Nuclear Medicine, Psychiatry, and Radiochemistry). I co-authored several publications on human PET measures of dopamine function and decision making across the adult life span. Notably, two of these publications challenge long-held assumptions about associations between dopamine, BMI, and physiological proxy measures of dopamine function. During my time in the lab, I presented a conference talk and a poster exploring neural correlations of impulsivity in aging as well as research combining dopamine PET imaging and genetic phenotypes to predict social reward valuation.

Selected Publications and Presentations:

- a. Dang, L.C., Samanez-Larkin, G.R., **Castrellon, J.J.**, Perkins, S.F., Cowan, R.L., Newhouse, P.A., Zald, D.H. (2017). Spontaneous eye blink rate (EBR) is uncorrelated with dopamine D2 receptor availability and unmodulated by dopamine agonism in healthy adults. *eNeuro*. [PMC5602106]
- b. Dang, L. C., **Castrellon, J.J.**, Perkins, S. F., Le, N. T., Cowan, R. L., Zald, D. H., & Samanez-Larkin, G.R. (2017). Reduced effects of age on dopamine D2 receptor levels in physically active adults. *NeuroImage*, *148*, *123-129*. [PMC5344739]
- c. **Castrellon, J.J.**, Smith, C.T., Perkins, S.F., Samanez-Larkin, G.R., Zald, D.H., Monoamine oxidase A: a genetic marker of social reward preferences. Oral presentation at the annual Interdisciplinary Symposium on Decision Neuroscience. Temple University. Philadelphia, PA. June 2016.
- d. **Castrellon, J.J.**, Dang, L.C., Perkins, S.F., Samanez-Larkin, G.R., Zald, D.H., Aging contributes to grey matter volume and attentional impulsivity correlates in frontoparietal functional connectivity. Poster presented at the annual meeting of the Society for Neuroscience. Chicago, IL. October 2015.
- 3. Graduate Research in Decision Neuroscience: My graduate research focuses on characterizing dopaminergic mechanisms of reward-related decision making in humans. Through research in the Samanez-Larkin lab, I have begun to unravel the complicated nature of individual differences in human reward discounting behavior and neural representations of subjective value. I have led several papers published and under review that challenge long-held assumptions about the role of dopamine receptors in reward discounting using PET measures of dopamine, fMRI, and a meta-analysis of rodent pharmacology. Currently, I am extending this work to evaluate whether ecologically valid methods can capture the link between PET measures of dopamine and resistance of everyday desires. Notably, I gained recognition for my presentation of all this work twice in a row with the Best Poster Award and selection for a data blitz talk at the Society for Neuroeconomics annual meetings in 2018 and 2019.

Selected Publications & Presentations:

- a. Castrellon, J.J., Meade, J., Greenwald, L., Hurst, K. (2020). Dopaminergic modulation of reward discounting in healthy rats: A systematic review and meta-analysis. Psychopharmacology. [PMID 33215269] DOI: 10.1007/s00213-020-05723-5
- Castrellon, J.J., Young, J.S., Dang, L.C., Cowan, R.L., Zald, D.H., Samanez-Larkin, G.R., (2019).
 Mesolimbic dopamine D2 receptors and neural representations of subjective value. Scientific Reports. [PMC6934551]
- c. Castrellon, J.J., Seaman K.L., Crawford, J.L., Young, J.S., Smith, C.T., Dang, L.C., Hsu, M., Cowan, R.L., Zald, D.H., Samanez-Larkin, G.R. (2019). Individual differences in dopamine are associated with reward discounting in clinical groups but not in healthy adults. *Journal of Neuroscience*. [PMC6325254]
- d. Castrellon, J.J., Zald, D.H., Samanez-Larkin, G.R., Individual differences in dopamine predict self-control of everyday desires. Spotlight poster and talk presented at the annual meeting of the Society for Neuroeconomics. Dublin, Ireland. October 2019. *Best Poster Award Winner

Complete list of published work:

PubMed

D. Additional Information: Research Support and/or Scholastic Performance Research Support

Duke University Bass Connections

Castrellon/Samanez-Larkin (Co-PI)

7/1/2018-8/31/2020

Using Neuroscience to Optimize Digital Health Interventions across Adulthood

Competitive internal pilot grant to determine whether neuroimaging can predict and optimize mobile motivational messaging with social features to increase physical activity. The outcome of this pilot research will support a larger R01 application to evaluate the neural basis of motivation for everyday healthy behaviors.

Role: Co-PI

NSF 1655445 Skene (PI) 8/15/2017-7/31/2021

Computational Modeling of Decision Making by Prosecutors and Jurors in Criminal Justice Research grant to support studies examining cognitive and neural mechanisms of jurors' biased decisions about guilt and punishment in mock criminal scenarios.

Role: Trainee

NSF DGE-1644868 9/1/18-8/31/21

National Science Foundation Graduate Research Fellowship

Independent fellowship to support training in decision making research in preparation for an academic career.

Role: PI

Scholastic Performance

Duke University Graduate School courses are graded A-F scale. Some courses are graded CR (credit) or NC (no credit). **University of Southern California GPA**: 3.63/4.00; **Duke University GPA**: 4.00/4.00

University of Southern California			
Neuroscience Major Courses	Political Science Major Courses		
Primate Social Behavior	Politics and Society I Honors Course		
Statistics I	Writing Seminar I Honors Course		
Introduction to Psychology	Culture and Values Honors Course		
The Process of Change in Science Honors Course	Politics and Society II Honors Course		
Minority Mental Health	Writing Seminar II Honors Course		
Behavioral Neuroscience	Theory and Practice of American Democracy		
Cell Biology and Physiology	Law, Politics, and Public Policy		
Systems Neuroscience	Change and the Future Honors Course		
Neurobiology of Aging Symbols and Conceptual Systems Honors			
Criminal Behavior Politics and the Economy			
Abnormal Psychology American Political Thought			
Psychology and Law	World Political Leadership		
	Regulation of Elections and Political Finance		
	Political Jurisprudence		

Duke University				
YEAR	COURSE TITLE	GRADE		
2017	First Year Seminar I	CR		
2017	Principles in Cognitive Neuroscience I	Α		
2017	Research Practicum	Α		
2018	First Year Seminar II	CR		
2018	Adult Psychopathology	A		
2018	Principles in Cognitive Neuroscience II	A		
2018	Research Practicum	A		
2019	Foundations of Cognitive Psychology	A		
2020	Functional Magnetic Resonance Imaging	A		

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Gregory R. Samanez Larkin

eRA COMMONS USER NAME: SAMANEZLARKIN.GREG

POSITION TITLE: Jack H Neely Associate Professor of Psychology and Neuroscience

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Michigan, Ann Arbor, MI	B.A.	05/2002	Psychology
Stanford University, Stanford, CA	M.A.	01/2008	Psychology
Stanford University, Stanford, CA	Ph.D.	08/2010	Psychology
Vanderbilt University, Nashville, TN	Post-Doc	06/2013	Neuroscience/Psychology

A. Personal Statement

Dr. Samanez-Larkin is a leading expert in the affective neuroscience and neuroeconomics of aging. His research is focused on individual and age differences in the function of neurobiological systems supporting motivation, learning, and decision making. His laboratory uses a combination of behavioral measures, computational modeling, structural (DTI) and functional (fMRI) brain imaging, and molecular brain imaging (PET). He conducted many of the foundational studies on reward processing in the aging human brain and the pioneering neuroimaging work that followed characterized adult age differences in motivation and decision making. He has been continuously supported by the National Institute on Aging for over 12 years (F31, F32, K99/R00, R24, R25, R01). His laboratory continues to focus on adult age differences in economic decision making but is extending this work into the study of social and health-related decision making and health behavior change. The long-term goal of this research is to improve health and well being in daily life.

- 1. Samanez-Larkin, G.R., Carstensen, L.L. (2011) Socioemotional functioning and the aging brain. In J. Decety and J. Cacioppo (Eds.) *The Oxford Handbook of Social Neuroscience* (pp. 507–521). New York: Oxford University Press.
- **2. Samanez-Larkin, G.R.** (2015) Decision neuroscience and aging. In T.M. Hess, J. Strough, and C.E. Löckenhoff (Eds.). *Aging and decision making: Empirical and applied perspectives*. New York: Elsevier.
- **3. Samanez-Larkin, G.R.**, Knutson, B. (2015) Decision making in the ageing brain: changes in affective and motivational circuits. *Nature Reviews Neuroscience*, 16 (5), 278-289. [PMC5645075]
- **4.** The Aging Brain: Functional Adaptation Across Adulthood (2019) **G.R. Samanez-Larkin** (Ed.). American Psychological Association.

A high priority focus of the Samanez-Larkin lab has been to facilitate the participation of individuals underrepresented in science. Samanez-Larkin has extensive experience successfully mentoring URMs. Since it's creation, the lab group has had a strong minority majority. Of the 13 current and 42 previous undergraduates, 3 current and 9 former post-bac researchers, 4 previous post-docs, and 6 current graduate students, 74% are women and 39% are Black and/or Hispanic (25% Black, 14% Hispanic/Latinx). An average of 1 in 5 members of his lab has been a Black woman, who are almost completely unrepresented among neuroscience faculty (<1%). Over 70% of his lab members have come from backgrounds that are under-represented in science in at least one way (e.g., racial/ethnic minority, LGBTQ, low-income, first-gen college, disability). Former Black and Latinx trainees at all levels have gone on to excellent faculty positions (e.g., UNC) and top post-bacc and graduate programs (e.g., Stanford, Princeton, Yale, Duke, USC, Cornell, UNC). Samanez-Larkin co-directs a

NSF-funded summer research experience at Duke for URM undergraduates and is involved in a range of diversity initiatives within and outside Duke. Samanez-Larkin also focuses on collecting data from diverse samples to generate more representative and generalizable discoveries. Most of his early studies were 50/50% Black/White and recent studies have all been 33/33/33% Latinx/Black/White. The current R01-funded study on memory and decision making in aging has a 40% Black adult sample. In spite of extensive experience and mentoring success, he lacks identity matching with many of these trainees. For this reason, he is deeply committed to creating opportunities for co-mentorship of trainees with relevant colleagues (as proposed in the current grant application).

B. Positions and

Honors Positions and

Employment

- 2013-2017 Assistant Professor of Psychology, Yale University
- 2017-2020 Assistant Professor of Psychology and Neuroscience, Duke University
- 2020- Jack H Neely Associate Professor of Psychology and Neuroscience, Duke University

Academic and Professional Honors

- 1999 Branstrom Prize for Freshman Scholars (top 10% of class), University of Michigan
- 2001 Psi Chi Psychology Honors Society
- 2002 University Honors, University of Michigan
- 2002 W.B. Pillsbury Thesis Award, University of Michigan
- 2006 NSF Graduate Research Fellowship, Honorable Mention
- 2006 Summer School in Neuroeconomics Fellowship, Stanford University
- 2007 Top Ten Scientific Advances, National Institute on Aging (for: Samanez-Larkin, et al., 2007)
- 2008 Department of Psychology Teaching Award, Stanford University
- 2009 Individual Pre-doctoral National Research Service Award (F31), National Institute on Aging
- 2010 Albert H. & Barbara R. Hastorf Prize for Teaching, Stanford University
- 2010 Adult Development and Aging Dissertation Award, APA Division 20
- 2010 Council of Graduate Schools / UMI Distinguished Dissertation Award in the Social Sciences
- 2011 Individual Post-doctoral National Research Service Award (F32), National Institute on Aging
- 2012 Rising Star, Association for Psychological Science
- 2012 Post-Doctoral Fellows Award, Cognitive Neuroscience Society
- 2012 Pathway to Independence Award (K99/R00), National Institute on Aging
- 2014 Theresa Seessel Postdoctoral Fellowship for Faculty, Yale University
- 2015 Poorvu Family Award for Interdisciplinary Teaching, Yale University
- 2019 Randolph Blake Early Career Award (for exemplary alumni), Vanderbilt University
- 2019 Early Career Award, Society for Neuroeconomics
- 2020 Bass Chair, Bass Society of Fellows, Duke University

C. Contributions to Science

- 1. I have led or collaborated on a range of studies investigating adult age differences in the processing of emotional stimuli and emotional experience in everyday life. This work has revealed that emotional experience improves with age, older adults are better at regulating temptation, and that higher emotional well being is associated with increased longevity. We've extended earlier findings demonstrating age- related positivity effects (i.e., increased attention and memory to positive relative to negative emotional material) by characterizing the neural systems associated with these effects and showing that positivity effects are also present in reward-based decision making in old age.
- a. **Samanez-Larkin, G.R.**, Gibbs, S.E.B., Khanna, K., Nielsen, L., Carstensen, L.L., Knutson, B. (2007) Anticipation of monetary gain but not loss in healthy older adults. *Nature Neuroscience*, 10(6), 787–791. [PMC2268869]
- b. **Samanez-Larkin, G.R.**, Robertson, E.R., Mikels, J.A., Carstensen, L.L., Gotlib, I.H. (2009) Selective attention to emotion in the aging brain. *Psychology and Aging*, 24(3), 519–529. [PMC2791508]

- c. Burr, D.A., Castrellon, J.J., Zald, D.H., **Samanez-Larkin, G.R.** (2020) Emotion dynamics across adulthood in everyday life: older adults are more emotionally stable and better at regulating desires. *Emotion*. [PMC In Process]
- d. Carstensen, L.L., Turan, B., Scheibe, S., Ram, N., Ersner-Hershfield, **Samanez-Larkin, G.R.**, Brooks, K.P., Nesselroade, J.R. (2011) Emotional experience improves with age: Evidence based on over 10 years of experience sampling. *Psychology and Aging*, 26(1), 21–33. [PMC3332527]
- 2. I have led a series of studies in which we examined how age differences in learning affect risky decision making. The studies show that older adults are impaired relative to younger adults when making decisions that require rapid learning from recent experience and this can sometimes lead to excessively risky decision making (even though many older adults self-identify as being more risk averse than they were when they were younger). We've linked these learning deficits to increases in striatal neural signal variability, reduced representation of prediction errors in the medial frontal cortex, and decreased white matter connectivity between the medial prefrontal cortex and ventral striatum. We've also shown that there are ways of displaying feedback in these tasks that enhance learning in old age, which we hope will inspire the development of decision aids that can be adapted for use in everyday life.
- a. **Samanez-Larkin, G.R.**, Kuhnen, C.M., Yoo, D.J., Knutson, B. (2010) Variability in nucleus accumbens activity mediates age-related suboptimal financial risk taking. *Journal of Neuroscience*, 30(4), 1426–1434. [PMC2821055]
- b. **Samanez-Larkin, G.R.**, Wagner, A.D., Knutson, B. (2011) Expected value information improves financial risk taking across the adult life span. *Social Cognitive and Affective Neuroscience*, 6(2), 207–217. [PMC3073388]
- c. **Samanez-Larkin, G.R.**, Levens, S.M., Perry, L.M., Dougherty, R.F., Knutson, B. (2012) Frontostriatal white matter integrity mediates adult age differences in probabilistic reward learning. *Journal of Neuroscience*, 32(15), 5333–5337. [PMC3744863]
- d. **Samanez-Larkin, G.R.**, Worthy, D.A., Mata, R., McClure, S.M., Knutson, B (2014) Adult age differences in frontostriatal representation of prediction error but not reward outcome. *Cognitive Affective and Behavioral Neuroscience*, 14 (2), 672–682. [PMC4072917]
- 3. Although many studies in the behavioral economics and neuroeconomics literatures use small amounts of real money in experimental tasks, shockingly few measures of performance on these laboratory tasks have been directly linked to real-world behavior. Highly relevant to the current proposal, my collaborators and I believe that validation of these tasks and prediction of real-world behavior is critical. Over the years, we have documented that many laboratory measures are related to real-world financial behavior (e.g., long-term financial saving, borrowing / credit card usage, credit scores).
- a. **Samanez-Larkin, G.R.**, Knodt, A.R., Richmond-Rakerd, L.S., Caspi, A., Moffit, T.E., Hariri, A.R. (2020, in prep) Brain structural correlates of practical financial knowledge and credit scores in a longitudinal birth cohort.
- b. Ersner-Hershfield, H., Garton, M.T., Ballard, K., **Samanez-Larkin, G.R.**, Knutson, K. (2009) Don't stop thinking about tomorrow: Individual differences in future self-continuity account for saving. *Judgment and Decision Making*, 4(4), 280–286. [PMC2747683]
- c. Knutson, B., **Samanez-Larkin, G.R.**, Kuhnen, C.M. (2011) Gain and loss learning differentially contribute to life financial outcomes. *PLoS ONE*, 6(9), e24390. [PMC3167846]
- d. Kuhnen, C.M., **Samanez-Larkin, G.R.**, Knutson, B. (2013) Serotonergic genotypes, neuroticism, and financial choices. *PLoS ONE*, 8(1), e54632. [PMC3559795]
- 4. In addition to contributions to the specific topics above, I am also an active contributor to the development of new tools and methods for studying age differences in affective and cognitive function. We've created a collection of dynamic socioemotional stimuli freely available to the scientific community, developed a set of guidelines for conducting neuroimaging studies comparing adults of various ages, co-developed (with Doug Garrett) new methods for measuring neural signal variability (which was a measure previously ignored in human brain imaging), and demonstrated ways of using structural equation modeling to examine neuromodulatory networks in human PET data.
- a. Holland, C.A.C., Ebner, N.C., Lin, T., Samanez-Larkin, G.R. (2019) Emotion identification across

- adulthood using the Dynamic FACES database of emotional expressions in young, middle-aged, and older adults. *Cognition and Emotion*, 33(2), 245–257. [PMC6599511]
- b. **Samanez-Larkin, G.R.**, D'Esposito, M. (2008) Group comparisons: Imaging the aging brain. *Social Cognitive and Affective Neuroscience*, 3(3), 290–297. [PMC2563421]
- c. Garrett, D.D., **Samanez-Larkin, G.R.**, MacDonald, S.W.S., Lindenberger, U., McIntosh, A.R., Grady, C.L. (2013). Moment-to-moment brain signal variability: A next frontier in human brain mapping? *Neuroscience and Biobehavioral Reviews*, 37(4), 610–624. [PMC3732213]
- d. **Samanez-Larkin, G.R.**, Buckholtz, J.W., Cowan, R.L., Woodward, N.D., Li, R., Ansari, M.S., Arrington, C.M., Baldwin, R.M., Smith, C.E., Treadway, M.T., Kessler, R.M., Zald, D.H. (2013). A thalamocorticostriatal dopamine network for psychostimulant-enhanced human cognitive flexibility. *Biological Psychiatry*. [PMC3615042]

Complete list of published work:

PubMed Google Scholar

D. Additional Information: Research Support

Active

NSF 1950651 Wilbourn (PI) 3/1/2020–2/28/2023

REU: Lifespan Approaches to Diverse Psychological Science

Grant to support annual summer Research Experience for Undergraduates (REU) under-represented in science across three research groups that study children, adults, and aging adults from social, developmental, and cognitive neuroscience perspectives.

Role: Co-PI

NIA/NIH R01-AG058547 Samanez-Larkin, Cabeza (MPI) 8/15/2018-3/31/2023

Effects of Aging on Episodic Memory-Dependent Decision Making

Research grant to examine how individual differences in episodic memory are related to adult age differences in multi-attribute and future-oriented decision

making. Role: PI

NIA/NIH R24-AG054355 Samanez-Larkin (PI) 9/15/2016-3/31/2021

Scientific Research Network on Decision Neuroscience and Aging

Network grant to support dissemination and training activities related to the emerging multidisciplinary science of decision making and aging.

Role: PI

NIA/NIH R25-AG053213 Samanez-Larkin (PI) 9/15/2016-4/30/2021

Short Courses in Neuroeconomics and Social Neuroscience

Grant to support preconference workshops and an annual summer school in neuroeconomics and social neuroscience.

Role: PI

NIA/NIH R25-AG053252 Carstensen, Samanez-Larkin (MPI) 9/15/2016-4/30/2021

Forming Science-Industry Partnerships to Link Everyday Behaviors to Well-Being

Grant to support an initiative that would facilitate collaborations between scientists and the private sector focused on improving financial and physical health and well being.

Role: PI

Recently Completed

NIA/NIH R01-AG043458 Zald, Samanez-Larkin (MPI) 2/15/2014–1/31/2019

Dopaminergic Neuromodulation of Decision Making in Young and Middle-Aged Adults

Project aims to characterize individual and age differences in motivation and decision making in young and late middle-aged adults using multimodal neuroimaging techniques to assess dopamine receptors, transporters,

and release. Role: PI

NIA/NIH R21-AG049293 Levy (PI) 9/30/2015–3/31/2018

Medical Decision Making Under Uncertainty in Older Adults

Research grant to examine the behavioral and neurobiological processes that characterize decision making under risk and ambiguity by younger and older adults in financial versus medical domains.

Role: Co-Investigator

NIA/NIH R00-AG042596 Samanez-Larkin (PI) 9/30/2014–3/31/2018

Neuromodulation of Motivated Cognition and Decision Making Across Adulthood

Pathway to Independence Award supporting research on the influence of motivation and cognition on decision making using multimodal neuroimaging including fMRI and PET imaging of dopamine receptors.

Role: PI

OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Hsu, Ming

eRA COMMONS USER NAME (credential, e.g., agency login):

ming hsu POSITION TITLE: Associate Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Arizona California Institute of Technology	B.A. Ph.D.	05/2001 07/2006	Political Science Economics
University of Illinois at Urbana-Champaign	Postdoctoral	07/2008	Economics and Neuroscience

A. Personal Statement

My research focuses on the interdisciplinary areas of decision neuroscience and neuroeconomics. I am part of the first generation of researchers to have received graduate training in both neuroscience and economics. In this, I have been highly successful in bridging the gap between the two fields to study the brain basis of decision- making, and have a track record of successful collaboration with researchers in neuroscience, psychology, and economics. Specifically, I am an expert in studying the neural mechanisms involved in decision-making. These studies involved combining economic models of choice behavior with a variety of neuroscientific experiment modalities, including neuroimaging, psychophysiology, and lesion patients. In addition, I successfully administered the projects (e.g. staffing, research protections, budget), collaborated with other researchers, and produced several peer-reviewed publications from each project. Currently I am extending the scientific framework developed from this research to issues relevant for public health, in particular mental health. Specifically, this involves building quantitative frameworks that bridge brain and behavior that will enable development of biomarkers and new ways of classifying mental disorders based on dimensions of observable behavior and neurobiological measures.

I am active in equity and inclusion activities. This includes both components of my research dealing with neural and cognitive underpinnings of unequal treatment, as well as in my mentoring, which strives to provide a welcoming training environment for our graduate students. I served as primary mentor for 4 PhD students, 3 of them are tenure-track or research faculty working in academic research, and 1 of whom entered postdoc.

- a. Hsu, Ming, Meghana Bhatt, Ralph Adolphs, Daniel Tranel, and Colin Camerer. "Neural Systems Responding to Degrees of Uncertainty In Human Decision Making." <u>Science</u>, 310: 1624-1625, 2005.
- b. Hsu, Ming, Cédric Anen, and Steven Quartz. "The Right and the Good: Distributive Justice and Neural Encoding of Equity and Efficiency." <u>Science</u>. 320: 1092-1095, 2008.
- c. Zhu, Lusha, Adrianna Jenkins, Eric Set, Donatella Scabini, Robert Knight, Pearl H. Chiu, Brooks King-Casas, and Ming Hsu. "Damage To Dorsolateral Prefrontal Cortex Affects Tradeoffs Between Honesty And Self-Interest." Nature Neuroscience, 17: 1319-1321, 2014. PMCID: PMC4177007
- d. Jenkins, Adrianna, Pierre Karashchuk, Lusha Zhu, & Ming Hsu. "Predicting human behavior toward members of different social groups". <u>Proceedings of the National Academy of Sciences</u>. 2018. PMCID: PMC6166817

B. Positions and Honors Positions and Employment

2006-2008	Beckman Fellow, Beckman İnstitute, University of Illinois at Urbana-Champaign
2008-2009	Assistant Professor of Economics, University of Illinois at Urbana Champaign
2008-2009	Affiliate Faculty, Neuroscience Program, University of Illinois at Urbana-Champaign
2008-2009	Affiliate Faculty, Beckman Institute, University of Illinois at Urbana-Champaign
2009-2016	Assistant Professor, Haas School of Business, University of California, Berkeley
2010-2016	Assistant Professor, Helen Wills Neuroscience Institute, University of California
2016-	Associate Professor, Haas School of Business, University of California, Berkeley
2016-	Associate Professor, Helen Wills Neuroscience Institute, University of California, Berkeley

Other Experience and Professional Memberships

2005-	Member, Society for Neuroeconomics
2007-	Member, Society for Neuroscience
2011-	Editorial Board, Frontiers in Decision Neuroscience
2011-	Editorial Board, Journal of Neuroscience, Economics, and Psychology
2012-	Editorial Board, New Mathematics and Natural Computation
2013	Society for Neuroscience, Working Group on Open-Access Publication
2013-	Ad Hoc Reviewer NSF, NIH

Co-chair, CRCNS Principle Investigator Annual Meeting

Honors

2018

2001-

2006	Everhart Lecture Series
2006-2008	Beckman Fellow
2010	Kavli Fellow
2015	Society for Neuroeconomics Early Career Award
2016	UCSF-UC Berkeley Sabbatical Exchange Award
2018	Barbara and Gerson Bakar Faculty Fellow

Member. Economic Science Association

C. Contributions to Science

- 1. Individual Decision-Making: My first contributions addressed the neurobiological basis of economic decision-making under uncertainty. Every day we make decisions about the goals we like to pursue, but we still know little about how the brain processes the simplest parameters that determine our decisions. This set of research developed out of my doctoral training at Caltech, where I applied formal economic models of choice behavior to shed light on how the brain weights different forms of risk and reward, and continue to this day. I served as primary investigator or co-investigator in all of these studies.
 - a. Hsu M, Bhatt M, Adolphs R, Tranel D, Camerer C. "Neural Systems Responding to Degrees of Uncertainty In Human Decision Making." <u>Science</u>, 310: 1624-1625, 2005.
- b. Jenkins A, Hsu, M. "Dissociable contributions of imagination and willpower to the malleability of human patience." <u>Psychological Science</u>. 28: 894-906, 2017. PMCID: PMC5507764
- c. Kenji K, Hsu M. "Neural mechanisms of updating under reducible and irreducible uncertainty". <u>Journal of Neuroscience</u>. 37: 6972-6982, 2017. PMCID: PMC5518424
- d. Saez I, Lin J, Stolk A, Chang E, Parvizi J, Schalk G, Knight RT, Hsu M. "Encoding of multiple reward-related factors in transient and sustained high-frequency activity in human OFC". <u>Current Biology</u>. 2018. PMCID: PMC6590063
- 2. **Social Decision-Making:** In addition, I extended my research topics to encompass social decision-making and decisions in interpersonal contexts. These studies emphasize cognitive components of social behavior that are in common with and or distinct from those involved in individual decision-making. In particular, they highlight distinct computational processes that subserve competitive and cooperative behavior in humans. I served as primary investigator or co-investigator in all of these studies.
 - a. Hsu M, Anen C, Quartz S. "The Right and the Good: Distributive Justice and Neural Encoding of Equity and Efficiency." Science. 320: 1092-1095, 2008.
 - b. Set E, Saez I, Zhu L, Houser D, Myung N, Zhong S, Ebstein R, Chew S, Hsu M. "Dissociable Contribution of Prefrontal And Striatal Dopaminergic Genes To Learning In Economic Games." <u>Proceedings of the National Academy of Sciences</u>, 111: 9615-9620, 2014. PMCID: PMC4084431

- c. Zhu L, Jenkins A, Set E, Scabini D, Knight R, Chiu PH, King-Casas B, Hsu M. "Damage To Dorsolateral Prefrontal Cortex Affects Tradeoffs Between Honesty And Self-Interest." Nature Neuroscience, 17: 1319-1321, 2014. PMCID: PMC4177007
- d. Jenkins A, Karashchuk P, Zhu L, Hsu M "Predicting human behavior toward members of different social groups". <u>Proceedings of the National Academy of Sciences</u>. 2018. PMCID: PMC6166817
- 3. Translational Applications: Build upon my work in basis cognitive and behavioral processes, I have started to translate findings from the above studies to questions with direct health relevance. In particular, changes in financial decision-making and interpersonal relationships are often the first symptoms of a striking array of neuropsychiatric disorders. However, whereas disruptions in memory, motor, or emotional functioning are readily recognized as symptoms of more serious underlying conditions, decision-making deficits are often overlooked and quantitative measures are largely lacking. With collaborators in medical schools, we have shown that a number of experimental paradigms developed out of my research have potential to serve as quantitative probes of behavioral deficits and potential tool for pharmacological intervention.
 - a. Zhu L, Walsh D, Hsu M. "Neuroeconomic Measures of Social Decision-Making Across the Lifespan." <u>Frontiers in Neuroscience</u>, 6: 1-7, 2012. PMCID: PMC3448294
 - b. Winston C, Hsu M, Wudka D, Miller B, Rosen H. "Financial errors in dementia: Testing a neuroeconomic conceptual framework." NeuroCase, 2013. PMCID: PMC3770748
 - c. Winston C, Wood K, Beagle A, Hsu M, Kayser A, Miller B, Kramer J. "Neuroeconomic dissociation of semantic dementia and behavioral variant fronto- temporal dementia." <u>Brain</u>, 139: 578-87, 2015. PMCID: PMC4861653
 - d. Saez, I, Set E, Zhu L, Kayser A, Hsu, M "Dopaminergic modulation of human egalitarianism". <u>Current Biology</u>, 25: 912–919, 2015. PMCID: PMC4627633

Complete List of Published Work:

http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/47244507/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

R01 MH110477 Carver & Johnson (PI)

6/1/2017 - 5/31/2022

Approach motivation, effortful control, and internalizing and externalizing problems

This proposal seeks to examine two RDoC constructs (effortful control and approach motivation) and their potential interactions, using fMRI, behavioral, and self-report measures.

Role: Co-Investigator

R01 AG058817 Chiong (PI)

9/1/2018 - 4/30/2023

Decision-making abilities in ADRD: From clinical standards to decision neuroscience

The major goal of this project is to bridge translational gaps between recent cognitive neuroscience on human decision-making and clinical standards used in the assessment of decisional capacity.

Role: Co-Investigator

R01 AA026587 Kayser (PI)

1/4/2019 – 1/3/2024

Behavioral and Neural Correlates of Social Function in Alcohol Use Disorders

The major goal of this project is to understand deficits in social decision-making in individuals with alcohol use disorder at behavioral and neural levels.

Role: Co-Investigator

DRMS 1851902

Hsu, Jenkins & Camerer (PI)

9/1/2019 - 8/31/2022

Collaborative Research: An Interdisciplinary Approach to Predicting Unequal Treatment

The major goal of this project is to use a combination of computational and neuroimaging methods to model and predict social discrimination and unequal treatment in laboratory and field data.

Role: Co-PI

R01 MH112775 Hsu (PI) 1/4/2019 –1/3/2024

Dopaminergic Mechanisms Underlying Human Social Behavior: A Multimodal Approach

The major goal of this project is to elucidate the role of dopaminergic circuits in human social behavior using a combination of computational, neuroimaging, and molecular tools.

Role: PI

Completed Research Support (last 3 years)

R01 NS092079 Ivry (PI) 4/1/2015 – 3/31/2020

Embodied Decision Making: The Influence of Action Errors on Reinforcement Learning

This proposal explores the interaction of processes involved in action selection and action execution subserved by the basal ganglia and cerebellum.

Role: Co-Investigator

R01 DA043196 Hsu (PI) 10/29/2016 – 10/29/2019

CRCNS: Neurocomputational substrates of monetary exchange

The research proposal focuses on studying how objects come to acquire value, and their neurocognitive underpinnings.

Role: PI

NSF 1822572 Hsu (PI) 4/15/2018 – 3/31/2019

2018 CRCNS Principal Investigators Meeting

This proposal is to organize the annual PI meeting for the Collaborative Research in Computational Neuroscience (CRCNS) program.

Role: PI

R01 MH098023 Hsu (PI) 4/1/2013 – 1/31/2018

Neurobiological Substrates of Social Behavior: A Neuroeconomic Framework

The goal of this proposal is to study neural mechanisms of social learning in healthy adults as a precursor to understanding the impact of mental illnesses on social functioning.

Role: PI

R21 MH109851 Hsu (PI) 8/1/2016 – 7/31/2018

Cortical Oscillatory Dynamics and Human Decision-Making

This proposal uses electrophysiological recordings from neurosurgical patients to understand oscillatory mechanisms reflecting local valuation and global top-down control processes in decision-making.

Role: Co-PI

PHS Fellowship Supplemental Form

OMB Number: 0925-0001 Expiration Date: 02/28/2023

	Expiration Date: 02/28/2023			
Introduction				
Introduction to Application (for Resubmission applications)	00_IntroToApp.pdf			
Fellowship Applicant Section				
2. Applicant's Background and Goals for Fellowship Training*	02_Background_Goals_for_Fellowship_Training.pdf			
Research Training Plan Section				
3. Specific Aims*	03_Specific_Aims.pdf			
4. Research Strategy*	04_Research_Strategy.pdf			
5. Respective Contributions*	05_Respective_Contributions.pdf			
6. Selection of Sponsor and Institution*	06_SponsorInstitutionSelect.pdf			
7. Progress Report Publication List (for Renewal applications)				
8. Training in the Responsible Conduct of Research*	07_Responsible_Conduct.pdf			
Sponsor(s), Collaborator(s) and Consultant(s) Section				
9. Sponsor and Co-Sponsor Statements	08_SponsorInfo_Rev.pdf			
10. Letters of Support from Collaborators, Contributors and Consultants	09_LOS_All.pdf			
Institutional Environment and Commitment to	Training Section			
11. Description of Institutional Environment and Commitment to Training	10_InstitutionEnvironTraining.pdf			
12. Description of Candidate's Contribution to Program Goals	DSPAN_CandContribution_Ltr.pdf			
Other Research Training Plan Section				
Vertebrate Animals				
The following item is taken from the Research & Related Other Project Information form and repeated here for your reference. Any change to this item must be made on the Research & Related Other Project Information form.				
Are Vertebrate Anim	nals Used?			
 13. Are vertebrate animals euthanized? If "Yes" to euthanasia Is method consistent with American Veterinary Medical Association (AVMA) guidelines? If "No" to AVMA guidelines, describe method and provide scientific justification 14. Vertebrate Animals 				

PHS Fellowship Supplemental Form

	• • •				
Other Research Training Plan Information					
15. Select Agent Research					
16. Resource Sharing Plan	12_ResourceSharingPlan.pdf				
17. Authentication of Key Biological and/or Chemical Resources	· · · · ·				
Additional Information Section					
18. Human Embryonic Stem Cells					
Does the proposed project involve human embryonic s	stem cells?* Yes No				
	m cells, list below the registration number of the specific cell line(s), using the registry r, if a specific stem cell line cannot be referenced at this time, please check the box me. One from the registry will be used.				
Cell Line(s):					
19. Alternate Phone Number: 661 537 3546					
20. Degree Sought During Proposed Award:					
Degree: If	f "other", indicate degree type: Expected Completion Date (MM/YYYY):				
PHD: Doctor of Philosophy	05/2022				
21. Field of Training for Current Proposal*:	160 Neurosciences & Neurobiology				
22. Current or Prior Kirschstein-NRSA Support?*	☐ Yes ✓ No				
If yes, identify current and prior Kirschstein-NRSA supp	pport below:				
Level* Type* S	Start Date (if known) End Date (if known) Grant Number (if known)				
23. Applications for Concurrent Support?*	☐ Yes ✓ No				
If yes, describe in an attached file: 24. Citizenship*	02.5_Concurrent_Support.pdf				
U.S. Citizen or Non-Citizen National?	? ☑ Yes □ No				
Non-U.S. Citizen	With a Permanent U.S. Resident Visa				
☐ With a Temporary U.S. Visa					
If you are a non-U.S. citizen with a temporary visa applying for an award that requires permanent residency status, and expect to be granted a permanent resident visa by the start date of the award, check here:					
25. Change of Sponsoring Institution	Name of Former Institution:*				

PHS Fellowship Supplemental Form

Budget Section				
All Fellowship Applican	ts:			
26. Tuition and Fees*:				
■ None Requested	✓ Funds Requested			
	Year 1	\$21,510.00		
	Year 2			
	Year 3			
	Year 4			
	Year 5			
Year 6 (wh	en applicable)			
Total Fund	s Requested:	\$21,510.00		
Senior Fellowship Appli	cants Only:			
27. Present Institutional Base Salary:		Amount	Academic Period	Number of Months
28. Stipends/Salary Durin	g First Year of Proposed Fel	lowship:		
a. Federal Stipend Req	uested:	Amount	Number of Months	
b. Supplementation from	n Other Sources:	Amount	Number of Months	
		Type (e.g.,sabbatical leave, salary)		
		Source		
Appendix				
29. Appendix				

INTRODUCTION TO APPLICATION

The reviewers of the previous application (1 F99 NS120412-01) pointed out minor concerns and generously offered a number of suggestions for improvement. The following issues have been addressed in this revision (and marked in margins):

Revisions to Research Plan

The reviewers raised concerns about the ability of human PET imaging to resolve dopamine dynamics of decision making. It is true that PET cannot adequately account for time-resolved changes related to decision making. The research plan has been revised to more specifically and clearly state that PET is used to measure individual differences in stable measures of dopamine rather than dynamic fluctuations. Nevertheless, Aim 2B measures amphetamine-induced dopamine release. Although this is not task-related, it is a dynamic measure of dopamine function (on/off drug). A point was raised that hypotheses for each Aim were unclear and written as predictions. Hypotheses are now more explicit and motivated by potential mechanisms. An additional concern was raised about language used to describe general families of dopamine receptors visualized by the PET radiotracer [18F]fallypride. This has now been clarified by stating that fallypride binds to and measures availability of all D2-like family receptors.

Revisions to Training Plan

Reviewers expressed concern about communication with the co-sponsor, Dr. Ming Hsu, at UC Berkeley, and more importantly his ability to provide mentorship. To address these concerns, the sponsor statement more clearly indicates Dr. Hsu's extensive and successful experience mentoring a number of graduate and postdoctoral trainees who have continued academic careers. In addition, Dr. Hsu has provided an additional statement affirming his commitment to providing the necessary mentorship remotely. The applicant provides additional support for this remote mentorship by highlighting that the applicant has already collaborated and co-authored a published paper with Dr. Hsu on work in Aim 1A and an additional published paper. Dr. Hsu's role is made more explicit in training the applicant in designing and running computational models of social decision making for Aim 2 and generating a reading list for a formal independent study course at Duke on behavioral economics and game theory. Further concern may have arisen from his role as "Other Significant Contributor." This is due to internal grant management software at Duke that does not allow the "co-sponsor" title for non-Duke faculty. Reviewers pointed out that the K00 phase training goals are vague. The training plan now more specifically states the applicant plans to train in methods to acquire ecologically-valid dynamic inperson interactions between humans. Importantly, this training is different from Aim 2 which studies social decisions using computerized tasks. Specific training in other neuroimaging tools including human magnetic resonance spectroscopy is described as a potential way to specifically study neuromodulatory systems that interact with dopamine such as glutamate and GABA. Reviewer #2 raised a concern that grant-writing goals were overly-ambitious. These goals are modified to focus on a single career-transition award application (K22 or K99/R00). To address Reviewer #2's concern about confusion in projected milestone completion dates, timeline figures are now labeled by months rather than seasons and dates are more linearly organized.

Additional training consultants Dr. Makeba Wilbourn and Dr. Sarah Gaither have been added to provide guidance in mentoring and teaching. Drs. Wilbourn and Gaither will provide mentorship both in navigating a science career as a URM and in mentoring fellow URMs primarily through the applicant's participation in an NSF REU program at Duke. Dr. Wilbourn will provide additional mentorship related to centering teaching on equity, inclusion, and diversity and Dr. Gaither is co-advising the applicant on a research project outside of his dissertation evaluating the effects of racial and ethnic representation among university faculty in the US.

Progress since previous submission

The applicant received a departmental research grant to study the effects of racial and ethnic diversity among faculty in psychology and neuroscience departments in collaboration with Dr. Sarah Gaither, a social psychologist at Duke. The applicant participated as a mentor in an NSF REU organized by Dr. Makeba Wilbourn, Dr. Gregory Samanez-Larkin, and Dr. Sarah Gaither. The applicant completed his final teaching assistantship requirement with Dr. Makeba Wilbourn. The application published a paper as the first author from the results of Aim 1C in *Psychopharmacology* and is a co-author on a large-scale collaboration on the reliability of fMRI analyses published in *Nature*. The applicant also submitted a paper for peer review on neural mechanisms of biased juror decision making. The applicant has presented research findings at the Society for Neuroeconomics (virtual) where he participated in a mentorship networking event to begin identifying potential postdoctoral mentors. Finally, the applicant has successfully proposed his dissertation to his committee.

Introduction Page 32

A. DOCTORAL DISSERATION AND RESEARCH EXPERIENCE

Education

December 2013 – B.A., Neuroscience and Political Science; University of Southern California December 2019 – M.A., Psychology and Neuroscience; Duke University

Research Experience

Emotion & Cognition Lab, University of Southern California January 2012 – May 2014 PI: Mara Mather During my initial year, I contributed to ongoing studies of socially shared emotional memory and conducted an independent project to study mechanisms of social memory conformity. For these projects, I applied for and received two competitive research grants. During my second year, I advanced my skillset by learning psychophysiological and neuroimaging data collection and analysis for projects examining dietary effects on memory and fear conditioning responses. Once again, for these projects, I applied for and received a competitive research grant. My involvement in the lab culminated with a poster presentation demonstrating my knowledge of brain imaging analysis and a co-authored paper from my work examining social memory.

Barber, S.J., **Castrellon, J.J.**, Opitz, P., & Mather, M. (2017). Younger and older adults' collaborative recall of shared and unshared emotional pictures. *Memory & Cognition*. DOI: 10.3758/s13421-017-0694-3

Castrellon, J., Ponzio, A., Faskowitz, J., Mather, M., The impact of caloric restriction on subcortical structures. Poster presented at the annual meeting of the Western Psychological Association. Portland, OR. April 2014.

Affective Neuroscience Lab, Vanderbilt University June 2014 - October 2016 PI: David H. Zald As a full-time research analyst, I contributed to two large-scale studies of dopamine function and decision making. For these projects, I was involved in the planning, coordination, collection, and analysis of behavioral, fMRI, PET, and pharmacological measures in humans across the adult life span. I also sought out and trained in conducting structured clinical interviews (SCIDs) for mental disorders, optimized hospital-wide protocols for radiopharmaceutical safety during PET scans, and I supervised several undergraduate students in data collection. To support my interest in connecting large-scale social issues with neuroscience research, I audited a course on Neuroscience and Law at the Vanderbilt Law School, In addition, I was selected for a competitive fellowship at the Sackler Summer Institute of Developmental Psychobiology whose topic that year was on law and neuroscience. As a fellow, I met with, learned from, and debated researchers and leaders in this field. This experience has allowed me to build a network of colleagues and mentors with whom I currently turn to for mentorship. I presented a poster at the Society for Neuroscience on fMRI data analysis and presented a talk at the Interdisciplinary Symposium on Decision Neuroscience on the relation between social reward and dopamine function. I co-authored four publications of research that I collected and analyzed during that time.

- Dang, L.C., Samanez-Larkin, G.R., Smith, C.T., **Castrellon, J.J.,** Perkins, S.F., Cowan, R.L., Claassen, D.O., Zald, D.H. (2018). FTO affects food cravings and interacts with age to influence age-related decline in food cravings. *Physiology & Behavior*. DOI: 10.1016/j.physbeh.2017.12.013
- Dang, L.C., Samanez-Larkin, G.R., **Castrellon, J.J.**, Perkins, S.F., Cowan, R.L., Newhouse, P.A., Zald, D.H. (2017). Spontaneous eye blink rate (EBR) is uncorrelated with dopamine D2 receptor availability and unmodulated by dopamine agonism in healthy adults. *eNeuro*. DOI: 10.1523/ENEURO.0211-17.2017
- Dang, L. C., **Castrellon, J.J.,** Perkins, S. F., Le, N. T., Cowan, R. L., Zald, D. H., & Samanez-Larkin, G. R. (2017). Reduced effects of age on dopamine D2 receptor levels in physically active adults. *NeuroImage*, *148*, *123-129*. DOI: 10.1016/j.neuroimage.2017.01.018
- Dang, L.C., Samanez-Larkin, G.R., **Castrellon, J.J.**, Perkins, S.F., Cowan, R.L., Zald, D.H. (2016). Associations between dopamine D2 receptor availability and BMI depend on age. *NeuroImage*, *138*, 176-183. DOI: 10.1016/j.neuroimage.2016.05.044
- **Castrellon, J.J.**, Smith, C.T., Perkins, S.F., Samanez-Larkin, G.R., Zald, D.H., Monoamine oxidase A: a genetic marker of social reward preferences. Oral presentation at the annual Interdisciplinary Symposium on Decision Neuroscience. Temple University. Philadelphia, PA. June 2016.

Castrellon, J.J., Dang, L.C., Perkins, S.F., Samanez-Larkin, G.R., Zald, D.H., Aging contributes to grey matter volume and attentional impulsivity correlates in frontoparietal functional connectivity. Poster presented at the annual meeting of the Society for Neuroscience. Chicago, IL. October 2015.

Cognitive & Clinical Neuroscience Lab, UCLA October 2016 – August 2017 PI: Katherine H. Karlsgodt As the lab's first member, I helped coordinate and establish the lab's behavioral and neuroimaging data analysis pipelines and protocols, staff and undergraduate hiring and training, and day-to-day operations. I oversaw the development of a large-scale project to characterize social cognition and reinforcement learning in adolescents with psychosis. To do this, I developed novel tasks and coordinated data-sharing with collaborators across campus and institutions. I also developed a novel analytic plan for brain imaging that estimated cellular and myelin composition from MRI scans. I presented this ongoing novel work at the Society for Neuroscience annual meeting in 2017. While at UCLA, I attended lectures, job talks, and colloquiums to familiarize myself with research at the intersection of social cognition and psychopathology.

Castrellon, J.J., Karlsgodt, K.H., Diffusion-imaging derived cell density in the nucleus accumbens core predicts delay discounting in humans. Poster presented at the annual meeting of the Society for Neuroscience. Washington, D.C. November 2017.

Motivated Cognition & Aging Brain Lab, Duke September 2017 – Present PI: GR Samanez-Larkin I entered my PhD program at Duke with an NSF Graduate Research Fellowship. During my time in the lab, I have developed statistical skills in multilevel modeling, blind source separation, multivariate fMRI analysis, and meta-analysis. During this time, I have investigated associations between dopamine function and impulsive decision making in humans using an individual differences approach. This includes quantification of dopamine receptor availability and release with PET and estimation of responsivity to the psychostimulant damphetamine. Specifically, my work has sought to identify links between delay discounting, subjective valuation, and dopaminergic mechanisms with pharmacology, fMRI, PET, and experience sampling in everyday life. I also received funding to conduct a pilot study to test whether fMRI-related brain activation patterns can predict real-world changes in physical activity in response to socially motivating messages. I have trained and mentored 10 undergraduate students in data analysis, writing of results, and conference presentations. Nearly all of these students have received competitive funding to support their research. My mentorship was recognized in March 2020 with the Duke Bass Connections Outstanding Mentor Award. I have presented my research at the Cognitive Neuroscience Society, Society for Neuroeconomics, the Social Affective Neuroscience Society, and the Organization for Human Brain Mapping. For two years in a row, I have won the Best Poster Award from the Society for Neuroeconomics. My travel to some of these conferences has been supported by competitive awards from the Lafitte Foundation and the Society for Neuroeconomics. Each summer, I have participated in competitive programs like the Summer School in Social Neuroscience and Neuroeconomics and the Kavli Summer Institute for Cognitive Neuroscience. At these summer schools, I have expanded my knowledge of social decision-making and developed a network of potential collaborators for future research. As part of my graduate training, I have served as an instructor for introductory statistics, cognitive neuroscience, neurobiology research methods, and developmental psychology. Thus far, I have authored/co-authored seven manuscripts and have personally delivered six conference presentations.

Castrellon, J.J., Young, J.S., Dang, L.C., Smith, C.T., Cowan, R.L., Zald, D.H., Samanez-Larkin, G.R., Individual differences in dopamine support self-control of everyday desires. *In Prep, Planned Submission March* 2021.

Castrellon, J.J., Meade, J., Greenwald, L., Hurst, K., Samanez-Larkin, G.R. (2020). Dopaminergic modulation of reward discounting in healthy rats: A systematic review and meta-analysis. *Psychopharmacology*. DOI: 10.1007/s00213-020-05723-5

Botvinik-Nezer, R., Holzmeister, F., Camerer, C.F.,... Castrellon, J.J.,... Samanez-Larkin, G.R., ..., Nichols, T., Poldrack R., Schonberg, T. (2020). Variability in the analysis of a single neuroimaging dataset by many teams. *Nature*. DOI: 10.1038/s41586-020-2314-9

Burr, D.A., **Castrellon, J.J.,** Zald, D.H., Samanez-Larkin, G.R. (2020). Emotion dynamics across adulthood in everyday life: older adults are more stable in their affective experiences and better at regulating desires. *Emotion*. DOI: 10.1037/emo0000734

Castrellon, J.J., Young, J.S., Dang, L.C., Cowan, R.L., Zald, D.H., Samanez-Larkin, G.R., (2019). Mesolimbic dopamine D2 receptors and neural representations of subjective value. *Scientific Reports*. DOI: 10.1038/s41598-019-56858-1

Castrellon, J.J., Seaman K.L., Crawford, J.L., Young, J.S., Smith, C.T., Dang, L.C., Hsu, M., Cowan, R.L., Zald, D.H., Samanez-Larkin, G.R. (2019). Individual differences in dopamine are associated with reward discounting in clinical groups but not in healthy adults. *Journal of Neuroscience*. DOI: 10.1523/JNEUROSCI.1984-18.2018

Castrellon, J.J., Zald, D.H., Samanez-Larkin, G.R., Individual differences in dopamine predict self-control of everyday desires. Spotlight poster and talk presented at the annual meeting of the Society for Neuroeconomics. Dublin, Ireland. October 2019. *Best Poster Award Winner

Castrellon, J.J., Dang, L.C., Smith, C.T., Cowan, R.L., Zald, D.H., Samanez-Larkin, G.R., Latent organization of dopamine D2 receptors. Poster presented at the annual meeting of the Organization for Human Brain Mapping. Rome, Italy. June 2019.

Castrellon, J.J., Samanez-Larkin, G.R., Parsing the role of dopamine in reward discounting and subjective valuation. Spotlight poster and talk presented at the annual meeting of the Society for Neuroeconomics. Philadelphia, PA. October 2018. *Best Poster Award Winner

Castrellon, J.J., Dang, L.C., Young, J.S., Zald, D.H., Samanez-Larkin, G.R., Individual differences in dopamine D2 receptors and neural representations of subjective reward value. Poster presented at the annual meeting of the Cognitive Neuroscience Society. Boston, MA. March 2018.

Brains & Computation Lab, Duke University January 2018 – Present PI: John M. Pearson My involvement in the Pearson lab grew from a practicum rotation to learn online survey programming methods. I have been involved with leading an ongoing project on neuroimaging juror decision making. By studying social decisions under an ecologically-valid context, the results shed light on neural mechanisms that account for biased juror decisions. Through personal meetings with Dr. Pearson and collaborators at the Duke University School of Law and the University of Colorado, I have enhanced my skillset in multilevel statistical models of complex social behavior and multivariate fMRI pattern analysis. I presented preliminary findings from this work at the Society for Neuroeconomics and submitted a manuscript for peer-review of the final results.

Castrellon, J.J., Hakimi, S., Parelman, J.M., Yin, L., Law, J.R., Skene, J.A.G., Ball, D., Malekpour, A., Pearson, J.M., Skene, J.H.P., Carter, R.M. (*Under review*). Distinct brain mechanisms linked to evidence accumulation and crime-type bias in juror decisions. Preprint DOI: 10.1101/2020.11.11.378935

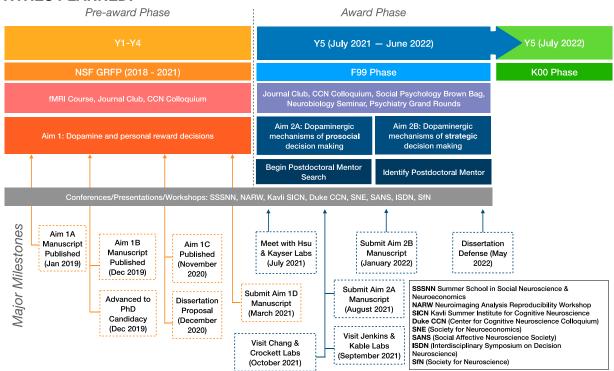
B. GOALS FOR FELLOWSHIP TRAINING AND CAREER

My ultimate goal is to lead a research lab that focuses on characterizing neurobiological mechanisms of motivated social decision making in humans. Thus far, my research has supported this goal by using neuroimaging to study the role of dopamine in human decisions for personal rewards. My proposed research under the F99 examines how dopamine supports decisions for social rewards. My future research will programmatically investigate whether dopamine dysfunction mediates observed differences in features of social decisions in psychopathology. This transdiagnostic approach is consistent with the RDoC framework because it seeks to link a common neural substrate (dopamine) measured at the molecular level with economic games that approximate behaviors under the Positive Valence and Social Processes domains. This line of research would place me in a position to lead as an interdisciplinary scientist by combining tools from neuroscience, behavioral economics, and psychiatry to probe social decision making. As an independent researcher in a faculty position, I will build an inclusive environment for future trainees to conduct interdisciplinary science while fostering practices that promote "open science" and accelerate discoveries. The goal of the F99 portion of this fellowship is to advance my intellectual, technical, and professional skills to succeed in the next step of my career.

Intellectual Skills: In order to succeed in the next phase of my training, I plan to broaden my knowledge in a way that allows me to synthesize theories and methods from social psychology, neurobiology, and psychiatry. As a student in the Duke Center for Cognitive Neuroscience (CCN), I regularly attend a weekly CCN journal club and colloquium that emphasizes core aspects of human cognitive neuroscience. During the F99 phase, I plan to continue attending these CCN weekly events

and alternate weekly attendance among the Social Psychology Brown Bag seminar, the Neurobiology seminar, and the weekly Psychiatry Grand Rounds. Exposure to a diversity of seminar talks will help me develop a rounded understanding to become a successful researcher. In addition to weekly meetings with Dr. Samanez-Larkin, I will have at least one meeting per semester with my dissertation committee members (Dr. Scott Huettel, Dr. Alison Adcock, and Dr. John Pearson) that is focused on identifying content areas I need to know better (e.g., social decision making) and discussing career navigation issues (e.g., which activities to prioritize to achieve long-term career success). I will work with co-sponsor Hsu to expand my knowledge of game theory and models of social decision making. **Technical Skills:** I am trained in experimental design, data collection, and neuroimaging data analysis. Under the F99, my technical training will focus on learning methods to apply computational models of decision making to draw inferences about underlying motivations of social behavior. I will have monthly one-on-one meetings with dissertation committee member, Dr. Pearson, a professor of Biostatistics, on the implementation of computational models and statistical inference including Bayesian statistics. **Professional Skills:** The resources available at Duke will further provide me with the opportunities to grow my skills in communicating science, mentoring trainees, and improve my teaching. During the F99 phase, I will give talks in local seminars, lab meetings, and at international conferences. I will further develop mentoring and teaching abilities through the supervision of undergraduate research assistants at Duke and from other institutions through an NSF REU program for URM undergrad trainees. I will also develop a teaching statement based on my experience teaching undergraduate statistics, cognitive neuroscience, and methods in neuroscience research. I will seek the advice of my faculty mentorship team as well as current D-SPAN scholars in the selection of a post-doc institution.

C. ACTIVITIES PLANNED:



Year 4 (December 2020 - May 2021)

- Research: I will continue running preliminary analyses for Aim 2A testing links between PET measures of DA and prosocial behavior from a dictator game that I collected. I will also contribute to side-projects that emerged from internal funding mechanisms that I applied for that seek to leverage neuroimaging data to motivate people to be physically active using socioemotional messages. I presented a dissertation proposal to my committee in December 2020.
- Conferences, Workshops, and Colloquiums: I will continue to attend the Duke Center for Cognitive Neuroscience journal club and colloquium series to network with visiting faculty. These presentations are attended by students and faculty across the University and by local students and faculty at the

University of North Carolina, Chapel Hill. I will present preliminary data from Aim 2A at the Social Affective Neuroscience Society meeting in May 2021.

- Publications: In March 2021, I will submit and revise as necessary a manuscript as a first-author with my sponsor, Dr. Samanez-Larkin, as part of Aim 1D on associations between dopamine receptor availability and self-control of everyday desires. Data collection and analysis for this manuscript is complete. A preprint for this manuscript will be immediately shared on an open-access preprint server. I anticipate this will be accepted for publication by the end of 2021. I will revise as necessary an additional manuscript I recently submitted for peer-review as a first-author with Dr. John Pearson. This manuscript is part of a project that evaluates fMRI-measured neural mechanisms of juror decisions. I anticipate this manuscript will be accepted by the end of 2021.
- Teaching/Mentorship: I will serve on an honors thesis committee for an undergraduate student (as I have done before). I am mentoring this student in analyses that characterize associations between dopamine function and subjective appetitive responses to amphetamine. This student will be a coauthor on a manuscript being prepared for publication outside my dissertation. I will include this student in meetings to discuss the submission and revision process to learn more about academic publishing. I will continue mentoring undergraduate students who are underrepresented in research careers as part of Duke's NSF Summer Research Experience for Undergraduates (NSF award no. 1950651) and through the Científico Latino Graduate Student Mentorship Initiative. Mentorship includes assistance in preparing applications for graduate school, fellowship awards, and postbaccalaureate job positions.

Year 5 (June 2021 – September 2021)

- Research: I plan to meet with my co-sponsor, Dr. Ming Hsu, at UC Berkeley in July 2021 to seek his advice on Aim 2A revisions, Aim 2B analysis strategies, and discuss academic career goals. During this time, I will also meet with my consultant, Dr. Andrew Kayser, at UC San Francisco Medical School to discuss translational research goals at the intersection of molecular neuroimaging and social decision making. Second, I will meet with the labs of Dr. Adrianna Jenkins and Dr. Joseph Kable at Penn in September 2021 to discuss how to best integrate contemporary behavioral economics with this line of research on social behavior. Dr. Jenkins and Dr. Kable can also provide unique advice for my postdoc search for an interdisciplinary environment given their affiliation with multiple academic communities at the University of Pennsylvania (Psychology, Psychiatry, Marketing, and Economics).
- Conferences, Workshops, and Colloquiums: During the academic year, I will begin attending the Social Psychology Brown Bag series, the Department of Neurobiology seminar, and the Duke Psychiatry Grand Rounds (one per week in addition to the Center for Cognitive Neuroscience Colloquium).
- <u>Publications:</u> I intend to have a complete draft of my results from Aim 2A on associations between PET-measured dopamine and prosocial decisions following feedback from Hsu and colleagues at the Social Affective Neuroscience Society meeting in May 2021. I plan to submit this manuscript in August 2021.
- Teaching/Mentorship: To help prepare for the postdoctoral phase, I will seek opportunities to mentor junior graduate students in my program and in the Center for Cognitive Neuroscience (CCN) at Duke. As a senior graduate student, I will assist new graduate students with neuroimaging data analysis and the use of our computing cluster. During the summer, I will again mentor visiting undergraduate students who are underrepresented in research careers as part of Duke's NSF Summer Research Experience for Undergraduates (NSF award no. 1950651). I will train students in neuroimaging data analysis and presenting research findings.

Year 5 (October 2021 – June 2022)

- Research: I will begin work on Aim 2B by analyzing pharmacological dopamine PET data and strategic behavior from a patent race game. I will meet with the labs of Dr. Molly Crockett and Dr. Steve Chang at Yale in October 2021 to discuss theoretical models of neuromodulation of social behavior in humans and to seek their counsel navigating the postdoc search.
- Conferences, Workshops, and Colloquiums: As part of the Duke Center for Cognitive Neuroscience Colloquium series, I will give a research talk in November 2021. I will attend the Society for Neuroscience meeting in November 2021 where I will propose a mini-symposium on neuromodulation of social decision making. I will solicit abstracts from relevant experts in the field. If the proposal is accepted, I will present my research from Aim 2 and network with co-presenters. I also will attend the Interdisciplinary Symposium on Decision Neuroscience in June 2022 to present my research before an

audience of academics from diverse academic fields including neuroscience, consumer psychology, behavioral economics, law, and finance as well as representatives from industry. This will further allow me to enrich my network as an interdisciplinary investigator. During the academic year, I will continue attending the Social Psychology Brown Bag colloquium series, Neurobiology seminar, and the Duke School of Medicine Psychiatry Grand Rounds. Finally, I will defend my dissertation in May 2022.

 <u>Publications:</u> Following feedback from colleagues at the Society for Neuroscience annual meeting in November 2021, I intend to have a complete draft of my results from Aim 2B on associations between pharmacological PET-measured dopamine and strategic decision making by January 2022.

Activities Planned for K00 Phase

As a postdoctoral scientist, I will apply the skills gained in the F99 phase to learn about and investigate neuromodulatory mechanisms of social decision making in clinical populations. Specifically, impairments in social cognition have been identified in ADHD and psychosis spectrum psychopathologies. While these psychopathologies are often treated with dopaminergic medication (e.g. antipsychotics, stimulants, etc.), it is unknown whether dopamine neurotransmission mediates differences in social behavior. During the K00 phase. I will use techniques like PET imaging and pharmacology to identify markers of dopamine function across individuals who vary in clinical symptoms and social decision making tasks. In addition, I will use this phase of the award to broaden my knowledge and research investigating alternative neuromodulatory mechanisms of social decisions. I intend to gain methodological skills in running experiments with dynamic social interaction to identify how participants naturally interact with each other (as opposed to computerized tasks with hypothetical players used in Aim 2). Learning how to acquire in-person social interaction data will enhance my research goals of linking everyday social decisions to dopamine function and psychopathology. While this plan will identify links between dopamine and social decisions, I also intend to account for potential interactions between dopamine and neurotransmission of glutamate and GABA, which are known to interact with dopamine in circuits that support social cognition and decision making. Training in advanced human MR imaging methods could include learning magnetic resonance spectroscopy to measure individual differences in cortical glutamate and GABA which will allow me to account for these links. In addition to pursuing this research, I will use the K00 phase toward professional development as an independent investigator. To this end, I will apply for a career transition award (K22 or K99/R00), seek teaching opportunities, and apply for faculty positions.

- Research: I will programmatically build links between neuromodulatory function, psychopathology, and social decision making. By applying methods from computational psychiatry, I will identify specific motivational factors that contribute to social decisions. I will gain experience with clinical research including drug manipulation studies and data collection from clinical populations (e.g., psychosis spectrum and ADHD). I will learn experimental methods that can help test dynamic social interactions between dyads and groups of individuals (e.g. using in-person dynamic economic decision tasks that require cooperation or competition). I will also seek to broaden my understanding of neuromodulatory mechanisms that may interact with dopamine such as glutamate and GABA potentially using magnetic resonance spectroscopy. I will submit at least 1 manuscript per year and at least 1 review article.
- Conferences & Workshops: I will attend new conferences to build my scientific network with colleagues in clinical neuroscience and social psychology. Candidate conferences that fulfill this goal include annual meetings of the Society of Biological Psychiatry, the American College of Neuropsychopharmacology, the Society for Personality and Social Psychology, and the Society of Experimental Social Psychology.
- <u>Teaching/Mentoring:</u> I will mentor graduate students in my postdoctoral lab and department and seek opportunities to continue teaching undergraduates in cognitive neuroscience and statistical methods.
- Grant Writing: I will submit an NIH training grant application per year. Specifically, I will apply for a K99/R00 or K22 diversity transition award with the assistance of post-doctoral mentors. If funded, this grant would provide additional support for continuity of my research program as I transition to an independent tenure-track faculty position. In addition to this, I will apply for internal institutional seed grants as PI.
- Job applications: During the K00 phase, I will identify ideal institutions that can support my line of research. I will prepare faculty position application materials, deliver job talks, and negotiate eventual offers. Throughout this process, I will be supported by K00 phase postdoctoral mentors and F99 phase co-sponsors.

Specific Aims

Research has shown that humans' decisions in interpersonal economic games recruit neural structures associated with both social cognition and reward valuation. While previous studies have shown that dopamine function is paramount to decisions involving rewards for oneself, its role in social decisions like sharing rewards and learning from adversaries is much less well understood. To address this, the F99 phase of this proposal will investigate the relationship between dopamine 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 function relates to prosocial and strategic social decisions. In this F99/K00 application, I propose three aims to complete my dissertation research and extend my training as a post-doctoral researcher studying dopaminergic neuromodulation of social decisions. By combining theories and tools from neuroscience, psychology, behavioral economics, and psychiatry, I will emerge from this training with a unique combination of approaches to support an independent research program on the neural mechanisms of human social decision making.

Aim 1 Dissertation Research Project Progress to date: My dissertation work focuses on identifying links between dopamine function and personal reward decision making in humans. Aim 1A reveals that individual difference associations between dopamine D2-like receptors and behavioral preferences for discounted rewards depend on psychopathology. Aim 1B demonstrates that subjective value functional magnetic resonance imaging (fMRI) neural signal in the medial prefrontal cortex and midbrain are associated with individual differences in dopamine D2-like receptors. Given mixed findings from past pharmacological studies, Aim 1C is a pharmacology meta-analysis demonstrating that D1-like and D2-like receptor antagonism but not agonism increases discounting and that psychostimulants decrease discounting. The findings are consistent with an emerging view that these receptor have similar roles in mediating value-based decisions. Finally, Aim 1D seeks to evaluate whether ecologically-valid methods can capture associations between impulsivity over desires experienced in daily life and individual differences in PET-measured D2-like receptors. This research uses measures of individual differences in D2-like receptor availability from the lab to predict self-control over desires for rewards in everyday life using experience sampling methods.

Aim 2 Completing Dissertation Research Project: Although prior work including the studies proposed in Aim 1 identified associations between dopamine function and decisions about personal rewards with costs like time, risk, or effort, it is unknown whether such associations exist for decisions with social trade-offs. Indirect evidence from human pharmacological studies indicate that increasing DA supports affiliative behaviors such as cooperation and fairness. Many social behaviors require optimal decision making that maximizes rewards for oneself while accounting for competitors' interests. Adaptive affiliative and competitive decisions are necessary for successful social relationships. Nevertheless, prosocial and strategic behaviors may conflict with dopamine's role in reward maximization out of self-interest alone. It is therefore unknown whether individual variability in dopamine function supports prosocial and strategic decisions to share rewards at one's own cost and learn from others' choices to optimize strategies that balance cooperation and self-interest. Given these associations, I hypothesize that individual differences in dopamine support prosocial and strategic behaviors. I will address this in the following sub-aims: 2A) characterize associations between dopamine D2like receptor availability measured with PET and prosocial behavior from the economic "dictator" game and 2B) characterize associations between dopamine D2-like receptor availability and dopamine release measured with pharmacological-challenge PET and strategic behavior from the economic "patent race" game. The overall goal of these studies is to better understand the specific role of human dopamine function in prosocial and strategic social decisions.

Aim 3 The Postdoctoral Research Direction: I am highly motivated to pursue interdisciplinary and translational research that bridges theories from social psychology, experimental design from behavioral economics, and measures of neurobiological function to better understand adaptive and maladaptive human behavior in everyday life. Although I am beginning to study social decisions in my dissertation, a postdoctoral fellowship would provide the necessary bridge to better understand the neuromodulatory mechanisms that mediate dynamic in-person social interactions in healthy adults and clinical populations. The ideal post-doctoral environment would include co-mentorship by scientists with expertise in social psychology, game theory, computational modeling, pharmacology, neuroimaging, and/or research with patient populations. I also seek a postdoctoral research environment that embraces diversity, allowing me to hone my mentoring and advising skills in the transition to a faculty position. The K00 phase would allow me to build a broader foundation of knowledge on social decision making while also developing new skills like acquiring ecologically-valid measures of social decisions essential for the development of my own independent research program.

Specific Aims Page 39

SIGNIFICANCE

Social interactions are fundamental to healthy living and many psychopathologies feature social deficits. It is imperative, therefore, to examine mechanisms that support individual variation in social decision about rewards. Over the past decade, a number of neuroimaging studies have highlighted specific social decision making circuits across the brain that depend on motivational and cognitive processes like reward value discounting, self-control, learning, and social cognition¹. While advances in human molecular neuroimaging have begun to reveal specific involvement of the neurotransmitter dopamine (DA) in personal reward-related decisions², considerably less is known about how DA modulates social reward-related decisions. This is of particular relevance to the goals of the NIH Research Domain Criteria (RDoC) Initiative since behaviors under the RDoC's Social Processes and Positive Valence (reward valuation) domains are disrupted in various psychopathologies³ and extremely few studies have tested whether social decisions are also mediated by the DA system. Research in this area can provide translational scientists with information to develop neurobiological targets for evidence-based therapies.

Whereas DA is largely known to support value-based decisions for oneself, this generalization is complicated in the face of reward outcomes with social contingencies that require trade-offs between self-interest and generosity and learning from others' choices. Indirect evidence from human pharmacological studies indicate that increasing DA increases prosocial giving⁴ and reduces aversion to harming others⁵. Anatomically, fMRI and lesion studies indicate that learning from competitors behaviors depends on the striatum and prefrontal cortex^{6,7}. These studies are not able, however, to identify which specific neuromodulatory systems and in which regions account for individual differences in social decisions involving rewards. This is important because DA neurons project to multiple regions in the striatum and frontal and temporal cortices^{8,9}. Critically, functional MRI (fMRI) studies suggest that prosocial choices and strategic social learning involve coordination between the ventral striatum, amygdala, ventromedial prefrontal cortex (vmPFC), anterior cingulate cortex (ACC), insula, and temporoparietal junction (TPJ)^{10,11}. Positron emission tomography (PET) can provide the neurochemical and spatial specificity to delineate the relationship between individual differences in DA and social decision making.

Ultimately, my goal is to lead a research lab that focuses on characterizing molecular mechanisms of motivated social decision making in humans with an emphasis on interpersonal decisions involving shared rewards in competitive and affiliative environments. My research will investigate the role of DA in social decisions by combining tools and knowledge from neuroscience, behavioral economics, and psychiatry. The research proposed here fulfills this goal with PET imaging, pharmacology, and computational modeling of behavior from economic interpersonal tasks with 3 primary aims. Aim 1 establishes new research on direct measures of dopaminergic modulation of personal reward-related decisions. Aim 2 uses the dictator game and the patent race game to model associations between direct measures of DA function and both prosocial and strategic reward-related decisions, respectively. Finally, Aim 3 broadens this research to study clinical populations to identify features of DA disruption that predict transdiagnostic impairments in dynamic in-person social decisions.

APPROACH

Aim 1 Dissertation Research Project Progress to date:

<u>Rationale:</u> In order to lay the groundwork to study DA and interpersonal reward processing and social decision making in humans, it is critical to first evaluate the role of DA in <u>personal</u> reward processing (rewards for oneself) and decision making. Whereas a number of investigations have evaluated dopaminergic mechanisms of reward valuation in rodents, these characterizations are less well-studied in humans¹². Some direct evidence from PET imaging studies and indirect evidence from pharmacology studies suggest that DA is important for personal value-based decisions^{13–15}. However, these results are mixed. The work described here evaluates DA and decision-making among healthy and clinical populations with PET imaging of the DA system using an individual differences approach (static measures) and pharmacological manipulation (dynamic measures) of DA in animals.

Aim 1A: Individual differences in dopamine are associated with reward discounting in clinical groups but not healthy controls. Discounting is the tendency to devalue rewards that are relatively more costly than alternative options. This behavior is often conceptualized as a form of self-control and inhibition of impulsive actions. Importantly, DA and DA D2-like receptors (D2Rs) in particular are believed to regulate decisions to inhibit impulsive actions in motor control tasks ^{16–18}, which has led researchers to begin examining associations between reward discounting and PET measures of DA. Unfortunately, many of these studies have been limited by small sample sizes, a focus only on decisions involving time costs ^{13,19}, use of radiotracers with limited visibility across the brain, or a focus only on individuals with psychopathology²⁰. **Methods:** To address these gaps in the literature, this study assessed how measures of discounting (N=134 healthy adults) were related to DA using PET scans with radiotracers that provide complementary coverage of D2Rs across the whole brain. I performed kinetic modeling²¹ of tracer radioactivity across time to estimate receptor availability (binding potential). Healthy

Research Strategy Page 40

participants made decisions about preferences for rewards that are smaller and sooner/more certain/less effort-requiring (finger pressing task) or larger rewards that are later/less certain/more effort-requiring (82 trials for each

cost type: time/probability/effort). Hypothesis: I hypothesized that if D2Rs regulate impulsive motor actions, then individuals with higher D2R availability would exhibit greater patience, risk aversion, and effort allocation. **Findings:** Contrary to this, I did not observe any individual difference associations between DA and decision making. Since this finding was inconsistent with prior reports in humans^{13,19} and assumptions based on studies in rodents, I conducted a systematic review and meta-analysis of human PET studies to identify potential sources of heterogeneity of effects. The results of the meta-analysis indicated that my observed effects were consistent with prior reported associations in healthy adults but not clinical groups (**Fig. 1**)²². I speculated that variation in the association by clinical status could be due to systemic differences across multiple interacting

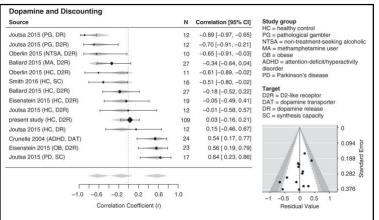


Figure 1: Meta-analysis of associations between in vivo PET measures of dopamine function and discounting in humans vary across clinical populations and healthy controls. Addiction populations show negative associations, whereas groups with obesity, ADHD, and Parkinson's disease show positive associations. Healthy controls do not show a relationship between dopamine and discounting.

neuromodulatory circuits²³ or differences in presynaptic DA synthesis²⁴. Importantly, the findings question our ability to draw generalizable inferences about individual difference associations across healthy and clinical populations. **Training Experience:** To perform this analysis and publish the results, I collected neuroimaging and behavioral data, learned how to preprocess PET data, learned how to organize data for reproducibility and sharing, and learned meta-analytic statistics. During the analysis stages, I gained mentorship experience through training research staff in voxelwise statistical analysis of PET data and data quality assessment.

Aim 1B: Dopamine D2 receptor availability is correlated with neural representations of subjective value. Aim 1B sought to more precisely characterize the functional neural circuitry of value-based personal decisions. Past research implicates two potential overlapping circuits critical for value-based choice: a cortiocostriatal loop²⁵ via medium spiny neuron (MSN) projections to the ventral pallidum \rightarrow thalamus \rightarrow vmPFC, and a ventral striatopallidal loop via MSN projections to the ventral pallidum \rightarrow midbrain²⁶. **Methods:** In this study, 25 healthy adults from a subsample included in the analysis of Aim 1A who underwent PET scanning with [18F]fallypride to measure D2-like receptor (D2R) availability (including D2 subtypes) also completed a delay discounting task for

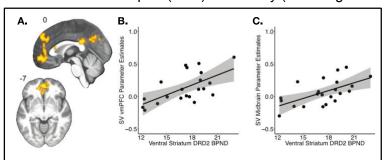


Figure 2: (A) fMRI signal linked to discounted subjective value. Ventral striatal D2R availability from PET was positively correlated with subjective value from fMRI in the vmPFC (B) and midbrain (C).

monetary rewards (as in Aim 1A) during an fMRI scan²⁷. **Hypothesis:** I hypothesized that although D2Rs may not predict overall average observed choices (as in Aim 1), D2Rs could still be related to trial-by-trial sensitivity of neural representations of subjective value for each choice. Specifically, I hypothesized that individual differences in ventral striatal D2R availability would be positively correlated with stronger neural representations of subjective value in the midbrain and vmPFC (core nodes of subjective value circuits as discussed above). **Findings:** Statistically significant (*p* < .05 threshold) positive associations were identified

between ventral striatal D2R availability and SV signal in the vmPFC (r = .624, p = .003) and midbrain (r = .597, p = .003) (**Fig. 2A-C**). The results converge with work in rodents suggesting that D2Rs in the ventral striatum functionally motivate behaviors through two DA signaling pathways (corticostriatal loop²⁸ and ventral striatopallidal loop²⁹) and suggest a role for DA in shaping individual differences in value sensitivity. **Training Experience:** In carrying out this analysis and publishing the results, I learned about and estimated discount rates with different assumptions about the rate of value decline over time (e.g. hyperbolic and exponential). I enhanced my fMRI skillset by preprocessing and running statistical models of brain function to identify neural representations of subjective value. I learned how to use open-source software and ensured that the data conformed to a new neuroimaging data format (BIDS) and shared all the data publicly through OpenNeuro.

Aim 1C: Quantitative meta-analysis of dopamine pharmacological effects on reward discounting. While Aims 1A and 1B focus on reward valuation associations with D2R availability, it is important to consider that DA modulates multiple binding sites at the synaptic level³⁰. This is particularly important for translational research since several medications that treat conditions like schizophrenia or ADHD work by modulating these different

DA sites^{31,32}. **Methods:** For my PhD qualification exam (and dissertation), I systematically reviewed and quantitatively meta-analyzed studies of DA drug effects on reward discounting in healthy humans, non-human primates, and rodents (121 DA drug effects on time, probability, and effort discounting from 1,710 animals). **Hypothesis:** I hypothesized that if D1-like (D1R) and D2-like receptors (D2R) have opposing function in increasing and decreasing motor function, respectively, then D1R agonism and D2R antagonism would increase reward discounting but that D1-like antagonism and D2-like agonism would decrease discounting. I also hypothesized that if DA transporters

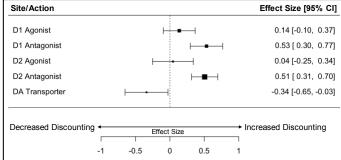


Figure 3: Summary of DA pharmacology meta-analysis results. D1 and D2 receptor antagonist drug increased discounting and DA transporter drugs decreased discounting.

regulate impulsive action, then DAT-binding drugs would decrease discounting. Findings: Contrary to my hypotheses, D1R and D2R drug effects were not dissociable: D1R and D2R agonists did not consistently modulate reward discounting but D1R and D2R antagonists increased discounting to a similar degree (Fig. 3)³³. Consistent with my hypothesis and the therapeutic effect of psychostimulants, DAT-binding drugs decreased reward discounting. Training Experience: I gained new technical and statistical knowledge from this analysis. I also expanded my understanding of DA function, pharmacology, and cross-species study design. I pre-registered methods and hypotheses on the Open Science Framework and gained experience with additional tools to support open and ethical science. I was able to enhance my mentorship skills by training 3 undergraduate students in data extraction, presentation of findings at a major international conference (Society of Biological Psychiatry), and co-authorship on a published paper in *Psychopharmacology* in November 2020³³.

Aim 1D: Individual differences in dopamine support self-control of everyday desires. Prior work suggests that valuation mechanisms also support self-control abilities³⁴ and that self-control decisions involve resisting temptations that conflict with personal goals (e.g. health goals may conflict with a desire to overeat)^{35,36}. Given DA's role in valuation from laboratory and neuroimaging studies (e.g. Aims 1A–C), it may be speculated that such associations are present for reward-related decisions outside the laboratory. **Methods:** 109 healthy adults

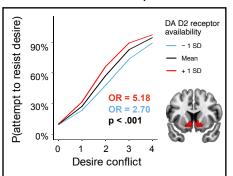


Figure 4: Individuals with lower ventral striatal D2R availability were less likely to resist a desire when conflict with personal goals was high. OR = odds ratio.

underwent a [18F]fallypride PET scan for D2-like receptors (D2Rs) before 10 days of experience sampling in everyday life³⁷. 3x/day for 10 days they were asked about desires recently experienced, the degree to which the desire conflicted with goals, whether they attempted to resist the desire, and if they behaved in line with their desire. **Hypothesis:** I hypothesized that if daily desires are subjectively valued according to how much they conflict with goals (like monetary rewards are subjectively valued across time delays as in Aim 1B), then D2Rs in the ventral striatum may similarly be associated with sensitivity to desire self-regulation value. Specifically, individuals with greater D2R availability in the ventral striatum would be better at attempting to resist daily desires that have greater subjective value (as a function of goal conflict). **Findings:** As hypothesized, individuals with greater D2R availability in the ventral striatum were more likely to attempt to resist desires under high conflict with personal goals (higher subjective value) (**Fig. 4**). This suggests that individual differences

in mesolimbic DA shape how people weigh personal goals in decisions to practice self-control and demonstrates that neural mechanisms of reward valuation have real-world implications beyond laboratory experiments. **Training Experience:** Through meetings with mentors in my department and lab, I learned how to run multilevel models of timeseries data. In collecting the data, I learned how to set-up an experience sampling study to obtain ecologically-valid measures. I will submit these findings for publication in March 2021.

Aim 2: Completing Dissertation Research Project (F99 Phase)

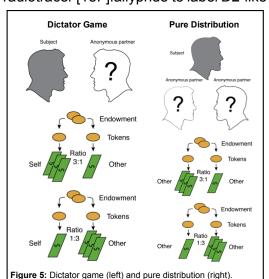
Whereas the work in Aim 1 evaluated DA function and reward valuation decisions at the cost of time, probability, effort, and personal goals, Aim 2 seeks to understand whether and how these DA associations contribute to

Research Strategy Page 42

reward valuation decisions with *social* costs. Game theorists have wrestled with the paradox that rational decisions to maximize rewards for oneself at the cost of others' welfare are not always optimal³⁸. Indeed, decisions to act against self-interest are prominent in prosocial choices and strategic social learning³⁹. Prosociality is hypothesized to arise from biological and social mechanisms. While kin selection may be a primary biological manifestation of prosociality in many species⁴⁰, primates and humans in particular also depend on social motivation to both increase the value placed on sharing rewards (e.g. desire for reciprocity or feelings of guilt^{41,42}) and to decrease the value placed on sharing rewards (e.g. feelings of envy⁴¹). Even though prosociality is supported by the same underlying motivational brain circuits that also support DA signaling (ventral striatum, ACC, vmPFC, amygdala, and insula)^{1,10}, no such link between DA and prosocial decisions has been investigated. In social situations, it is fundamental that an individual learn from and anticipate another person's actions in order to maximize personal rewards. Anticipating others' future choices requires second-order learning to draw inferences about a competitor's inference about oneself⁴³. Prior fMRI studies have implicated regions receiving DA such as the ventral striatum, amygdala, and insula, as well as the TPJ in this kind of belief learning (theory of mind)^{7,44,45}. It may be speculated that DA modulates these regions to support social decision making.

Aim 2A: Associations between dopamine D2 receptor availability and prosocial decision making

Decisions to act for the good of someone else (i.e. prosocially) or for one's own good (i.e. out of self-interest) are often mutually-exclusive. How, then, could DA simultaneously support rewards for oneself and others? One possibility is that specific brain regions that support self-interest have concurrent but dissociable DA-mediated effects on decisions from brain regions that support prosocial choices. fMRI studies indicate that the ventral striatum and ACC support self-interest and envy^{46,47} whereas the amygdala and insula support prosociality and guilt^{48,49} and the vmPFC may support both functions^{50,51}. DA signaling across these regions may modulate those respective functions. This work seeks to evaluate how DA relates to prosocial choices and to reveal underlying motivations. Computational models have been developed to explain generosity^{52,53}, self-interest^{39,48}, and equity^{48,54}. These models can distinguish whether behaviors are motivated by feelings of guilt and envy or aversion to unfairness to oneself or others. **Methods:** Healthy adults (N=81) underwent PET scanning with the radiotracer [18F] fallypride to label D2-like receptors (D2Rs) and on a separate visit completed the dictator game⁵⁵



and pure distribution task (Fig. 5). During the dictator game, participants were endowed with a number of tokens that varied from trial to trial. In each trial, participants distributed these tokens between themselves and an anonymous partner that were worth different amounts of money. On some trials, the tokens for the participant and the anonymous partner were worth the same amount of money but on other trials they were worth more for the participant or the anonymous partner (ratios of 1:1, 1:2, 1:3, 3:1, 2:1). Participants distributed tokens for 20 trials with 2 different anonymous partners (40 trials total). Importantly, during this task, the anonymous partner did not respond and distribute tokens. This prevents desire for reciprocity and social learning. Following this, participants completed the pure distribution task. The structure of this task is identical to the dictator game: however, here participants distributed endowed tokens between 2 different anonymous partners (with no tokens going to the participant) for 20 trials. I will use multilevel models to assess two primary measures: (1) generosity (mean amount of money given to

the anonymous partner) and (2) inequity (absolute difference between money kept by the participant and given to the anonymous partner). Specifically, I will test whether D2R availability predicts differences in generosity and inequity and whether the token-to-dollar exchange value ratio between the participant and other player modulates this effect. Presumably, variation in the ratio can mimic environments in which inequity is already present. I will use this analysis plan for the dictator game and pure distribution—where generosity to any particular player should be absent. I will also use computational models to describe guilt and envy motivations for prosociality as previously described. **Expected and Competing Hypotheses:** I hypothesize that if DA has dissociable concurrent circuit functions related to prosociality and self-interest as discussed above, then lower D2R availability in the ventral striatum and ACC but higher D2R availability in the amygdala and insula will be associated with greater generosity and lower self-interest. Alternatively, D2R availability may not relate to generosity but instead with equity (fair distributions of money) in general. This hypothesis accounts for the potential for individuals to be more concerned with the token exchange ratio when anonymous partners' tokens are effectively less valuable. I also hypothesize that computational model parameters will indicate a positive

association between guilt and D2R availability in the amygdala and insula as well as positive associations between D2R in the ACC and ventral striatum with envy parameters. Training Experience: I will expand my knowledge of game theory through a formal reading course of literature developed by my co-sponsor Ming Hsu. I plan to present preliminary findings from Aim 2A at the annual meeting of the Social Affective Neuroscience Society in May 2021. I will regularly meet with Hsu to gain experience running computational Bayesian models using R and Stan. I will also meet with Hsu's and consultant Andrew Kayser's labs to present these data in July 2021 and will submit a manuscript with 2A findings for peer-review in a publication in August 2021.

Aim 2B: Associations between dopamine receptors, dopamine release, and strategic decision making Whereas the studies described thus far largely used PET to evaluate D2Rs, this study goes further by also quantifying psychostimulant-induced DA release. Psychostimulant abuse has been linked to deficits in social cognition and theory of mind abilities⁵⁶. In addition to prosocial behaviors (Aim 2A), it is critical for an individual to learn to make social decisions that require understanding and predicting the choices of others (Aim 2B). Emerging work suggests that regions such as the ventral striatum, vmPFC, TPJ, and amygdala are as critical to social learning as they are to non-social learning^{6,7,57–59}. Whereas DA supports non-social reward learning, it is unclear whether such associations exist for strategic social learning. Simple reinforcement learning (RL) algorithms only account for an individual's own actions and not the possibility that competitors may exploit an individual decision maker. Belief-learning (BL) algorithms, however, can account for this by modeling an individual's beliefs about a competitor's expectations (second-order beliefs)⁶. This research seeks to understand whether DA could also support this kind of complex BL in addition to simple RL. Methods: Healthy adults (N=35) underwent PET scanning with [11C]FLB-457 to label D2-like receptors (D2Rs): (1) after oral placebo and (2) after a dose of the DAT modulating psychostimulant d-amphetamine (0.43 mg/kg). On a separate visit, participants completed the patent race game⁴³. Participants' neural responsivity to amphetamine was estimated as the change between radiotracer binding to D2Rs between amphetamine and placebo. During the patent race (Fig. 6), on each of 160 trials, participants were paired with a different past participant as an opponent. The

participant and opponent competed to develop a new product worth money and the participant and their opponent were endowed with money. After participants indicated how much they wish to spend, their opponent's choices programmed) were revealed. If the participant spent more than their opponent, they won the prize and if they spent less than their

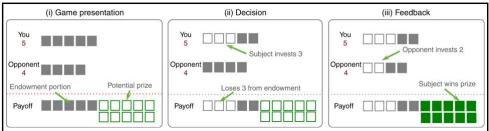


Figure 6: Patent race game. Participants compete with others to develop a new product worth a certain amount of money. If the participant spends more than their competitor, the participant wins the product and their remaining endowment and vice-versa with the competitor. If the participant and the competitor invest the same amount, then neither player wins the product.

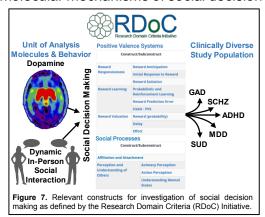
opponent, they lost the prize to the opponent. In both scenarios, the participant lost their investment. Participants received real payouts from 40 trials. I will use computational modeling to identify interactions between placebo D2R availability, DA release, and participants' social learning strategies. I will examine individual difference associations between regional DA measures and parameters from (1) simple RL and (2) complex social BL models. **Expected and Competing Hypotheses:** I hypothesize that higher ventral striatal and amygdala D2R availability and DA release will be associated with learning from both one's own and competitors' behaviors. Specifically, participants' whose behavior fits both the BL and RL model will show positive associations with DA measures whereas participants' whose behavior fits BL only or RL only will show negative associations with DA. **Training Experience:** Meetings with sponsors, dissertation committee, and consultants with experience in social decision making (Crockett, Chang, Jenkins) will enrich my understanding of social psychology and game theory. I will regularly meet with co-sponsor Ming Hsu to test and run computational models. I will meet with consultant labs in September and October 2021 to give talks about the study. I will present preliminary results at the Society for Neuroeconomics in October 2021 and submit a publication for peer-review in January 2022.

Aim 3: The Postdoctoral Research Direction (K00 Phase)

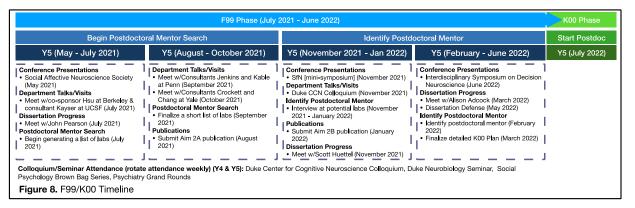
A number of studies indicate that performance in social decision making tasks is disrupted across a range of psychopathologies³, many of which have also been shown to exhibit disruptions in PET-measured DA function (e.g. addiction⁶⁰, schizophrenia⁶¹, ADHD⁶², depression^{63,64}, and anxiety^{65,66}). No research to date has explored whether DA abnormalities in these populations account for observed differences in social decisions. During my K00 phase of the award, I plan to evaluate dopaminergic mechanisms of social decision-making deficits across

a heterogenous sample of individuals with psychopathology using molecular neuroimaging and pharmacology. This approach will identify transdiagonstic neuromodulatory disruptions to social decisions. Consistent with the goals of the RDOC initiative (**Fig. 7**), this research will identify common molecular mechanisms of social decision

making across a spectrum of disorders. Principally, I will use the K00 to train in acquiring ecologically-valid measures of dynamic in-person social interaction and sample social decision-making behavior from participants outside the lab. Importantly, DA is only one of several neuromodulators disrupted in psychopathology. Indeed, glutamate and GABA are also important candidates for the study of molecular mechanisms of social decision making that interact with DA signaling. Therefore, during the K00 phase, I will expand my training and understanding of other neuromodulatory circuits involved in social decisions. If necessary, this could include training in magnetic resonance spectroscopy to measure glutamate and GABA in humans. **Desired Postdoctoral Lab Setting:** I will search for a postdoctoral mentor at an R1-level institution who either directly studies clinical



populations, collaborates with local researchers actively studying psychopathology, or open to my initiation of such collaborations. I will search for a mentor with a record of funding and assisting trainees in acquiring funding. My grantsmanship goals include writing a K99/R00 or K22 diversity transition award with post-doctoral mentors. If funded, this grant would provide additional support for continuity of my research program as I transition to an independent tenure-track faculty position. In addition to this, I will apply for internal institutional seed grants as PI. My desired postdoctoral mentor will help me network with colleagues in clinical neuroscience and social psychology. I hope to network and present research at conferences such as the annual meetings of the Society of Biological Psychiatry, the American College of Neuropsychopharmacology, the Society for Personality and Social Psychology, and the Society of Experimental Social Psychology. The ideal postdoctoral mentor will support me in seeking opportunities to mentor graduate students in the lab and department and opportunities to continue teaching undergraduates in cognitive neuroscience and statistical methods. Most importantly, I will seek a mentor who can provide guidance in transitioning into an independent scientist in a tenure-track faculty position.



Identification of a Postdoctoral Lab: My sponsors and I will generate a list of potential postdoctoral mentors. I will meet with Andrew Kayser at UCSF in October 2021 and continually consult with him to seek advice about advisors who can provide mentorship and research support in studying clinical groups. I will also seek advice from Adrianna Jenkins and Joe Kable at the University of Pennsylvania (September 2021) about identifying an interdisciplinary environment given their affiliation with multiple academic communities (Psychology, Psychiatry, Marketing, and Economics). I will meet with Molly Crockett and Steve Chang at Yale (August 2021) who can provide insight about identifying optimal research training environments to study the neurobiology of human social decisions. In both of these visits, I will give research talks and meet with faculty who may be on my list of potential mentors. At my home institution (Duke), I will seek advice from Makeba Wilbourn, Sarah Gaither, and my dissertation committee members who are seasoned in guiding students into successful postdoctoral and faculty positions. I will meet with visiting speakers at the Center for Cognitive Neuroscience Colloquium, Neurobiology Seminar, Social Psychology Brown Bag, and Psychiatry Grand Round (which I will rotate in attendance weekly). Finally, I will network at conferences including the annual meetings of the Society for Neuroeconomics, the Social Affective Neuroscience Society, and the Society for Neuroscience. I will also meet with graduate students familiar with potential mentors and departments who can speak to a faculty member's mentorship style, interest in collaboration, and commitment to fostering a diverse and inclusive lab.

RESPECTIVE CONTRIBUTIONS

The ideas and general research program have been developed primarily by the applicant. The applicant has been developing this line of research throughout all stages of his career so far from his time as an undergraduate and post-bacc research assistant to his current time as a graduate student. Although much of the proposed work for the F99 phase is applying new analytic techniques to previously collected data, some of these data being used in his current dissertation work were collected by him when he was a post-bacc research assistant before starting graduate school. After starting his PhD, he has taken charge of managing these data sets and leading analyses. He has been a leader on these projects before starting his PhD.

The research proposal was developed through an iterative process between the applicant and the primary sponsor Dr. Gregory Samanez-Larkin in consultation with the co-sponsor Ming Hsu. The applicant developed the initial draft of the proposal and subsequently made revisions according to suggestions from the mentorship team. The training and mentorship plan was developed collaboratively between the applicant and Dr. Samanez-Larkin who is a previous F31, F32, and K99/R00 recipient with experience and knowledge about what it takes to make these career transitional fellowships effective.

Mentorship Team	Role and Objectives
Gregory Samanez-Larkin (Duke University)	Sponsor, will provide mentorship in human neuroimaging methods and statistical analysis, overall project management, access to the research population and data, career advisement, mentorship training, manuscript and grant preparation, and will meet weekly with the applicant.
Ming Hsu (UC Berkeley)	Co-sponsor , will provide mentorship in computational modeling methods and statistical analysis of social decision making task data, manuscript preparation and career advisement, and will meet at least once a month and sometimes weekly with the applicant via phone or videochat.
Andrew Kayser (UC San Francisco Medical School)	Consultant on F99 phase studies of dopamine and social decision making will provide mentorship on designing clinical research studies, managing clinical research data, and pharmacological studies. The applicant will consult with Andy in preparation for identifying a post-doctoral lab to ensure that the training environment is optimal for gaining experience with clinical research.
Steve Chang & Molly Crockett (Yale University), Joseph Kable & Adrianna Jenkins (University of Pennsylvania)	Consultants on F99 phase studies of dopamine and social decision making will provide mentorship on theoretical understanding of social cognition and game theory. The applicant will also seek advice from these consultants in identifying a post-doctoral lab that can provide support in social decision making research.
Makeba Wilbourn & Sarah Gaither (Duke University)	Consultants on F99 phase of professional development including inclusive teaching and mentorship practices. The applicant will meet with these consultants as part of the Duke NSF REU program for underrepresented undergraduate researchers, for which the applicant is a mentor (NSF Award #1950651).
John Pearson, Alison Adcock, & Scott Huettel (Duke University)	The dissertation committee members will offer feedback on study results and manuscript preparation and will meet as needed with the applicant (on average 2-3 times per year, but more frequently during heavy phases of data analysis) and provide career navigation advice (at least once per semester).

SELECTION OF SPONSOR AND INSTITUTION

My interest in decision neuroscience began during my undergraduate years at USC. As a double-major in Neuroscience and Political Science, I became inspired to complete a PhD in a translational neuroscience lab. I am passionate about basic science and also strive to make broad connections to behavior in everyday life and larger scale social issues in all of my research projects. Under the guidance of undergraduate and post-bacc mentors, I built a strong foundation of skills and knowledge in emotion, reward processing, and cognitive and clinical neuroscience. For graduate school, I sought opportunities that would allow me to continue to gain deep expertise in molecular neuroimaging (PET) and computational modeling while also studying behavior in everyday life. Working with Drs. Gregory Samanez-Larkin and Ming Hsu has been an ideal fit, both in terms of the skills I am developing and my longer-term research interests.

Dr. Samanez-Larkin's work on motivation, cognition, and decision making, with extensive background in MR and PET neuroimaging techniques, made him an ideal choice as a pre-doctoral sponsor. In addition to his expertise in neuroimaging, we share interests in revealing the mechanisms of individual differences in motivation and decision making across adulthood. In additional to basic neuroscience research, the lab regularly conducts experience sampling studies and collects a wealth of real-world data (e.g., on self-control, emotional experience, and financial management in everyday life). Samanez-Larkin already has an outstanding track record in decision neuroscience, as validated by his winning an Early Career Award from the Society for Neuroeconomics in 2019. He also has experience with career transitional fellowships having previously been the recipient of a NIH Pathway to Independence Award (K99/R00). He had a highly productive graduate school career with his first first-author paper recognized as one of the National Institute on Aging Top 10 Scientific Advances of 2007 and then going on to publish 7 more papers as a graduate student. He has published research in top-tier journals such as Nature Neuroscience, Neuron, Psychological Science, the Journal of Neuroscience, and Biological Psychiatry as well as an invited review for Nature Reviews Neuroscience. In addition to his publication record, Dr. Samanez-Larkin is a fantastic role model for building an independent career; his impressive grantsmanship and previous success on the job market will be invaluable in guiding me to successfully obtain a top-tier post-doc and eventually an academic faculty position.

In addition to the scientific match, Dr. Samanez-Larkin has been highly committed to and successful mentoring students under-represented in science. Beyond the mentorship opportunities already available within the lab at Duke, Dr. Samanez-Larkin is co-PI on a NSF REU grant which brings under-represented undergraduate students to Duke campus for a summer research program and provides mentoring opportunities for graduate students. I will continue to be a mentor for this program throughout my time at Duke and hope to run my own program like this one day as a faculty member.

Dr. Ming Hsu is an ideal **co-sponsor**. As a decision neuroscientist with a primary faculty appointment in a business school, he has a clear track record of translational neuroscience research. He was a consultant and collaborator on a multi-institutional grant on dopamine and decision making written by Drs. Samanez-Larkin and Zald, so they have a *history of working together successfully despite being at different institutions*. Although Dr. Hsu is in California, we successfully collaborated on my first-author publication in the *Journal of Neuroscience*. We have demonstrated clearly the feasibility of working together across the country by publishing two papers together (Castrellon et al 2019; Seaman et al 2018) with another paper in preparation. Now that all of the data collection is complete for the grant, the three of us are working together closely on the studies proposed for the F99 phase of this award. Dr. Hsu is an expert in computational modeling and neuroimaging of social economic behavior with publications in *Science*, *PNAS*, *Nature Neuroscience*, the *Journal of Neuroscience*, and *Psychological Science*. He was also a Society for Neuroeconomics Early Career Award winner in 2015. In addition to collaborating on dopamine and decision-making projects with our lab, he has several of his own grants related to dopamine and social decision making. He will also provide guidance and advice on the transition to the post-doctoral K00 phase and is a potential post-doctoral mentor.

In addition to the mentorship described above, the intellectual environment and scientific resources available at Duke are unmatched. Various intellectual communities at Duke (e.g., Duke Center for Cognitive Neuroscience (CCN), Duke Center for Interdisciplinary Decision Science), will provide access to cutting edge research and theoretical perspectives. For instance, the Duke CCN hosts a weekly colloquium which I will regularly attend to see visiting speakers from around the world and in which I will give my own talks to the local community. These presentations will broaden my experience with cognitive neuroscience and expand my professional network of colleagues. This network will be invaluable as I move forward in my academic career.

RESPONSIBLE CONDUCT OF RESEARCH

Formal Training

As a graduate student before starting the F99 phase, I have already completed the Collaborative Institutional Training Initiative (CITI) series of courses on Human Research. This CITI online series contained five modules on the following topics: (1) History and Ethics, (2) Regulatory Overview, (3) Risk, Informed Consent, and Privacy and Confidentiality, (4) Vulnerable Subjects, (5) Education, International and Internet Research. These online courses emphasize the importance of ethical conduct by researchers and provided a strong set of guidelines for ensuring the welfare of all participants in our research. In addition, I completed the CITI courses on Biomedical Research with Good Clinical Practice (GCP). This CITI online series contained modules on topics including: (1) New Drug Development, (2) FDA Regulations, (3) Clinical Trials, (4) Detecting, Evaluating, and Reporting Adverse Events, and (5) Audits and Inspections of Clinical Trials.

In addition to these online trainings, I have attended in-person courses to enhance my knowledge of Responsible Conduct of Research (RCR) at Duke University. In August 2017, I attended an all-day (9am to 5pm) RCR workshop that reviewed topics such as: (1) Diversity and Inclusion, (2) Stress in Graduate School, (3) Responsible Digital Research, (4) Ethics, and (5) Case Study Discussions in Psychology & Neuroscience.

I have also continued to attend in-person RCR courses offered at Duke University throughout the year including: (1) a 2-hour course on Deconstructing Digital Scholarship to enhance skills in evaluating digital sources, (2) a 2-hour course on Research Reproducibility to learn foundational strategies to increase reproducibility of my work, and (3) a 2-hour course on Evaluating Publishers to evaluate and analyze publication contracts and predatory journals. I will continue to attend these kinds of in-person workshops throughout my graduate training.

Duke University is committed to the conduct of research and research training activities in a scientifically responsible and ethical manner. Duke University and the sub-communities in which we will conduct the proposed research, including the Department of Psychology & Neuroscience and Brain Imaging Analysis Center, believe that all individual research and research training activities should be conducted in a scientifically responsible and ethical manner. Towards this goal the University has developed principles and practices to ensure the highest possible standards for conducting research. The university offers both web-based and in-person training sessions that I will attend. During each year of training, I will complete the appropriate web courses on responsible conduct of research and be engaged in regular discussion of research ethics while working on projects and in lab meetings (as detailed below and in the Sponsor Information section of the training plan). Formal instruction as well as individual guidance through mentorship is a critical component of this plan. As a postdoctoral fellow during the K00 phase, I will continue training in the responsible conduct of research.

Informal Training

Faculty members and institutional officials not only bear responsibility for their own ethical behavior but they must also set a positive example to their trainees. Toward this end, faculty mentors are responsible for providing individual guidance and education. This will be achieved by establishing meaningful relationships between mentors and mentees, discussing expectations, setting concrete RCR goals, and fostering the development of meaningful professional networks. In addition to the formal online and in-person activities discussed above, under the guidance of Dr. Samanez-Larkin, lab members will meet at least weekly to discuss topics in responsible experimental design, data processing and presentation, recruitment and protection of research subjects, authorship and collaboration, peer review, conflict of interest, and research misconduct. These are regular topics of discussion in our lab meetings and during individual project meetings. For example, I regularly discuss open science methods in my own individual meetings with undergraduate research assistants. I am strongly committed to conducting responsible research and training future generations to do the same.

SPONSOR AND CO-SPONSOR STATEMENTS

A. Research Support Available SPONSOR – Samanez-Larkin

Charles Lafitte Foundation Program in Psych and Neuroscience Research at Duke 9/1/2019–12/31/2020

Using Neuroimaging to Optimize Mobile Interventions Targeting Healthy Brain Aging

Seed grant to examine how human neuroimaging can be used to enhance mobile digital health interventions that target physical activity with the long term goal of improving healthy brain aging.

Role: PI \$50,000

NIA/NIH R01-AG058547 Samanez-Larkin, Cabeza (MPI) 8/15/2018–3/31/2023

Effects of Aging on Episodic Memory-Dependent Decision Making

Research grant to examine how individual differences in episodic memory are related to adult age differences in multi-attribute and future-oriented decision making.

Role: PI \$3,052,360 (\$1,919,269 direct costs, \$1,133,091 indirect costs)

NIA/NIH R24-AG054355 Samanez-Larkin (PI) 9/15/2016–3/31/2021

Scientific Research Network on Decision Neuroscience and Aging

Network grant to support dissemination and training activities related to the emerging multidisciplinary science of decision making and aging.

Role: PI \$1,443,412 (\$861,738 direct costs, \$581,674 indirect costs)

NSF 1950651 Wilbourn (PI) 3/1/2020–2/28/2023

REU: Lifespan Approaches to Diverse Psychological Science

Grant to support annual summer Research Experience for Undergraduates (REU) across three research groups that study children, adults, and aging adults from social, developmental, and cognitive neuroscience perspectives.

Role: Co-PI w/ Sarah Gaither \$430,344 (\$350,331 direct costs, \$78,430 indirect costs)

NIA/NIH R25-AG053213 Samanez-Larkin (PI) 9/15/2016–7/30/2021

Short Courses in Neuroeconomics and Social Neuroscience

Grant to support workshops and an annual summer school in neuroeconomics and social neuroscience.

Role: PI \$650,025 (\$607,801 direct costs, \$42,224 indirect costs)

NIA/NIH <u>R25-AG053252</u> Carstensen, Samanez-Larkin (MPI) 9/15/2016–4/30/2021

Forming Science-Industry Partnerships to Link Everyday Behaviors to Well-Being

Grant to support an workshops that would facilitate collaborations between scientists and the private sector focused on improving financial and physical health and well being.

Role: PI \$646,959 (\$601,880 direct costs, \$45,079 indirect costs)

CO-SPONSOR - Hsu

NIMH/NIH R01-MH112775 Hsu (PI) 1/4/2019 –1/3/2024

Dopaminergic Mechanisms Underlying Human Social Behavior: A Multimodal Approach

Research grant to elucidate the role of dopaminergic circuits in human social behavior using a combination of computational, neuroimaging, and molecular tools.

Role: PI

DRMS/NSF 1851902 Hsu, Jenkins & Camerer (PI) 9/1/2019 – 8/31/2022

Collaborative Research: An Interdisciplinary Approach to Predicting Unequal Treatment

The major goal of this project is to use a combination of computational and neuroimaging methods to model and predict social discrimination and unequal treatment in laboratory and field data.

Role: Co-PI

NIAA/NIH R01-AA026587 Kayser (PI) 1/4/2019 – 1/3/2024

Behavioral and Neural Correlates of Social Function in Alcohol Use Disorders

The major goal of this project is to understand deficits in social decision-making in individuals with alcohol use disorder at behavioral and neural levels.

Role: Co-Investigator

NIMH/NIH R01 MH110477 Carver & Johnson (PI)

6/1/2017 - 5/31/2022

Approach motivation, effortful control, and internalizing and externalizing problems

This proposal seeks to examine two RDoC constructs (effortful control and approach motivation) and their potential interactions, using fMRI, behavioral, and self-report measures.

Role: Co-Investigator

NIA/NIH R01 AG058817 Chiong (PI)

9/1/2018 - 4/30/2023

Decision-making abilities in ADRD: From clinical standards to decision neuroscience

The major goal of this project is to bridge translational gaps between recent cognitive neuroscience on human decision-making and clinical standards used in the assessment of decisional capacity.

Role: Co-Investigator

B. Sponsor's Previous Fellows/Trainees

Dr. Samanez-Larkin has sponsored 6 pre-doctoral (6 current) and 5 post-doctoral (0 current) individuals. Examples:

Candace Brown, Ph.D., Post-Doc 2018–2019. Assistant Professor, University of North Carolina, Charlotte.

Kendra Seaman, Ph.D., Post-Doc 2015–2019. Assistant Professor, University of Texas Dallas.

Marissa Gorlick, Ph.D., Post-Doc 2014–2015. Senior Data Scientist, Mozilla.

Christopher T Smith, Ph.D. (co-mentor), Post-Doc 2016–2018. Postdoctoral Program Manager, NCSU.

Linh Dang, Ph.D. (co-mentor), Post-Doc 2013–2017. Quantitative UX Researcher, Google.

Dr. Ming Hsu has sponsored 6 pre-doctoral (2 current) and 6 post-doctoral (3 current) individuals.

Examples:

Kenji Kobayashi, Ph.D., Pre-Doc 2012–2017. Post-doctoral Scholar, University of Pennsylvania.

Yu-Ping Chen, Ph.D., Pre-Doc 2010–2015. Assistant Professor, National Taiwan University.

Eric Set, Ph.D., Pre-Doc 2012–2017. Lecturer in economics at NYU Shanghai.

Lusha Zhu, Ph.D., Pre-Doc 2009-2012. Assistant Professor, Peking University.

Anne Berry, Ph.D., Postdoc. Assistant Professor, Brandeis.

Adrianna Jenkins, Ph.D., Post-Doc. Assistant Professor, University of Pennsylvania.

Ignacio Saez, Ph.D., Post-Doc. Assistant Professor, University of California, Davis.

C. Training Plan, Environment, Research Facilities

Training will focus on learning new research methods, broadening the base of knowledge, honing teaching and mentoring skills, building project management skills, networking to further establish reputation in the field, and preparing for the job market. The overarching goal of the training plan is to ensure that the applicant is extremely competitive when entering the post-doctoral job market and eventually faculty job market and fully equipped with the necessary tools to independently direct a unique and comprehensive research program.

Expanding Research Toolbox

The proposed studies will build on the applicant's existing skills and knowledge related to functional neuroimaging and reward processing to expand into the study of social decision making. The applicant will gain new expertise in integrating multimodal neuroimaging data with computational models in a new content area. This training will occur through hands-on experience while completing the proposed studies. All research activities from data processing and analysis to manuscript preparation will be carried out with the advice and counsel of the **sponsor**, **Dr. Samanez-Larkin**, and **co-sponsor**, **Dr. Hsu**. The research conducted in the Motivated Cognition and Aging Brain Laboratory at Duke is highly integrative and thus there will be many collaborative training opportunities. Dr. Samanez-Larkin will contribute to all aspects of the applicant's training. The applicant will have individual weekly hour-long meetings with Dr. Samanez-Larkin to discuss progress. The applicant will have individual hour-long remote meetings via Zoom with Dr. Hsu as needed but at least once per month (more frequently, likely weekly, during times of manuscript writing or application of new analytic techniques). Additionally, the applicant will regularly attend the bi-weekly hour-long Samanez-Larkin

lab meetings where labmates provide updates and discuss research in progress, manuscripts in progress, funding opportunities and grantsmanship, ethical conduct of research, scheduling and human subjects issues, and general lab business. Dr. Hsu will provide additional education in the use of Bayesian statistics, computational modeling, theories of neuromodulation of motivation, and theories of social decision making. The applicant will have, at minimum, one meeting per semester with at least one of the dissertation committee members (Pearson, Adcock, Huettel) and will meet with the whole committee for milestone meetings once per year (i.e., dissertation proposal meeting, dissertation defense). The meetings with Duke faculty will be used to discuss progress, data analyses, and manuscript preparation. The meetings with remote co-sponsor Dr. Hsu will primarily occur via Zoom, although the applicant will visit Northern California (if travel is permitted) to work directly with Dr. Hsu on manuscript preparation and the post-doc search. In general, the sponsor and co-sponsor will continually provide feedback and guidance to the trainee throughout the pre-doctoral fellowship. The sponsor and co-sponsor will remain as advisors throughout the K00 period as needed. The K00 mentors (TBD) will also introduce the applicant to new research methods and research areas to even more significantly expand his expertise in the transition to independence.

Increasing Knowledge Base

A key training activity will focus on increasing the applicant's knowledge base of social reward, social cognition, and social decision making and the detailed neurocircuitry and function of the dopamine system and related neuromodulatory motivational circuits. The applicant already has a well-developed expertise on the neuroscience of decision-making, so specialized readings will be aimed at broadening this knowledge base to understand social processes and the neural circuitry of social decision making. Although Dr. Samanez-Larkin has expertise in the neuroscience of motivation and decision making, he is not an expert in social decision making. The collaboration of Dr. Hsu is critical. Dr. Hsu will create a reading list for the applicant to get to know the core relevant literature during the first semester of the F99 award period. This reading list will be turned into a syllabus for a Special Reading course (PSY 990) in which the applicant will enroll. This course is available to all graduate students who seek specialized knowledge in specific content areas. Dr. Samanez-Larkin will be listed as the faculty instructor for this individualized reading course but Dr. Hsu will curate the reading list and have at least monthly discussions of the readings with the applicant. At the end of each semester the applicant will submit a written document in the form of a literature review of these readings. This review will ideally be used for manuscripts in preparation and the applicant's dissertation. As a more general means of increasing the base of scientific knowledge, the applicant will attend the weekly Center for Cognitive Neuroscience colloquium which features speakers from all over the world who conduct research on a broad range of topics. During the F99 period, the applicant will additionally attend one weekly talk in a new series such as the Neurobiology Seminar, Social Psychology Brown Bag, or Psychiatry Grand Rounds. The applicant will attend on average two 1-hour talks per week. The applicant has similar plans for the K00 phase to request reading lists of core literature to discuss with K00 mentors (TBD).

Honing Teaching and Mentoring Skills

The applicant completed his final teaching assistantship for a total of four semesters of undergraduate teaching during his time as a PhD student. He has received outstanding teaching evaluations in challenging courses including Statistics, Cognitive Neuroscience, Contemporary Neuroscience Methods. The applicant is receiving initial training in inclusive teaching through his TAship with Dr. Makeba Wilbourn (see letter of support). In order to further his lecturing and presentation skills, the applicant will present at research forums once a semester. Potential forums include: the Social Psychology Brown Bag in the Department of Psychology and Neuroscience, the Center for Cognitive Neuroscience Colloquium, or the Fugua Behavioral Lab in the business school at Duke. The applicant will also continue to be a primary mentor and co-mentor to undergraduate and full-time research assistants and undergraduate distinction students with Dr. Samanez-Larkin. The applicant will be primarily responsible for supervising one to two undergraduate honors students during each grant period academic year and will mentor an additional student from outside Duke in the Duke Psychology and Neuroscience summer REU which recruits URM students from outside of Duke (prioritizing applicants from HBCUs, HSIs, Native and Tribal Colleges, and smaller schools) to campus for 10 weeks. The applicant is committed to providing mentored junior URM researchers with valuable experience that will adequately prepare them for graduate studies. In addition to providing junior researchers with hands-on training, the applicant will meet with at least one junior researcher at least once each week for an hour to discuss progress during the academic year and summer. The applicant will have monthly meetings with Dr. Samanez-Larkin to

discuss issues related to mentoring, such as supporting progress/productivity, building analytic thinking skills, and strengthening scientific writing skills.

Building Grant Writing and Management Skills

The applicant has written small internal grants at Duke and been awarded an NSF GRF so has some smaller-scale grant application experience (in addition to recent work on this somewhat larger F99/K00 application). During the K00 phase of training, the applicant will prepare a career award grant application (K22 or K99/R00) with his post-doc mentors and Dr. Samanez-Larkin will provide informal feedback as an external reviewer before submission. The applicant will continue to assist with grant management for pilot grants he wrote during the remainder of his PhD. The applicant and sponsor will meet monthly to discuss time and budget management and research progress. This will continue during the post-doc K00 phase with his post-doc mentors. He hopes to have the opportunity to learn about more active research grant management during the K00 phase including preparation of progress reports, expense tracking and planning, and personnel management. The latter skills are rarely taught but essential for survival in an independent career.

Networking / Establishing Scientific Reputation

The applicant will attend and present at 2-3 scientific meetings per year and any highly relevant smaller conferences that occur during the training period. He has some initial visibility from receiving poster awards from the Society for Neuroeconomics. A focus of the F99 and K00 phase will be to give talks at conferences. He also plans to organize a symposium proposal which will provide him with additional visibility and allow him to connect with other relevant senior faculty in his field. His F99 and K00 mentors will facilitate networking at conferences by introducing him to relevant scientists in the field.

Preparing for the Job Market

During the final year of pre-doctoral training in the F99 phase the applicant will apply for post-doc positions. The training supported by this fellowship will make the applicant a strong candidate and will ensure his success in this next phase. The sponsor, Dr. Samanez-Larkin, and co-sponsor, Dr. Hsu, will assist the trainee with the application process. The applicant will meet with Samanez-Larkin and Hsu at least 6 months before applying for post-docs to begin preparing materials and identify candidate positions (however, it should be noted that he already has a great list of options). During this time, the applicant will have at least bi-weekly meetings with Samanez-Larkin and Hsu and consultants Drs. Kayser, Wilbourn, and Gaither to discuss strategies for interviewing and choosing an optimal site. Dr. Kayser will help the applicant ensure that he identifies a training site that will provide optimal training in clinical research and Drs. Wilbourn and Gaither will help ensure the applicant identifies a training site that has demonstrated commitment to training URMs in science. The applicant will also present initial drafts of a post-doc job talk in the Samanez-Larkin lab meeting. There additionally will be routine opportunities for the applicant to attend job talks and practice job talks in the department and CCN. During the final year of the K00 post-doctoral training phase, the applicant will apply for a junior faculty position. The training supported by this fellowship will make the applicant a strong candidate for a faculty position and will ensure his success after securing a job offer. For example, through mentoring and grant management as a post-doc, the applicant will gain necessary laboratory management experience. The pre-doc F99 and post-doc K00 sponsors will assist the applicant with the preparation of application materials (e.g., research and teaching statements). The F99 sponsors (and likely K00 sponsors) have served on several search committees for junior faculty and have had great success on the job market themselves. The applicant will meet with sponsors and co-sponsors 6 months before applying for jobs to begin preparing materials and identify candidate positions. During this time, the applicant will have at least bi-weekly meetings with the F99 and K00 sponsors to discuss strategies for interviewing and negotiating offers. The applicant will also present initial drafts of a job talk in his post-doc lab's regular meeting and will later practice a final version in a relevant area seminar (e.g., Cognitive Neuroscience Area Seminar). Ideally, there also will be routine opportunities for the applicant to attend job talks and practice job talks in his eventual post-doc department.

The training plan described above will assist the trainee in successfully completing the proposed research projects as well as further developing a strong base of training to achieve his career goals. This combination of training experiences is ideally suited for the applicant. The primary goal of the fellowship is to broaden the research and lab management skill set and knowledge base of the applicant. Castrellon is developing an independent line of research on neuromodulation of social decision making. There are very few (maybe a handful?) of researchers in the field who are able to successfully combine all of the methods that he will be

able to combine after emerging from training (computational modeling, behavioral pharmacology, PET, fMRI, experience sampling). After completion of the pre- and post-doctoral fellowships, the applicant will enter the job market with a highly unique combination of skills. Thus, the training plan holds tremendous potential for impact throughout the applicant's career. Combining skills and experiences gained through collaboration with other faculty within and outside of the department, mentoring, and grant writing will set the foundation for a productive and successful career in academic research.

Contingency plan / modifications related to COVID-19: Should social distancing be required during the training period, all (individual, committee, and degree milestone) meetings listed as in-person will be virtual via Zoom. All essential data are collected already for the proposed F99 studies so current and any additional social distancing will have no major impact on progress. Mentorship of undergraduate students will continue remotely. The applicant will speak at and attend virtual conferences when available. Proposed visits to collaborators and potential post-doc labs will become virtual Zoom visits.

d. Number of Fellows/Trainees to be Supervised During the Fellowship

Dr. Samanez-Larkin will supervise no more than 5 other pre-doctoral fellows (3 co-mentored with other faculty) at a time during the span of this grant, and it is expected that there will be at most one post-doctoral fellow during the applicant's fellowship. Dr. Samanez-Larkin will not admit graduate students until 2022. **Dr. Hsu** will supervise no more than 3 other pre-doctoral fellows (currently 2) at a time during the span of this grant, and it is expected that there will be around 3 post-doctoral fellows during the applicant's fellowship.

e. Applicant's Qualifications and Potential for a Research Career

We express our highest possible support for Jaime Castrellon for a D-SPAN F99/K00 fellowship. He is on a trajectory to become a quickly rising star. I (Greg S-L) first met Jaime several years ago when David Zald and I jointly hired him as a post-bacc project coordinator to collect data for an aging study of dopamine and decision making collected at Vanderbilt. I was delighted when he expressed interest in pursuing a PhD in my lab at Duke. In comparison to other students in a related field who have had approximately the same amount of experience and training, Jaime is likely among the top 1%. I am confident that he will be one of the most successful students in our program, even relative to his high achieving peers.

Jaime joined the PhD program in Psychology and Neuroscience in the fall of 2017 to work primarily in our lab, which focuses on motivation and decision making in the Center for Cognitive Neuroscience. I reviewed Jaime's graduate application before I arrived at Duke. I was moving my lab from Yale at the time and was hesitant to accept new graduate students right away. However, I already worked well with Jaime and had first-hand experience with his motivation and work ethic. He had the ideal combination of training for work in our lab. He was an undergraduate student at USC working in Mara Mather's lab and completed two post-bacc research assistantships, one at Vanderbilt studying dopamine and decision making and one at UCLA studying clinical neuroscience of schizophrenia where he was lab manager of a new lab. During the interview process, Jaime won a US National Science Foundation Graduate Research Fellowship. He was the only incoming student in the Department of Psychology and Neuroscience that year to come in with this award.

As expected, Jaime hit the ground running when he started graduate school. He has been working mostly with previously collected data — most of which he himself collected through the joint projects with the Zald lab at Vanderbilt. By his second year, he was leading multiple projects in the lab. Normally there would be concerns about burnout or lack of completion of any one project, but Jaime thrives when juggling. Six months into graduate school he had a rough draft of a research paper that included PET data from three studies. The paper, his first first-author paper, was published in 2019 in the *Journal of Neuroscience* and featured on the cover. He currently has a second first-author paper published which included making public the first ever open fMRI and dopamine PET data set. He has another first-author meta-analysis in review and two other nearly completed drafts that will soon be ready for submission in addition to several co-authored papers.

Jaime's research projects might seem quite diverse, but all of his projects are truly complementary. There is an impressive variety of data types from behavior to fMRI and PET to a meta-analysis of dopamine drugs effects on impulsive choice (which includes an extensive review of rodent and other non-human animal literature). We are very much looking forward to supporting him in completing the proposed studies and writing all of this up. It would not be unreasonable for him to finish graduate school with a dozen high-quality papers. Certainly, quantity is never preferred over quality. However, we are confident that Jaime's work will land in top journals and be highly cited. He is an excellent data analyst and is quickly developing impressive scientific writing skills. He seems to enjoy the writing and revision process, which is a promising indicator that he may

remain in science and run his own lab doing high quality research. Jaime has also assisted with several mentored manuscript reviews, obtained small grants, and mentored several students. He is quickly developing all of the skills to become an independent scientist.

Jaime has embraced open science. He is publicly sharing behavioral and brain imaging data and has registered multiple pre-registrations for both data analysis projects and a meta-analysis. He was the first in the Samanez-Larkin lab to publicly preprocess fMRI data on <u>openneuro.org</u> for full transparency, and will make all the full data sets publicly available when we finish analyses. Everyone else in the Samanez-Larkin lab who is analyzing imaging data is now also using these tools. Jaime has helped others get started. He is generous with his time and mentorship of students and peers in the lab.

Jaime goes above and beyond in his mentoring. He is a research superstar who is quite self-sufficient. He is incredibly productive and could generate many papers almost single-handedly without ever engaging an undergraduate student. However, Jaime is incredibly passionate about teaching and mentoring. He is deeply invested in mentoring students from backgrounds under-represented in science. Many of Jaime's mentees have been Latinx or Black, first-generation college students, and/or LGBTQ+. In addition to the research mentoring Jaime does in the lab, in his free time he is a mentor for Duke's F1rst program where he provides academic and career support for undergraduate students from similar backgrounds. Undergraduate students who have worked directly with Jaime in the lab have received excellent training. Jaime spends significant time meeting with students one-on-one to go over the basics of experimental design and data analysis. He is committed to making sure that everyone he mentors develops confidence as a researcher and doesn't just feel like a good helper. He seriously engages every student in data analysis and pushes them to read the literature and creatively make sense of results. In his three years at Duke, Jaime already has mentored 10 undergrads. 7 out of 10 of those students have presented research they conducted in the lab at national or international conferences. Many of them will become co-authors on his papers; two already have. This past year Jaime was recognized with a Duke-wide Bass Connections Award for Outstanding Mentorship.

Jaime is taking on a lot as a student and he is thriving. He is clearly motivated and committed to the work. The more he learns, the more excited he gets about his studies. His ability to juggle multiple projects at various stages with the long-term goals of each always clearly in mind will serve him well long term as a scientist. He is well suited for a career in science. His plan is ambitious but feasible. If he doesn't get the proposed papers published as planned during the F99 phase, we both commit to working with him on these papers during K00.

We successfully co-mentor Jaime even though one of us (Hsu) is at a different institution. The distance has not yet imposed any barriers. Jaime was previously critiqued for having a remote mentor in his initial application, so we would like to reconfirm that this collaboration has been highly successful already resulting in multiple co-authored papers led by Jaime. We are both highly committed to making this work and Jaime has been expert at taking advantage of both of our expertise. This will continue throughout the F99/K00 phases.

Jaime is done with his teaching at Duke. He was a TA for undergraduate statistics, two neuroscience courses and developmental psychology. He has received some of the highest teaching evaluations in the department for the past several years. It won't be surprising if he wins a university teaching award. Jaime is also an excellent speaker in lab meetings and with larger audiences. We have seen him give conference talks and many faculty have commented on his impressive presentation skills. He presents as clearly knowledgeable and confident yet has an approachable and open speaking style. Not only does he communicate his work well, he is also open and gracious about critical feedback. As validation of his excellent presentation skills, Jaime has received the Best Poster Award at the Society for Neuroeconomics meeting for the past two years in a row. Jaime has the potential to be an excellent independent scientist. The field will be lucky to have him and we are grateful for the opportunity to support him on this journey.

Jaime has a strong foundation and truly impressive potential for a productive independent future research program. His research program has great potential and direct implications for public health and well-being. He is an ideal candidate for an F99/K00. At this early career stage, he has demonstrated a strong commitment to basic research and a deep commitment to supporting fellow under-represented students. His strong foundation combined with the set of research and teaching skills he is developing as a graduate student will set him on the path to great long-term success as a professor and scientist. He is a quickly-rising star that deserves all of the support we can give him. The expertise available in our labs and affiliated centers will provide Jaime with invaluable opportunities to take his career to the next level. There are few sites in the world where he could acquire this combination of research skills. When combined with the impressive skills that he has already acquired, he will emerge from this fellowship with prepared for a truly outstanding and unique research career.

Gregory Samanez-Larkin (SPONSOR) and Ming Hsu (CO-SPONSOR)

Yale University

Steve W. C. Chang, Ph.D.
Associate Professor of Psychology & Neuroscience
Department of Psychology
Department of Neuroscience
Kavli Institute for Neuroscience
Cognitive Science, Child Study Center
Yale University

Campus Address: 2 Hillhouse Avenue New Haven, CT 06511





Nov 12th, 2020

Dear F99/K00 application review committee,

I am writing in enthusiastic support of Mr. Jaime Castrellon's application for an F99/K00 to study neuromodulation of social decision making. My laboratory at Yale University is focused on investigating neural mechanisms underlying social decision-making in both nonhuman primates (electrophysiological studies in rhesus macaques and marmosets) and humans (functional neuroimaging investigations). Jaime's interests are well-aligned with the research goals of our lab and several other labs here at Yale with overlapping research interests, such as the laboratory of Dr. Molly Crockett. There is also a growing neuroscience initiative at Yale which would provide Jaime with extraordinary opportunities to network with many leaders in the field through seminars and workgroup meetings. I would look forward to hosting Jaime for a visit to learn more about his current and future research direction and career goals as well as providing advice about his post-doc search so that he can successfully transition from the F99 to K00 phase.

All the best,

Steve W. C. Chang, Ph.D.

Yale University

Molly J. Crockett, Ph.D. Assistant Professor of Psychology 2 Hillhouse Avenue New Haven, CT 06511 mj..crockett@yale.edu

11/12/20

Dear review committee,

I am writing in support of Jaime Castrellon's application for an F99/K00 to study neuromodulation of social decision making. I have followed Jaime's work for several years and have found his trajectory to be extremely impressive. My lab at Yale University is focused on the cognitive and neural mechanisms of social cognition and decision-making. Jaime's interests are well-aligned with the research goals of our lab. There is also a growing neuroscience initiative at Yale which would provide Jaime with opportunities to network with many leaders in the field. We would be delighted to host Jaime for a research visit to learn more about his research and career goals as well as providing advice about his very promising career.

Sincerely,

Molly Crockett, Ph.D.

Molly of Crockett



Solomon Labs 3720 Walnut Street Philadephia, PA 19104-6241

Dec 2, 2020

Dear Colleagues,

I am very happy to offer my support to Jaime Castrellon in his pursuit of a F99/K00 award. His proposed research and training will equip him with a strong foundation on which to pursue an independent program of research in social decision-making.

My specific role in Jaime's proposal lies in the transition from the predoctoral to the postdoctoral phase. During the F99 portion, Jaime proposes to visit several potential postdoctoral labs, and I am very enthusiastic about the possibility of his visiting my lab at the University of Pennsylvania. Jaime's proposed research and training goals are highly compatible with my lab's ongoing research on social cognition and decision-making. I would happily work with Jaime and with other potential collaborators here at Penn to facilitate a visit in which Jaime gives talks in our labs, meets our lab members, and learns more about our ongoing programs of research. Additionally, Jaime would have the opportunity to learn about the broader research community and resources at Penn, which would be highly conducive to his proposed training given its synergistic relationships between neuroscience, psychology, and the business school (Wharton), along with relevant interdisciplinary initiatives like MindCORE (Penn's integrative hub for the study of the mind).

As a graduate student, Jaime is already a promising scientist, and he has put together a proposal for further training that will build upon his existing strengths and expand his expertise into relevant new areas – areas that are directly relevant to ongoing work in my lab. I would look forward to welcoming Jaime for a visit to Penn and discussing his possible postdoctoral research plans.

Sincerely,

Adrianna (Anna) Jenkins, Ph.D.

Assistant Professor

Department of Psychology

University of Pennsylvania



Department of Psychology Stephen A. Levin Building 425 S. University Avenue Philadelphia PA, 19104-6018

December 3, 2020

Dear reviewers.

Thank you for your consideration of Jaime Castrellon's application for an F99/K00 award to create a foundation for research on social decision making. As you will read in his application, he plans to visit a few potential post-doc labs during the F99 phase. I would be very enthusiastic about his visiting Penn as part of this process. Jaime's emerging research program is highly compatible with the current and planned research in our lab. I have also been very impressed with the research he has completed so far – for example, Jaime has won the best poster award at the Society for Neuroeconomics for two years running (!). Beyond my lab, Penn is a growing hub for interdisciplinary neuroscience research, especially in the domain of decision making, including a new center for the integrative study of the mind, mindCORE. On a visit to campus, Jaime would have the opportunity to meet with members of my lab group and related labs in the Department of Psychology, as well as to connect with faculty in Wharton Marketing and the Annenberg School for Communications and Journalism. I look forward to having the opportunity to connect with Jaime and discuss his plans for a post-doc and independent research career.

Sincerely,

Joseph W. Kable

Baird Term Professor of Psychology & Marketing

Director, mindCOPE (Pann's hub for the integrative study of

Director, mindCORE (Penn's hub for the integrative study of the mind)

University of Pennsylvania

Joseph W. Kable

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

BERKELEY • DAVIS • IRVINE • LOSANGELES • RIVERSIDE • SANDIEGO • SANFRANCISCO

SANTABARBARA • SA

SANTACRUZ

ALCOHOL AND ADDICTION RESEARCH GROUP DEPARTMENT OF NEUROLOGY UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

PHONE: (415) 502-7333 FAX: (415) 502-7332

EMAIL: And rew. Kayser@ucsf.edu

November 16, 2020

Andrew Kayser, M.D., Ph.D. Associate Professor Department of Neurology U.C. San Francisco 675 Nelson Rising Lane San Francisco, CA 94143

Dear colleagues,

It is my pleasure to serve as a consultant in support of Jaime Castrellon's F99/K00 application. Jaime is an exceptionally strong cognitive neuroscientist in training whose work addresses the complex interactions between dopamine measures and valuation processes. He now aspires to extend his graduate work through a post-doctoral fellowship that will not only provide him with new analytic tools, but will also explore the clinically relevant applications of his work. I am looking forward to discussing strategies for testing clinical populations, and for identifying optimal training environments for his post-doctoral fellowship. I plan to meet with him by phone or videocall to assist him in these efforts. In addition, I look forward to consulting with him during the K00 phase as he begins to identify institutions at which to continue his independent research program as a new faculty member. With his track record to date and the research team he has assembled in support of this proposal, I am confident that he will be successful in both completing the experiments proposed here and transitioning into a productive post-doctoral fellowship.

Sincerely,

Andrew Kayser, M.D., Ph.D.



Dear review committee,

We are writing to commit to continuing our mentorship of Jaime Castrellon on issues related to navigating an academic career as a an under-represented minority (URM) in science and related to mentoring URMs. The three of us are co-directors of a National Science Foundation funded summer Research Experience for Undergraduates (REU) in the Duke Department of Psychology and Neuroscience: Lifespan Approaches to Diverse Psychological Science (Award#: 1950651). Through this program we bring URM students from outside Duke to join our labs at Duke for the summer. The primary focus of the program is to provide transformational research experiences (full-time engagement in a project for several months) while also providing critical training in the vast hidden curriculum of navigating a scientific career. The programming is focused on preparing undergrads for grad school, but there are critical mentoring opportunities for grad students.

Each undergraduate in the program has a post-bacc or PhD student mentor. The mentors and mentees meet weekly one-on-one outside of our weekly seminars and regular programming. Jaime was one of the PhD student mentors this past summer and will continue to be a mentor in the program throughout this time at Duke. In the program, we aim for approximate identity matching between mentors and mentees. This past summer Jaime mentored a first-generation college student Latinx woman – whose family ended up being from the same part of Mexico as Jaime's father (we didn't know this before the program started!). Jaime and Rebeca have continued working together on their project after the program ended and she regularly seeks his advice about her senior project back at ASU and navigating the post-bacc job search. This program allows unique mentoring opportunities that complement the mentoring Jaime does during the academic year in his own lab at Duke.

The program has provided critical opportunities for Jaime to benefit from mentoring by Professors Wilbourn and Gaither. Outside of the core scientific mentoring Jaime has been getting from his dissertation committee, he is picking up valuable academic navigation skills. Participation in the program led to Jaime serving as a teaching assistant for Professor Wilbourn's Developmental Psychology course. This course provided Jaime with an example of how to infuse issues of diversity, equity, and inclusion into classroom teaching for even the most foundational introductory coursework. Jaime has described this teaching assistantship as "inspirational" and has said it has "changed the way he thinks about teaching in general" and how he "plans to teach neuroscience courses in the future". Jaime also received a grant this year with Dr. Gaither for a research project on diversity among psychology and neuroscience faculty. Jaime will continue to build these relationships throughout the proposed F99 period of this grant, which will position him well for his own career navigation and mentoring of junior URMs in the K00 phase. We look forward to continuing to mentor Jaime and support him in whatever way we can throughout his career.

Sincerely,

Makeba Wilbourn, Ph.D.

Associate Professor of the Practice

makeba.wilbourn@duke.edu

Sarah Gaither, Ph.D.

Assistant Professor

sarah.gaither@duke.edu

Gregory R. Samanez-Larkin, Ph.D.

Jack H Neely Associate Professor

g.samanezlarkin@duke.edu



November 20, 2020

Members of the F99/K00 scientific review group,

The following Description of Institutional Environment and Commitment to Training is jointly approved by the chair of Jaime Castrellon's PhD granting department, Dr. Scott Huettel, and the Director of the center in which Jaime's research is conducted, Dr. Alison Adcock. Duke University will serve as the sponsoring institution for the F99 phase of this award. Duke is a world-renowned research university with world-class experts in all the fields relevant to this award including cognitive neuroscience, decision neuroscience, and health and well-being. With its many research institutes and centers, Duke is an ideal training environment for this proposal.

Duke has world-class facilities for conducting the research proposed in this award. The Brain Imaging and Analysis Center (BIAC) is a highly active neuroimaging facility continually developing new methodological techniques. As a member of the Samanez-Larkin lab within the Center for Cognitive Neuroscience, the candidate will have full access to all of the BIAC equipment and resources for structural and functional neuroimaging. In addition to the neuroimaging resources, BIAC also houses extensive computing facilities to support data analysis. All data in the Samanez-Larkin lab are being processed using the BIAC High-Performance Computing (HPC) cluster.

The Duke Center for Cognitive Neuroscience (CCN) is a leading center for interdisciplinary research and training. The 22 core faculty have primary appointments in 9 different departments (Psychology and Neuroscience, Psychiatry, Neurology, Neurobiology, Statistical Science, Biostatistics, Biomedical Engineering, Evolutionary Anthropology, Philosophy). The center offers the ideal training environment for interdisciplinary brain research. Past graduate and post-doctoral trainees of the center have had a long history of great career success, routinely going on to excellent positions running their own cognitive neuroscience research groups or centers. The center hosts a weekly colloquium of visiting speakers, which the applicant will regularly attend. These talks will broaden the applicant's understanding of cutting-edge cognitive neuroscience research and expand his professional network through interactions with visiting faculty during student lunches. Between the Department of Psychology and Neuroscience (the candidate's PhD granting department) and the Center for Cognitive Neuroscience, there are many regular seminars, workshops, and talk series available to the candidate.

The candidate has assembled a complementary team of mentors from within Duke and outside of the university. The local primary advisor is Dr. Gregory Samanez-Larkin and the co-mentor is Dr. Ming Hsu at the University of California Berkeley. Samanez-Larkin and Hsu have been collaborating on studies of dopamine and decision making in humans since the first grant they wrote together 8 years ago. Both advisors are recent Early Career Award recipients from the Society for Neuroeconomics who have strong track records of obtaining independent research grants from the NIH and high scientific productivity. The candidate is currently working with both advisors on new studies of social decision making detailed in this application. The candidate also has a broader local team of advisors on his dissertation committee that includes John Pearson and ourselves (Alison Adcock and Scott Huettel). John Pearson is a rising expert in computational neuroscience with research spanning from single cell measurement of brain function in non-human animals to the neural systems supporting legal decision making. Alison Adcock is the current Director of the CCN, Associate Director of the Duke Institute for Brain Sciences, and a leading expert on motivation and memory in the healthy and disordered brain. Scott Huettel is current Chair of the Department of Psychology and Neuroscience and a leading expert in the fields of cognitive neuroscience and decision neuroscience, publishing one of the first textbooks on fMRI and serving as

past president of the Society for Neuroeconomics. The candidate will have the opportunity to continue building relationships with his committee members through the dissertation process where he will present his work and seek our advice as needed on data analysis, manuscript preparation, and general career development. The skills and expertise that the candidate will obtain through working with these experts will contribute greatly to his future work, allowing him to apply computational modeling and neuroimaging to the study of self-control and social decision making. This network of advisors will provide the ideal mentorship team to support the candidate in his transition to a post-doctoral fellowship and eventual faculty position throughout the F99 and K00 award periods.

We are highly committed to Jaime's training. One indication of our ongoing commitment is the fact that Jaime is already well integrated into the Department and CCN communities as a current predoctoral trainee. He has given public talks in the CCN colloquium series and at our annual retreat and has been regularly featured in Departmental news for awards received in the past three years. As an excellent public speaker with a strong commitment to open science, we recently asked him to moderate a campus-wide discussion of research ethics and open science. As he transitions to the mentored phase of the F99 Award, we can guarantee that Jaime's time will be protected so that he can focus on the proposed research and the training components outlined in his proposal. Jaime has already completed all 4 out of 4 required teaching assistantships. Our commitment to his training is not dependent on the funding of this award. In fact, Jaime has previously funded himself through an NSF GRF. We are committed to doing everything we can to support his training.

In summary, beyond the commitment of traditional resources (i.e., computing, office space, research assistants, research funding) and mentorship within the Samanez-Larkin lab, the candidate will have ample opportunity for career development within the institutional environment at Duke and beyond from his assembled team of advisors. The Department of Psychology and Neuroscience and CCN are both highly committed to the development of the candidate as a productive, independent investigator. The training and mentorship that this award will provide will allow him to take full advantage of the available resources and achieve great success in his own independent career.

Sincerely,

Scott Huettel, Ph.D.

Chair, Department of Psychology and Neuroscience

Duke University

scott.huettel@duke.edu

(919) 668-5286

R. Alison Adcock, M.D., Ph.D.

RAlin Adrock

Director, Center for Cognitive Neuroscience

Duke University

alison.adcock@duke.edu

(919) 681-7486

PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001

Expiration Date: 02/28/2023

П	lse o	f I	Human	S	pecimens	and/or	Data
•	3C U	"	Iuliaii	•	Decilion	allu/Ol	Data

Does any of the proposed research in the application involve human specimens and/or data *

Provide an explanation for any use of human specimens and/or data not considered to be human subjects research.

Are Human Subjects Involved

Is the Project Exempt from Federal regulations?

Exemption Number

Other Requested Information

• Yes	O No				
11.1_ProtHuma	anSubjectsRev_	notHS.pc	df		
• Yes	O No				
• Yes	O No				
$\Box 1 \Box 2$	□3 🖬4	□ 5	□ 6	□ 7	_ 8

EXPLANATION OF ANY HUMAN SPECIMENS/DATA THAT IS NOT HUMAN SUBJECTS RESEARCH

All human subjects data are already collected for the F99 phase. No new data collection is proposed during the F99 phase.

Justification for Exemption

This Human Subjects Research falls under <u>Exemption 4</u>. This study involves secondary data analysis of anonymized behavioral and neuroimaging data that were previously collected as part of 3 completed studies. One of the three neuroimaging datasets is already publicly available

(https://openneuro.org/datasets/ds002041) and the other two are being prepared for public release. None of the data analyzed contains identifiers linked to the subjects. No contact will be made with participants whose data will be analyzed. The data is already stored "on the shelf" on a secure server at the research site where secondary data analysis will be conducted.

Explanation Page 64

Human Subject Studies

Study#	Study Title	Clinical Trial?
1	Dopaminergic neuromodulation of social decision making	No

Section 1 - Basic Information (Study 1)

OMB Number: 0925-0001 Expiration Date: 02/28/2023

1.1. Study Title *

Dopaminergic neuromodulation of social decision making

1.2. Is this study exempt from Federal Regulations *	• Y	'es	O N	10				
1.3. Exemption Number	□ 1	□ 2	□ 3	4	□ 5	□ 6	□ 7	□ 8
1.4. Clinical Trial Questionnaire *								
1.4.a. Does the study involve human participants	?			•	Yes		O No	
1.4.b. Are the participants prospectively assigned	d to an inte	rvention?		0	Yes		No	
1.4.c. Is the study designed to evaluate the effect participants?	t of the inte	ervention	on the	0	Yes		• No	
1.4.d. Is the effect that will be evaluated a health-	related bid	omedical o	or	0	Yes		No	

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 1)

- 2.1. Conditions or Focus of Study
- 2.2. Eligibility Criteria
- 2.3. Age Limits Min Age: Max Age:
- 2.3.a. Inclusion of Individuals Across the Lifespan
- 2.4. Inclusion of Women and Minorities
- 2.5. Recruitment and Retention Plan
- 2.6. Recruitment Status
- 2.7. Study Timeline
- 2.8. Enrollment of First Participant

2.9. Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location			
The study does not have any IERs					

Section 3 - Protection and Monitoring Plans (Study 1)

3.1. Protection of Human Subjects	11.2	!_ProtHu	ıma	nSubjects	Rev	/.pdf
3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?	О,	Yes	0	No	•	N/A
If yes, describe the single IRB plan						
3.3. Data and Safety Monitoring Plan						
3.4. Will a Data and Safety Monitoring Board be appointed for this study?	о,	Yes	•	No		
3.5. Overall structure of the study team						

PROTECTION OF HUMAN SUBJECTS

All human subjects data are already collected for the F99 phase. No new data collection is proposed during the F99 phase. The following is a general description of the data that will be analyzed for the proposed research.

Our research methods are safe, entail minimal risk, are non-invasive, and entail minimal discomfort. When the discomfort and risk is balanced against the value of using humans as subjects as opposed to model organisms, the use of humans to meet the goals of our proposal is justified.

1. Justification for Exemption

This Human Subjects Research falls under Exemption 4. This study involves secondary data analysis of anonymized behavioral and neuroimaging data that were previously collected as part of 3 completed studies. One of the three neuroimaging datasets is already publicly available (https://openneuro.org/datasets/ds002041) and the other two are being prepared for public release. None of the data analyzed contains identifiers linked to the subjects. No contact will be made with participants whose data will be analyzed. The data is already stored "on the shelf" on a secure server at the research site where secondary data analysis will be conducted.

2. Human Subjects Involvement, Characteristics & Design

The following is a description of the data to be analyzed that is already collected.

Only subjects who were medically healthy with no significant psychiatric or neurological history were eligible for studies. *Inclusion criteria:* Medically and psychiatrically healthy, estimated IQ greater than 80. *Exclusion criteria:* For both MRI and PET studies, any condition which would interfere with MRI or PET studies, e.g. extreme obesity, claustrophobia, cochlear implant, metal fragments in eyes, cardiac pacemaker, neural stimulator, metallic body inclusions or other metal implanted in the body, pregnancy, anemia, or hematocrit below 34. Subjects were additionally excluded if they participated in any research studies in the past year that involved radiation, or if they were exposed to radiation on a routine basis due to their occupation. For PET studies, history of substance abuse, current tobacco use, alcohol intake greater than 8 ounces of whiskey or equivalent per week, any psychotropic medication for the past 6 months (other than occasional use of benzodiazepines for sleep), history of psychiatric illness, significant medical condition, and high blood pressure (Systolic B.P. > 135, Diastolic B.P. > 85).

Recruitment procedures: Healthy participants were recruited from university mailing lists and local advertisements in the community. Any individual meeting pre-screening criteria (age, free of self-reported psychiatric problems, imaging contraindicators or history of head trauma) could contact the lab to participate.

Clinical Trials Definition: After reviewing the definition and case studies provided by the NIH, the studies in our proposal do not meet the criteria for clinical trials. All data collection is already complete for the proposed F99 studies. These studies were meant to explore how people behave under different naturally occurring conditions (e.g. receiving material/monetary or social feedback and adjusting future behavior based on that feedback). Thus, our studies are observational in nature and do not meet the criteria for clinical trials.

3. Sources of Materials

Subjects provided the following specimens and data: self-report of mood, personality, cognitive assessment, medical, and psychiatric history. For PET studies blood samples for metabolic assessment (CMP), and complete blood count (CBC) were performed both at baseline to determine eligibility and before and after each PET scan. Women provided additional blood samples to ensure they were not pregnant prior to every PET scan. The subjects additionally provided data from PET scans, as well as structural and functional MRI scan data, neuropsychological data, and vital signs. All data was solely collected for research purposes only.

All subject information is kept in a locked file cabinet in the offices of PI and/or co-investigators. Image data are only accessible to study personnel on password-protected computers. Wherever possible, data are stored as a study ID number and not linked to the subject identification information. Only de-identified data is analyzed in the proposed studies.

Section 4 - Protocol Synopsis (Study 1)

4.1	Study De	esign						
	4.1.a. De	etailed Des	cription					
	4.1.b. Pr	imary Purp	oose					
	4.1.c. Int	erventions						
	Туре		Name		Description			
	4.1.d. St	udy Phase						
	Is	this an NIH	H-defined Phase III Clir	nical Trial	? Yes	O No		
	4.1.e. Int	ervention l	Model					
	4.1.f. Ma	sking			O Yes	O No		
			Participant	t	☐ Care Provider	☐ Investigator	☐ Outcomes Assessor	
	4.1.g. All	ocation						
4.2	. Outcome	e Measures	S					
Ту	pe	Name		Time Fr	ame	Brief Description		
4.3	. Statistica	al Design a	nd Power					
4.4	. Subject F	Participatio	n Duration					
4.5	. Will the s	study use a	an FDA-regulated interv	vention?	O Yes	O No		
	Product	(IP) and In	be the availability of Investigational New Drugice Exemption (IDE) st	g (IND)/	nal			
4.6	. Is this an	applicable	e clinical trial under FD	AAA?	→ Yes	O No		
4.7	7. Dissemination Plan							

Contact PD/PI: Castrellon, Jaime J.

Tracking Number: GRANT13258952

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification			
The form does not have any delayed onset studies						



December 4, 2020

Dear reviewers,

Duke University is pleased to support Jaime Castrellon's application for a NIH Blueprint Diversity Specialized Predoctoral to Postdoctoral Advancement in Neuroscience (D-SPAN) Award (F99/K00). The applicant, Jaime Castrellon, is Hispanic/Latinx and a first-generation college student. His mother was born in Uruguay and immigrated to the United States. His father was born in southern California to Mexican day-laborer parents. Neither parent attended college. Jaime received dual undergraduate degrees in Neuroscience and Political Science from USC and will earn his PhD in Psychology and Neuroscience here at Duke. Nationwide, less than 10% of undergraduate neuroscience degrees are awarded to Hispanic students (10% Hispanic male, 9% Hispanic female) and less than 6% of PhDs in neuroscience are awarded to Hispanic students (4% Hispanic female, 6% Hispanic male).

Jaime is a PhD student in the Department of Psychology and Neuroscience (P&N) who conducts research in the Center for Cognitive Neuroscience. Among neuroscience applicants to P&N and the Cognitive Neuroscience Admitting Program (CNAP) over the past 5 years, fewer than 10% of applications have come from under-represented students of color (Hispanic/Latinx or Black students). Once under-represented students enter our training programs, we do everything we can to support their career development. The Office of Research Support is highly committed to assisting the applicant with the management of this F99/K00 award throughout the F99 phase and assisting with the institutional transition for the K00 post-doctoral phase if necessary.

Jaime is completing his PhD with Dr. Samanez-Larkin who has a track record of success in training individuals under-represented in science. The vast majority of his lab members come from backgrounds that are under-represented in science in at last one but often multiple ways (e.g., race/ethnicity, LGBTQ, low-income background, first-gen college, disability). The commitment to diversity within this lab and broader Duke environment will provide Jaime with an ideal level of support while also providing many opportunities for mentoring more junior under-represented students.

Jaime advanced to candidacy having completed his Doctoral Preliminary Examination in December 2019. He completed this milestone several months earlier than normal and is on track to finish his PhD within the standard five-year period. The proposed timeline in this grant application is both feasible and reasonable given Jaime's already productive track record to date.

Sincerely,

Jennifer Bolognesi

Jennifer Bolognesi

Assistant Director of the Office of Research Support, Duke University jennifer.bolognesi@duke.edu, (919) 681-4932

Gregory Samanez-Larkin

Jack H Neely Associate Professor of Psychology and Neuroscience, Duke University g.samanezlarkin@duke.edu, (650) 799-5715

RESOURCE SHARING PLAN

The proposed research will include behavioral, MRI, and PET data from healthy adults. For the sake of reproducibility and transparency we will publicly share all deidentified data and analysis code for the proposed studies as has been done by the applicant https://osf.io/582bx/ and the Samanez-Larkin lab https://osf.io/faets/. Our brain imaging data will be in BIDS format for easy sharing to public repositories (e.g., OpenNeuro). The applicant has already publicly shared one multimodal (MRI+PET) neuroimaging data set publicly: https://openneuro.org/datasets/ds002041/versions/1.2.0

CONCURRENT SUPPORT

The applicant is currently "on-tenure" for the final year of a National Science Foundation Graduate Research Fellowship which provides funds for tuition and stipend. This NSF funding will expire August 30, 2021. If the applicant is awarded the F99/K00 DSPAN fellowship, which is planned to begin July 1, 2021, then the applicant will immediately forfeit the NSF award for the months of July and August 2021.