

APPLICATION FOR FEDERAL ASSISTANCE  
**SF 424 (R&R)**

		<b>3. DATE RECEIVED BY STATE</b>	State Application Identifier
<b>1. TYPE OF SUBMISSION*</b>		<b>4.a. Federal Identifier</b> MH122091-01	
<input type="radio"/> Pre-application <input type="radio"/> Application <input checked="" type="radio"/> Changed/Corrected Application		<b>b. Agency Routing Number</b>	
<b>2. DATE SUBMITTED</b> 2019-08-07	<b>Application Identifier</b> 265563	<b>c. Previous Grants.gov Tracking Number</b> GRANT12916039	
<b>5. APPLICANT INFORMATION</b>			Organizational DUNS*: 0571231920000
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<b>6. EMPLOYER IDENTIFICATION NUMBER (EIN) or (TIN)*</b> 1231365971A1			
<b>7. TYPE OF APPLICANT*</b> X: Other (specify)			
Other (Specify): Public, Nonprofit, State-related Inst of Higher Ed			
<b>Small Business Organization Type</b> <input type="radio"/> Women Owned <input type="radio"/> Socially and Economically Disadvantaged			
<b>8. TYPE OF APPLICATION*</b>		If Revision, mark appropriate box(es).	
<input type="radio"/> New <input checked="" type="radio"/> Resubmission		<input type="radio"/> A. Increase Award <input type="radio"/> B. Decrease Award <input type="radio"/> C. Increase Duration	
<input type="radio"/> Renewal <input type="radio"/> Continuation <input type="radio"/> Revision		<input type="radio"/> D. Decrease Duration <input type="radio"/> E. Other (specify):	
Is this application being submitted to other agencies?*		<input type="radio"/> Yes	<input checked="" type="radio"/> No      What other Agencies?
<b>9. NAME OF FEDERAL AGENCY*</b> National Institutes of Health		<b>10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER</b> TITLE:	
<b>11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*</b> Learning to fear social interactions: Dysregulated neural mechanisms of social learning in adolescent social anxiety			
<b>12. PROPOSED PROJECT</b> Start Date* 04/01/2020		<b>13. CONGRESSIONAL DISTRICTS OF APPLICANT</b> Ending Date* 03/31/2022 PA-002	

**SF 424 (R&R)** APPLICATION FOR FEDERAL ASSISTANCE**Page 2****14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION**

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**15. ESTIMATED PROJECT FUNDING**

a. Total Federal Funds Requested*	\$68,910.00
b. Total Non-Federal Funds*	\$0.00
c. Total Federal & Non-Federal Funds*	\$68,910.00
d. Estimated Program Income*	\$0.00

**16. IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?\***

- a. YES  THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:  
 DATE:
- b. NO  PROGRAM IS NOT COVERED BY E.O. 12372; OR  
 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)**

I agree\*

\* 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.

**18. SFLLL or OTHER EXPLANATORY DOCUMENTATION**

File Name:

**19. AUTHORIZED REPRESENTATIVE**

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**Signature of Authorized Representative\***

MS. KAREN D. MITCHELL

**Date Signed\***

08/08/2019

**20. PRE-APPLICATION** File Name:**21. COVER LETTER ATTACHMENT** File Name:Cover Letter.pdf

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## Project/Performance Site Location(s)

**Project/Performance Site Primary Location**

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: Temple University - Of The Commonwealth System of  
Duns Number: 0571231920000  
Street1\*: 1701 N. 13th Street  
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Province:  
Country\*: USA: UNITED STATES  
Zip / Postal Code\*: 19122-6011  
Project/Performance Site Congressional District\*: PA-002

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**Additional Location(s)**

File Name:

## RESEARCH &amp; 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 — 4 — 5 — 6 — 7 — 8

If NO, is the IRB review Pending?  Yes  No

IRB Approval Date: 07-23-2019

Human Subject Assurance Number 00004964

**2. Are Vertebrate Animals Used?\***  Yes  No

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending?  Yes  No

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 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 collaborators?\***  Yes  No

6.a. If yes, identify countries:

6.b. Optional Explanation:

Filename

**7. Project Summary/Abstract\*** 2.Project Summary\_FINAL\_ClarksonTe.pdf**8. Project Narrative\*** 3.Project Narrative\_FINAL\_ClarksonTe.pdf**9. Bibliography & References Cited** Bibliography\_References.pdf**10. Facilities & Other Resources** Facilities and other Resources.pdf**11. Equipment** Equipment.pdf

## PROJECT SUMMARY/ABSTRACT

Social anxiety (SA) disorder is prevalent<sup>1</sup>, chronic<sup>2</sup>, and impairs quality of life<sup>3,4</sup>. Typical onset occurs in early adolescence<sup>2</sup>, when social relationships become more salient and complex. Thus, difficulty learning from nuanced interactions may potentiate SA<sup>6–11</sup>. Although SA is associated with suboptimal adaptive learning rates in non-social<sup>9–11</sup> and uncertain/volatile contexts<sup>8,9</sup>, little is known about relations between SA and learning during symptom-eliciting social interactions with peers<sup>6,12–14</sup>. Moreover, in SA, social feedback is associated with dysregulated engagement of neural circuits implicated in salience and reward processing<sup>15–17</sup>, which are critical hubs for learning<sup>9,10,18–21</sup>. Despite this overlap, the neural mechanisms that support learning from social feedback remain relatively unexplored in SA. Treating deficits in social learning may diminish acute SA symptoms before they become chronic, thereby reducing the high societal cost of adult SA<sup>22</sup>. Progress towards this goal has been hindered by the limited extension of well-established computational methods to isolating the neural mechanisms of social learning. The proposed project addresses these limitations by pairing computational modeling with fMRI to determine the extent to which peer value, valence of peer feedback and volatility of peer feedback modulate the neural bases of social learning about peers and their relation to adolescent SA. The proposed project will study the behavioral and neural responses of adolescents (N=60; age 10-15yrs) with a range of SA to real-time social interactions with purported peers while undergoing an fMRI scan. Aims of this study are consistent with the NIMH strategic plan (Objective 1): defining the mechanisms of complex behaviors, specifically how environmental factors, such as social experiences, and neural mechanisms influence socially anxious behavior. The proposed study will determine neural circuits involved in complex social learning through interactions that are associated with SA. Such findings will provide novel treatment targets for SA. The proposed training plan, which consists of workshops, experiential learning, and mentorship, are designed to develop the applicant's expertise in computational modeling, neuroimaging and clinical assessment of SA disorder. The proposed study will take place within Temple University's clinical psychology program, which has a successful track record of conducting impactful NIMH-funded research and training research scientists.

## PROJECT NARRATIVE

Social anxiety (SA) disorder increases in adolescence as social relationships become more salient and complex; therefore, difficulty learning from nuanced social interactions may potentiate SA. Although SA is associated with impaired learning in non-social contexts, little is known about relations between SA and learning during symptom-eliciting social interactions with peers. The proposed study pairs computational modeling with fMRI to determine the extent to which peer value, valence of peer feedback and volatility of peer feedback modulate the neural bases of social learning about peers and their relation to SA.

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## FACILITIES AND OTHER RESOURCES

The Clinical Psychology Program of the Department of Psychology at Temple University is an APA- and PCSAS-accredited clinical doctoral program designed to produce high-caliber independent researchers. The university is considered a R1 research institute on the Carnegie classification, meaning that it is in the top four percent of institutions for research activities. Institutional support includes: (1) financial support for conferences and workshops and (2) classes intended to provide professional development and training to become an independent researcher (i.e., courses on grant writing). Temple's location in Philadelphia facilitates additional training opportunities given its proximity to the University of Delaware, University of Pennsylvania, Drexel University, Philadelphia College of Osteopathic Medicine, and LaSalle University, thus creating an intellectually stimulating environment that will allow the applicant to expand her professional network. Overall, these facilities and resources will provide the applicant with an excellent institutional environment for executing the proposed study, along with strong mentorship that will support the applicant's development towards a career as an independent researcher.

**Neuroimaging.** The Temple University Brain Research and Imaging Center (TUBRIC), is a 3400sf, multi-modal, research imaging center serving the neuroimaging research community on Temple's main campus. TUBRIC is a fully functional research-dedicated facility with immediately adjacent participant preparation, testing, and interview space, furnished with a range of integrated and supplemental research instruments (e.g., mock fMRI scanner, eye tracker, EEG equipment) to complement basic imaging work. Integrated tools include MRI compatible stimulus delivery (e.g., visual projection, audio, liquid delivery, electric shock delivery), response collection, physiological monitoring, and eye-tracking devices. All data acquisition will be completed at TUBRIC, and funded by Dr. Jarcho. The facility is staffed by a director (Dr. Jason Chein), MRI physicist (Dr. Huiling Peng), neuroimaging supervisor, and administrative and IT support personnel. Scanning will be conducted on a Siemens MAGNETOM Prisma 3-Tesla whole-body MRI scanner, supporting a collection of structural MRI, fMRI, and DTI sequences.

**Clinical.** Diagnostic assessments will be conducted at the Child and Adolescent Anxiety Disorders Clinic (CAADC), directed by Dr. Kendall, located directly across the hall from TUBRIC. The CAADC is both a laboratory and a clinic specializing in the research and treatment of youth with anxiety disorders, and has been home to multiple NIH-funded grants examining the treatment of youth anxiety. Thus, the CAADC is well equipped to provide the necessary infrastructure for conducting the Anxiety Disorders Interview Schedule (ADIS) and recruitment of youths with social anxiety symptoms for the applicant's proposed study. The CAADC occupies a large amount of space in the Department of Psychology (approximately 3000 square feet) and includes seven assessment/treatment rooms that are all equipped with secure digital audio and video recording equipment. Intake assessment sessions for the proposed study will be conducted in these rooms. Additionally, there is ample office space in the CAADC, and each graduate student has access to a private office. For the proposed project, the applicant will have access to networked desktop and laptop computers linked to a secured network server to review videos of assessments. Additionally, weekly lab meetings are held in the in-house conference room to review all diagnostic assessments, included those for the proposed study, with the clinical graduate student team and Dr. Kendall.

**Laboratory.** The Social Developmental Neuroscience (SDN) Lab led by Dr. Jarcho is located in the same building as TUBRIC and the CAADC. The lab has 15 computers, including the applicant's encrypted Mac Mini desktop and MacBook Pro laptop computers, that are equipped with standard software for designing experiments (e.g., EPrime 2.0), analyzing data (e.g., SPSS, R, MPLUS), and preparing presentations and manuscripts (e.g., Microsoft Office), and fMRI data analysis (e.g., Analysis of Functional NeuroImages (AFNI), Statistical Parametric Mapping (SPM12), the FMRIB Software Library (FSL), and Free-Surfer. The SDN lab also has a secure server administered and supported by Temple University for the storage and backup of all study data.

The College of Liberal Arts IT Department (CLA IT) provides the SDN Lab with Network Attached Storage services for file storage. The servers are protected from disk failure by using a Redundant Array of Independent Disks (RAID) Level 6. This protection allows for multiple disks to fail and file services remain uninterrupted with no data loss. CLA IT staff have spare disks on hand to replace failed disks immediately upon failure to avoid a wait time for the vendor to ship out a replacement. CLA IT also maintains a backup system that resides in a separate data center 0.5 miles across campus which holds approx. 100 days of backups for restores upon request. User data access is controlled using security groups managed through

Microsoft Active Directory. Users only see the files and folders in which they should have access to and full auditing of access is enabled. The file server is connected via four 1 Gigabit Ethernet connections configured with jumbo frames that are bonded together to provide high availability and allow for a high amount of bandwidth. The server also has redundant power in case of a power supply failure and is connected to an uninterruptible power supply to protect against a power outage. All server equipment is secured in high security data centers that require card access to prevent unauthorized entry. The file server can be accessed remotely using a VPN client and Duo 2 Factor Authentication for a secure connection. CLA IT staff actively monitor the server and receive immediate email notifications regarding system warnings and failures.

**Computational Modeling.** In addition to the resources offered in the Temple University, the applicant and proposed study will benefit from support provided by co-sponsor, Dr. Platt. Dr. Platt will provide access to resources and computational modeling supervision at his lab located at the University of Pennsylvania's main campus. The Department of Neuroscience at University of Pennsylvania, Perelman School of Medicine houses the offices and laboratories of Dr. Platt's data analysis laboratory (~2000 square feet). The Platt lab has desk space for 20 people, each outfitted with high-end Macintosh or PC computers for computational modeling. The Platt lab also has dedicated networked storage devices, SMART Boards for presentations, as well as dedicated rooms for conducting psychophysiological tests and patient interviews. Computer and printing resources as well as conference rooms are available both within the lab and in shared office space. General-function computers are available at each of the research, testing, and office sites on the Penn campus. Full-time IT staff provide support for the general computing needs of faculty and staff. Computers dedicated to experimental control, data acquisition, and online data supervision are available in the Smilow center at U Penn and in the Richards Building as well as the Wharton Behavior Lab. Through regularly individual and lab-based meetings, the applicant will work closely with Dr. Platt and his team to develop and optimize the computational models proposed in this study. The applicant's will have access to lab computers and her personal computer, which is equipped with software for running computational modeling (RStudio and Matlab).

**Mentorship.** In her role as the primary sponsor for this project, Dr. Jarcho will continue to facilitate data collection by being available on Temple's main campus for continued oversight, and will offer her mentorship and support on every dimension of this proposal via weekly in-person meetings. The applicant's co-sponsor, Dr. Platt, will be available on University of Pennsylvania's main campus for bi-weekly meetings and additional in-person consultation when necessary. Drs. Smith and Kendall, professors in the Psychology department at Temple University, will be available for consultation on best practices for neuroimaging and clinical assessment via bi-weekly in-person meetings.

## EQUIPMENT

The Temple University Brain Research and Imaging Center (TUBRIC), a 3400sf, multi-modal, research imaging center is serving the neuroimaging research community on Temple's main campus. Neuroimaging will be performed on a Siemens MAGNETOM Prisma 3-Tesla whole-body MRI scanner, supporting the collection of structural MRI, fMRI, and DTI sequences. This instrument provides the strongest commercially available gradient field (80mT/m) in combination with the fastest available gradient switching rate (200mT/m/s). The magnet is equipped with advanced active shielding capabilities, using Siemen's MRITimTX TrueForm, to overcome B1 inhomogeneities at 3T, providing a maximally stable and linearly uniform imaging field of view. The magnet's coil uses an ultra-high-performance cooling and force-compensated design to reduce vibrations, which results in a minimization of eddy currents and acoustic noise. The advanced fully-dynamic parallel transmit RF technology in this system integrates all transmit and receive components within the magnet housing, providing industry leading signal-to-noise performance and high image stability with minimal RF noise artifact. The complete system is equipped with a 64-channel phased-array parallel transmit and receive RF head/neck coil, providing maximal image quality with exceptionally high spatial and temporal resolution for all brain imaging pulse sequences. The center also houses three testing rooms equipped with desktop computers for administering behavioral aspects of the LEARN task and a waiting room, equip with ipads, for parents to comfortably complete questionnaires. The facility is staffed by a director (Dr. Jason Chein), MRI physicist (Dr. Huiling Peng), neuroimaging supervisor, and administrative and IT support personnel. All data for the proposed project will be acquired by the applicant.

The Child and Adolescent Anxiety Disorders Clinic (CAADC) is located directly across the hall from TUBRIC, which will facilitate visit scheduling and completion for CAADC participants. The CAADC has two computer labs with nine desktop computers and two laptop computers. All computers are linked to a secured network server with access to treatment videos and training materials for clinical training during the study. The center has seven treatment rooms for use in video-taped Anxiety and Related Disorders Interview Schedule for DSM-5 (ADIS-5) assessments for the proposed study.

The Social Developmental Neuroscience (SDN) lab, directed by Dr. Johanna Jarcho is located in the same building as TUBIRC and the CAADC. The lab is equipped with 15 secure computers with standard software for designing experiments (e.g., EPrime 2.0), analyzing data (e.g., SPSS, R, MPLUS), preparing presentations and manuscripts (e.g., Microsoft Office), and fMRI data analysis (e.g., Analysis of Functional NeuroImages (AFNI), Statistical Parametric Mapping (SPM12), the FMRIB Software Library (FSL), and Free-Surfer. The SDN lab also has a secure server administered and supported by Temple University for the storage and backup of all study data (see Facilities & Resources). In addition to physical supplies, the SDN lab employs a master's level research coordinator who provides additional supervision to advanced undergraduate and masters students who serve as research assistants. The applicant will recruit up to six undergraduate and one master's level students whose primary responsibility will be to serve as research assistants on the proposed project.

The Platt labs, directed by Dr. Platt, is located in the department of Neuroscience at University of Pennsylvania, Perelman School of Medicine. The lab houses the offices and laboratories of Dr. Platt's data analysis laboratory (~2000 square feet), which has desk space for 20 people, each outfitted with high-end Macintosh or PC computers for computational modeling.

With regard to security, all mentioned facilities are all under video surveillance, require keycard access, and remain locked when staff members are not present to ensure safety of confidential materials.

## RESEARCH &amp; RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator				
Prefix:	First Name*: TESSA	Middle Name	Last Name*: CLARKSON	Suffix:
Position/Title*:	GRADUATE RESEARCH ASST W/DAB			
Organization Name*:	Temple University - Of The Commonwealth System of			
Department:	CLA:PSYCHOLOGY (18110)			
Division:				
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Street2:	Weiss Hall			
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County:	Pennsylvania			
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Degree Type:	Degree Year:			
Attach Biographical Sketch*:	File Name:	7.Clarkson Biosketch_ClarksonTNRSA.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix:	First Name*: JOHANNA	Middle Name	Last Name*: JARCHO	Suffix:
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Department:	CLA:PSYCHOLOGY (18110)			
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Street2:	Weiss Hall			
City*:	Philadelphia			
County:	Philadelphia			
State*:	PA: Pennsylvania			
Province:				
Country*:	USA: UNITED STATES			
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Project Role*:	Other (Specify)		Other Project Role Category: Sponsor	
Degree Type:	Degree Year:			
Attach Biographical Sketch*:	File Name:	7.Jarcho_Biosketch_Clarkson_NRSA_jj.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix:	First Name*: Michael	Middle Name L	Last Name*: Platt	Suffix:
Position/Title*:	Professor			
Organization Name*:	University of Pennsylvania			
Department:	Psychology			
Division:				
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City*:	Philadelphia			
County:				
State*:	PA: Pennsylvania			
Province:				
Country*:	USA: UNITED STATES			
Zip / Postal Code*:	19104-6018			
Phone Number*:	736.712.5083		Fax Number:	
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Project Role*:	Other (Specify)		Other Project Role Category: Other Significant Contributor	
Degree Type:	Degree Year:			
Attach Biographical Sketch*:	File Name:	7.Platt_Biosketch_ClarksonTNRSA.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix: DR.	First Name*: DAVID	Middle Name V.	Last Name*: SMITH	Suffix:
Position/Title*:	ASSISTANT PROFESSOR			
Organization Name*:	Temple University - Of The Commonwealth System of			
Department:	CLA:PSYCHOLOGY (18110)			
Division:				
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Street2:	825 Weiss Hall			
City*:	Philadelphia			
County:				
State*:	PA: Pennsylvania			
Province:				
Country*:	USA: UNITED STATES			
Zip / Postal Code*:	19122-6011			
Phone Number*:	215-204-1552		Fax Number: ()	
E-Mail*:	dvsmit@temple.edu			
Credential, e.g., agency login:	dvsmit84			
Project Role*:	Other (Specify)		Other Project Role Category: Other Significant Contributor	
Degree Type:	Degree Year:			
Attach Biographical Sketch*:	File Name:	Smith_Biosketch.pdf		
Attach Current & Pending Support:	File Name:			

PROFILE - Senior/Key Person				
Prefix: DR	First Name*: PHILIP	Middle Name	Last Name*: KENDALL	Suffix:
Position/Title*:	PROFESSOR			
Organization Name*:	Temple University - Of The Commonwealth System of			
Department:	CLA:PSYCHOLOGY (18110)			
Division:				
Street1*:	1701 North 13th Street			
Street2:	Temple University			
City*:	Philadelphia			
County:	Philadelphia			
State*:	PA: Pennsylvania			
Province:				
Country*:	USA: UNITED STATES			
Zip / Postal Code*:	19122-6011			
Phone Number*:	2152041558		Fax Number: 6108961955	
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Credential, e.g., agency login:	PKENDALL			
Project Role*:	Other (Specify)		Other Project Role Category: Other Significant Contributor	
Degree Type:	Degree Year:			
Attach Biographical Sketch*:	File Name:	Kendall_Biosketch.pdf		
Attach Current & Pending Support:	File Name:			

**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: Clarkson, Tessa

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

POSITION TITLE: Pre-doctoral researcher

**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 <i>(if applicable)</i>	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Boston University, Boston, MA	B.S.	09/2007	05/2011	Human Physiology
Stony Brook University, Stony Brook, NY	M.A.	09/2016	05/2018	Psychology
Temple University, Philadelphia, PA	Ph.D.	09/2016	05/2022 (expected)	Clinical Psychology

**A. Personal Statement**

My long-term career goal is to become a professor at a research-oriented institute, investigating etiopathogenic mechanisms that promote social impairment in youth. My proposed project supports this goal: I will isolate parameters of the social context that impair social learning in socially anxious adolescents using neural circuit-, behavioral-, and subjective report-level measures. My education, research, and clinical training have provided me with the foundational skills necessary to undertake this project and training plan. Specifically, through my work on 15+ studies involving youth with social impairments, 2 of which I designed and led, I have learned to acquire and analyze basic functional neuroimaging data, generate scripts for statistical analyses, conduct clinical assessments of social impairment, and design and implement ecologically valid experiments with a team of research assistances. These studies have resulted in 13 manuscripts, 10 of which isolate neural mechanisms of social/cognitive dysfunction in youths with social impairment. These opportunities have enabled me to use multiple methods to investigate mechanisms of social impairment in at-risk youth. In the interest of my long-term career goal, I plan to further incorporate computational modeling as an analytic tool for isolating parameters of social context important for social learning. Specifically, I am interested in developing models that can estimate how the peer value or valence and volatility of peer feedback can modulate social learning during real-time social interactions to promote social anxiety (SA). I aim to gain expertise in methodological training in neuroimaging to examine how functional connectivity within neural circuits of social learning promote SA in adolescents. To do this, I have assembled an exceptional mentorship team with expertise in fMRI-study design (Sponsor; Dr. Jarcho), computational modeling (co-sponsor; Dr. Platt), functional connectivity analyses (Dr. Smith), and diagnostic assessment of SA (Dr. Kendall) to facilitate my training. I have access to ideal facilities and resources necessary to conduct the proposed study including: The Temple University Brain Imaging Center (TUBRIC), funding for scans via Dr. Jarcho, the Platt lab computational modeling resources, and access to youth with clinically significant SA via Dr. Kendall's clinic. The support of an NRSA will provide me the time and opportunity to utilize these facilities and expertise to conduct the proposed research and training plan, which are commensurate with my career goals and the NIH's strategic plan.

**B. Positions and Honors****Positions**

- 2011-12 Research Coordinator. Neurology, Boston Children's Hospital/Harvard Medical (BCH/HMS), *Omar Khawaja, M.D., Ph.D., Walter Kaufmann, M.D.*
- 2012-14 Research Assistant. DevCogNeuro, BCH/HMS, *Charles A. Nelson, Ph.D.*
- 2014-16 Lab Manager. DevCogNeuro, BCH/HMS, *Susan Faja, Ph.D.*
- 2016-18 Teaching Assistant. Psychology, Stony Brook Univ. (SBU), *Ryan Parsons, Ph.D. Bonita London, Ph.D., Matthew Lerner, Ph.D.*
- 2014-16 Clinician. Psychology, SBU, *Kristin Bernard, Ph.D.; Nicholas Eaton, Ph.D.; Dina Vivian, Ph.D.*
- 2017-17 Instructor. Psychology, SBU, *Christian Luhmann, Ph.D.*

- 2018- Graduate Assistant. Psychology, Temple Univ. (TU), *Johanna Jarcho, Ph.D.*  
2018- Clinician. Psychology, TU, *Jay S. Efran, Ph.D., Jean Wright, Ph.D., Phil Kendall, Ph.D., A.B.P.P., Elizabeth Gosh, Ph.D., A.B.P.P.*

### **Academic and Professional Honors**

- 2017 Student Travel Award. Society for Research and Child Development (SRCD)  
2017 Student Award. International Meeting For Autism Research (INSAR)  
2018 Award for Excellence in Research (Second Year Research). Stony Brook University

### **Memberships in Professional Societies**

- 2014-present Member, Society for Research and Child Development  
2014-present Member, International Society for Autism Research  
2015-present Member, Society for a Science of Clinical Psychology  
2016-present Member, Association for Psychological Science  
2016-present Member, Social and Affective Neuroscience Society  
2017-present Member, Association for Psychological Association  
2017-present Member, Flux Society  
2017-present Ad Hoc Reviewer, Social Cognitive Affective Neuroscience  
2018-present Ad Hoc Reviewer, Autism  
2016-present Ad Hoc Reviewer, Journal of Intellectual and Developmental Disabilities  
2019-present Ad Hoc Reviewer, International Journal of Psychophysiology  
2019-present Ad Hoc Reviewer, Plus One

### **C. Contributions to Science**

1. *Neural mechanisms of anxiety in youth.* Understanding risk and maintenance factors of anxiety and the influence of comorbidity on these factors is vital for improving interventions and preventative care. Thus, a focus of my research has been to isolate neural mechanisms of risk and maintenance of anxiety disorders, and how neural mechanisms are altered in the presence of comorbidity. For example, in one manuscript I demonstrated that dysregulated neural responses to unpredictably positive social feedback mediate relations of *early risk*, in the form of childhood social reticence, and the *maintenance* of SA from pre- to mid-adolescence. I also co-authored another manuscript that revealed distinct influences of anxiety and *comorbid* depression on neural responses to social and intrinsic rewards that *maintain* symptoms. I have utilized electrophysiological measures of anxiety to assessing and predicting treatment responses in anxiety symptoms in youth with *comorbid* autism spectrum disorder (ASD). These studies underscore the value of neural measures in predicting persistence of and treatment response for anxiety symptoms in the presence of comorbidity. Less is understood about the mechanisms by which the social environment influences neural responses to promote anxiety. As such, I have developed a novel task that identifies how social environment factors modulate neural responses to promote SA.

- a. Clarkson, T., Eaton, N. R., Nelson, E.E., Fox, N.A., Leibenluft, E., Pine, D.S., Heckelman, A., Sequeira, S.L., Jarcho. J.M. (2019). Early Childhood Social Reticence and Neural Response to Peers in Preadolescence Predict Social Anxiety Symptoms in Mid-Adolescence. *Depression and Anxiety.* <https://doi.org/10.1002/da.22910>
- b. Quarmley, M., Rainville, B., Clarkson, T., Jarcho. J.M. (revise resubmit). *Special Issue: I Knew You Weren't Going to Like Me!* Anxiety and Depression are Associated with Neural Response to Accurately Predicting Rejection. *Frontiers in Neuroscience*
- c. Kang, E. ¥, ^ Clarkson, T. ¥, ^ Keifer, C.M., Rosen, T.E., Lerner, M.D.^ (2019) Discrete electrophysiological predictors of anxiety and anxiety-related treatment response in youth with autism spectrum disorder. (¥:joint first-authorship). *Biological Psychology.* <https://doi.org/10.1016/j.biopsych.2019.05.010>
- d. Clarkson, T.. Kang, E., Keifer, C., Rosen, T., Lerner, M.D, Gilbert, R., Vaidyanathan, A.\* Hyatt, D. Clarkson, T., Greco, G., Caroll, D., Faja, S., Key, A., Corbett, B. A., Jones, D., Schiltz, H. K., McVey, A. J., Haendel, A. D., Barrington, A., Dolan, B., Willar, K., Pleiss, S., Carson, A., Mata-Greve, F., Caiozzo, C. and Van Hecke, A. V. (May, 2018) *Translational Electrophysiological Predictors of Individualized Treatment Response in School-Age and Adolescent Individuals with ASD.* Clarkson, T. (Chair) Jeste, S. (Discussant). Symposium to be presented at the *International Society for Autism Research.* Rotterdam, Netherlands.

**2. Neural indices of executive functioning and error processing in ASD.** I am broadly interested in the role of error-processing in executive functioning and social learning. Thus, I have co-authored several manuscripts focused on establishing the construct validity, reliability, and use of neural and behavioral measures of error processing and executive functioning in youth with ASD. Additionally, I have co-authored another paper that describes methods I developed for a novel pipeline for decoding single-trial neural responses to errors in individuals with ASD. Together these studies lay the foundation for using neural measures for assessing the role of executive functioning and error processing in promoting social impairments in ASD, and could provide novel intervention targets. Moreover, my work on these projects have strengthen my ability to develop and validate neural measures, which will prove useful for the analysis of my novel task in the proposed study.

- a. Faja, S., **Clarkson, T.**, Gilbert, R., Vaidyanathan, A.\*., Greco, G.M., Rueda, R., Combita, L.M., Sideridis, G., Driscoll, K. (under review). Randomized, controlled trial of executive function training for children with autism spectrum disorder. *Autism Research*.
- b. Cremone, A., Vaidyanathan, A.\*., Hyatt, D., Gilbert, R., **Clarkson, T.**, Faja, S. (revise resubmit). Test-Retest Reliability of the N2 Event-Related Potential in School-Aged Children with Autism Spectrum Disorder (ASD). *Clinical Neuropsychology*.
- c. Mayor Torres, J.M., **Clarkson, T.**, Stepanov, E.A., Luhmann, C.C., Lerner, M.D., Riccardi, G. (2018). Enhanced Error Decoding from Error-Related Potentials Using Convolutional Neural Networks. In *Engineering in Medicine and Biology Society (EMBC)*, 2018 40th Annual International Conference of the IEEE. Honolulu, HI, July 17 - 21.
- d. Faja, S., **Clarkson, T.**, & Webb, S. J. (2016). Neural and behavioral suppression of interfering flankers by children with and without autism spectrum disorder. *Neuropsychologia*.  
<https://doi.org/10.1016/j.neuropsychologia.2016.10.017>

**3. Social processing across units of analysis.** An additional focus of my research has been to assess the utility and correspondence of measures social processing across units of analyses in youth. As such, I conducted a meta-analysis of studies on social processing in youth and found high correspondence between neural circuit measures using neuroimaging and subjective-report symptoms. Additionally, I co-authored a perspective paper highlighting the benefits of using neural and behavioral measures to pinpoint individualized profiles of social impairments in youth with ASD. I have also conducted studies utilizing neural measures to determine whether observed deficits of facial emotion recognition in ASD are due to problems encoding social information, or other stages of social processing. Finally, I have examined the correspondence between social and non-social neural mechanisms of social impairments and their role in SA. These studies have not only given me perspective on the literature, but also emphasize the need for more research examining the role of neural measures in pinpointing individual differences in social processing that can help inform individualized intervention programs.

- a. **Clarkson, T.**, Kang, E., Lerner, M.D., Jarcho, J., Prinstein, M.J. (conditionally accepted). *RDoC Special Issue: A Meta-Analysis of the RDoC Social Processing Domain Across Units of Analysis*. *Journal of Clinical Child and Adolescent Psychology*.
- b. Mayor Torres, J.M.¥., **Clarkson, T.** ¥, Luhmann, C.C., Hauschild, K.M., Stepanov, E.A., Danielli, M., Lerner, M.D., Riccardi, G. (In prep). Facial emotions are accurate and holistically encoded in Autistic brains: A Deep Learning approach. (¥: joint first-authorship). *Proceedings of the National Academy of Sciences of the United States of America*
- c. Libsack, E., **Clarkson, T.**, & Lerner, M.D. (2018). Unique perspectives: harnessing multimodal assessment to understand how children with autism decode the social world. *Behavioral Health News*, 6(1), 35.
- d. **Clarkson, T.**, Quarmley, M., Hajcak, G., Jarcho, J.M. (In prep). Gender differences in shared neural mechanisms of anxiety in social and non-social contexts. *Developmental Cognitive Neuroscience*.

**4. Novel assessments for individuals with Rett Syndrome.** I am also interested in using multiple measures across units of analyses to develop better clinical assessments for disorders characterized by severe deficits in functioning that prohibit the valid use of standardize assessments. Therefore, I conducted several studies evaluating the validity of behavioral, physiological and eye-tracking measures for assessing impairments in Rett Syndrome (RTT). These studies have resulted in the validation of novel assessments of development, cognition, and perceived pain in RTT, all of which could not previously be assessed due to impairments in motor skills and expressive language. These projects have established methods that are now used clinically to develop intervention plans that capitalize on individual strengths to improve areas of weakness, and improve

quality of life in reducing pain. My work on these projects afforded me the skills in developing and validating measures and translating such measures for clinical use.

- a. Clarkson, T., LeBlanc, J., Degregorio, G., Vogel-Farley, V., Barnes, K., Kaufmann, W.E., Nelson, C.A. (2017). Adapting the Mullen Scales of Early Learning for a Standardized Measure of Cognition in Children with Rett Syndrome. *American Journal on Intellectual and Developmental Disabilities*. DOI 10.1352/1934-9556-55.6
- b. O'Leary, H. M., Marschik, P.B., Khwaja, O.S., Ho, E., Barnes, K.V., Clarkson, T., Bruck, N. M., Kaufmann, W.E. (2015) Increased autonomic response to pain in Rett syndrome. *Developmental Neurorehabilitation*, Early Online: 1–7. <http://www.ncbi.nlm.nih.gov/pubmed/26457613>
- c. Clarkson, T., LeBlanc, J., Degregorio, G., Vogel-Farley, V., Barnes, K., Kaufmann, W.E., Nelson, C.A. (2015, October). Adapting the Mullen Scales of Early Learning in Rett Syndrome. Poster presented at Translational Neuroscience Conference, Boston, MA.
- d. Gregory, JC, Baczeski, LM, Clarkson, T., Nelson, CA. (2017, October). Determining the Validity of the Eye-Tracking Mullen Scales of Early Learning (MSEL) in Age-Matched Control Participants. Poster presented at: *Neurodevelopmental Disorders Symposium*. Boston, MA

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

YEAR	COURSE TITLE	GRADE
<b>TEMPLE UNIVERSITY</b>		
2019	Multicultural Issues in Clinical Psychology	A
2019	Social, Cognitive, and Developmental Aspects of Behavior	A
2019	Research	S
2019	Clinical Practicum	A
2018	Cognitive Core	A
2018	Topical Seminar Cognitive Psychology	A
2018	Research	S
2018	Clinical Practicum	A
<b>STONY BROOK UNIVERSITY</b>		
2018	Advanced Clinical Practicum	S
2018	Supervised Practice	S
2018	Research	S
2017	Multivariate Methods	A
2017	Intervention Practicum	S
2017	Supervised Practice	S
2017	Research	S
2017	Correlation and Regression	A-
2017	First-Year Lectures (Professional Development Series)	S
2017	Introduction to Computer Applications	S
2017	Method of Intervention	A
2017	Psychopathology: Externalizing	A-
2017	Assessment: Personality	A
2017	Ethics and Professional Issues	S
2017	Research	S
2016	Analysis of Variance and Experimental Design	A-
2016	First Year Seminar	S
2016	Introduction to Computer Applications	S
2016	Assessment: General Principles	A
2016	Methods of Intervention: Treatment	A
2016	Psychopathology: Internalizing	A-
2016	Research	S

YEAR	COURSE TITLE	GRADE
<b>HARVARD UNIVERSITY: EXTENSION SCHOOL</b>		
2014	Neurobiology of Emotion	A
2013	Introduction to Statistical Methods	A
<b>BOSTON UNIVERSITY</b>		
2011	Biochemistry 2	B-
2011	Psychology of Criminal Justice	B+
2011	Neuroanatomy and Physiology	B+
2011	Cardiopulmonary Pathophysiology	B+
2011	Visual arts and drawing	A
2010	Biochemistry 1	B
2010	Cell Biology	A-
2010	Music Theory	C
2010	Field Experience in Human Physiology	A
2010	Gross Human Anatomy	B
2010	General Physics 2	C-
2010	Exercise Physiology	B-
2010	General Physics 1	B
2010	Gross Human Anatomy	B
2010	Human Nutrition Sciences	B
2010	Voice Class	B+
2010	Statistics	B+
2010	Systems Physiology	B-
2008	Introduction to health professions	B+
2008	Writing and Research Seminar	C
2008	General Chemistry	C
2008	Biology 2	C+
2007	Physiological Psychology	B+
2007	Writing Seminar	C+
2007	General Chemistry	C+
2007	Biology 1	C+
<b>METROPOLITAN STATE COLLEGE OF DENVER</b>		
2009	Introduction to Psychology	A
2009	Organic Chemistry 1 & Lab	A
2009	Organic Chemistry 2 & Lab	A
<b>PORLAND STATE UNIVERSITY</b>		
2009	Community & Health	A
2009	Cultural Development & Awareness	B+
2009	Experiments in Environment and Geography 1	A
2009	Experiments in Environment and Geography 2	A
2009	Global Women's Studies	A

\*Temple and Stony Brook Courses are sometimes graded on a pass-fail basis, with S indicating satisfactory or pass.

**GRE Test Scores:** Verbal: 157, 74<sup>th</sup> percentile; Quantitative: 155, 60<sup>th</sup> percentile; Analytical Writing: 4.5, 80<sup>th</sup> percentile.

**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: Jarcho, Johanna Molly

ERA COMMONS USER NAME (credential, e.g., agency login): JARCHO2

POSITION TITLE: Assistant 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 <i>(if applicable)</i>	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Los Angeles	B.A.	06/2000	Psychology
University of California, Los Angeles	Ph.D.	06/2008	Social Psychology
University of California, Los Angeles	PostDoc	06/2010	Psychobiology
National Institute of Mental Health, Bethesda, MD	PostDoc	06/2015	Developmental Neuroscience and Psychopathology

**A. Personal Statement**

My research aims to isolate neurobiological and behavioral mechanisms implicated in social competence. I have paired my background in social psychology with training in clinically-relevant developmental cognitive neuroscience to develop novel behavioral and functional magnetic imaging tasks designed to test these relations in adults and children. I have successfully obtained competitive extramural and intramural funding (during my time as a post-doctoral fellow at NIMH) to conduct research using these paradigms to differentiate brain function and behavior during peer-based social acceptance and rejection. This work has demonstrated that the brain responds differently to social evaluation in healthy and socially anxious individuals, and those at high and low risk for psychopathology due to childhood social reticence and exposure to peer victimization. As an Assistant Professor in the Psychology Department with joint affiliations in the areas of Brain Cognitive Sciences and Social Psychology at Temple University, my research program extends and builds on this work. I have extensive experience leading teams of interdisciplinary team of researchers and am well equipped to provide the mentorship needed to ensure the successful completion of Tessa Clarkson's proposed research and training plan. I have also recently initiated collaborations with Drs. Smith and Kendall, both consultants on her application, therefore, I am well positioned to facilitate their consultant on Tessa's application.

**B. Positions and Honors****Positions and Employment**

- 2000-2001 Lab Manager, Department of Psychology, University of California, Los Angeles
- 2002-2008 Teaching Fellow, Department of Psychology, University of California, Los Angeles
- 2015-2018 Assistant Professor, Department of Psychology, Stony Brook University, NY
- 2018- Assistant Professor, Department of Psychology, Temple University, PA

**Other Experience and Professional Memberships**

- 2000- Member, Association for Psychological Science
- 2000- Member, American Psychological Association
- 2011- Member, Society of Biological Psychiatry
- 2014- Member, Flux Society
- 2015- Member, Social Affective Neuroscience Society
- 2018- Associate Member, American College of Neuropsychopharmacology

2012	Fellow, University of Maryland Summer Institute on Social Developmental Neuroscience
2014-2017	Planning Committee for annual Society of Biological Psychiatry meeting
2016-2019	Planning Committee for annual Social Affective Neuroscience Society meeting
2016	Career Development Institute for Psychiatry

## **Honors**

2000	Highest Departmental Honors, University of California, Los Angeles
2005-2007	Young Investigator Award, Oppenheimer Foundation
2006-2007	Pre-doctoral Ruth L. Kirschstein National Research Service Award
2013	Society for Biological Psychiatry, Travel Award
2013	American College of Neuropsychopharmacology, Travel Award
2013	NIMH Fellows Award for Research Excellence
2015	American College of Neuropsychopharmacology, Travel Award
2015	American Academy of Child and Adolescent Psychiatry Senior Researcher Award
2015	NARSAD Ellen Schapiro & Gerald Axelbaum Young Investigator
2016	Teacher of the Year: Department of Psychology

## **C. Contributions to Science**

- 1. Development of ecologically valid functional magnetic resonance imaging (fMRI) paradigms for studying social cognition.** Most studies probe neural circuits engaged by social cognition by presenting participants with photographs of unfamiliar emotional faces. A small number of paradigms lead participants believe they have been socially accepted/rejected or included/excluded by individuals depicted in these photographs. While this is a large improvement on traditional methods, several limitations remain, namely: 1) meaningful behavioral responses are not obtained in response to purported feedback; 2) when obtained, behavioral responses are often dichotomous and nature, and do not allow the participant flexibility in their response; 3) uncertainty about purported feedback is not specifically modeled. I developed the Virtual School Paradigm (a and b, below), to address each of these limitations. I have also been integral in developing several other fMRI-based paradigms with high levels of ecological validity, including those that target brain function during rationalization (c) and self-referential thought (d).
  - a. **Jarcho JM**, Davis MM, Shechner T, Degnan KA, Henderson HA, Fox NA, Leibenluft E, Pine DS, Nelson EE (2016). Early childhood social reticence predicts brain function in preadolescent youths during distinct forms of peer evaluation. *Psychological Science*. **27**: 821-835. doi: 10.1177/0956797616638319
  - b. **Jarcho JM**, Leibenluft E, Walker OL, Fox NA, Pine DS, Nelson EE (2013). Neuroimaging studies of social anxiety: Paradigms, pitfalls and a new direction for investigating the neural mechanisms of childhood social anxiety. *Biology of Mood & Anxiety Disorders* **3**:14.
  - c. **Jarcho JM**, Berkman ET, Lieberman MD (2011). The neural basis of rationalization: cognitive dissonance reduction during decision-making. *Social Cognitive and Affective Neuroscience* **4**: 460-467.
  - d. Lieberman MD, **Jarcho JM**, Satpute AB (2004). Evidence-based and intuition-based self-knowledge: an fMRI study. *Journal of Personality and Social Psychology* **87**: 421-435.
- 2. Application of ecologically valid fMRI paradigms for studying relations between clinically relevant symptoms and social cognition.** The neural correlates of psychopathology are often assessed using paradigms that bear little resemblance to contexts that actually elicit symptoms. Another contribution I have made is to extend my use of ecologically valid experimental paradigms to study clinical populations. In doing so, I have been able to demonstrate that neural circuits engaged during distinct aspects of social acceptance and rejection predict subsequent expression of anxious behavior (a), heightened caloric intake among adolescent girls with loss of control eating (b), and biases that diminish the likelihood of recalling unexpectedly positive peer feedback in socially anxious adolescents (c).
  - a. **Jarcho JM**, Davis MM, Shechner T, Degnan KA, Henderson HA, Fox NA, Leibenluft E, Pine DS, Nelson EE (2016). Early childhood social reticence predicts brain function in preadolescent

- youths during distinct forms of peer evaluation. *Psychological Science*. 27: 821-835. doi: 10.1177/0956797616638319
- b. **Jarcho JM**, Tanofsky-Kraff M, Nelson EE, Engel SG, Vannucci A, Field SE, Romer AL, Hannallah L, Brady SM, Demidowich AP, Shomaker LB, Courville AB, Pine DS, Yanovski JA (2015). Neural activation during anticipated peer evaluation and laboratory meal intake in overweight girls with and without loss of control eating. *NeuroImage*. 108:343-53.
  - c. **Jarcho JM**, Romer AL, Shechner T, Galvan A, Guyer AE, Leibenluft E, Pine DS, Nelson EE. (2015). Forgetting the best when predicting the worst: Preliminary observations on neural circuit function in adolescent social anxiety. *Developmental Cognitive Neuroscience*. 13:21-31.
- 3. Neural mechanisms of behaviorally inhibited temperament.** A third contribution defines the lasting neural correlates of behavioral inhibition, a temperament that manifests during infancy, and predicts increased risk of developing anxiety disorders later in life. Through collaborations with Dr. Nathan Fox (UMD, Collage Park), I performed fMRI studies on young adults characterized as behaviorally inhibited or non-inhibited during the first years of life. I demonstrated that while early childhood temperament was largely unrelated to behavior during adulthood, residual effects were clearly evident in the brain during affective, attentional, and social processing. These residual effects were influenced by other risk factors, such as parenting style, which may mitigate the lasting effects of temperament on brain function.
- a. **Jarcho JM**, Fox NA, Pine DS, Leibenluft E, Shechner T, Degnan KA, Perez-Edgar K, Ernst M (2014). Enduring influence of early temperament on neural mechanisms mediating attention-emotion conflict in adults. *Depression and Anxiety*. 31(1):53-62.
  - b. **Jarcho JM**, Fox NA, Pine DS, Etkin A, Leibenluft E, Shechner T, Ernst M (2013). The neural correlates of emotion-based cognitive control in adults with early childhood behavioral inhibition. *Biological Psychology*. 92(2):306-14.
  - c. Guyer AE, **Jarcho JM**, Perez-Edgar K, Degnan KA, Pine DS, Fox NA, Nelson EE (2015). Temperament and parenting styles in early childhood differentially influence neural response to peer evaluation in adolescence. *Journal of Abnormal Child Psychology* 43: 863-874. doi: 10.1007/s10802-015-9973-2.
- 4. Neural mechanisms of pain processing.** A fourth contribution stems from my earlier work focused on elucidating the neural correlates of pain processing. I demonstrated that expectations and endogenous neuropharmacology influence the experience of acute and chronic pain in patients with functional disorders. Each of these studies prompted hypothesis generation in the literature, and corresponding suggestions for novel treatment of functional disorders.
- a. **Jarcho JM**, Feier NA, Labus JS, Naliboff B, Smith SR, Hong J, Colloca L, Tillisch K, Mandelkern MA, Mayer EA, London ED (2016). Placebo analgesia: Self-report measures and preliminary evidence of cortical dopamine release associated with placebo response. *NeuroImage: Clinical*. 10: 107-114. doi:10.1016/j.nicl.2015.11.009
  - b. **Jarcho JM**, Feier NA, Bert A, Labus JA, Lee M, Stains J, Ebrat B, Groman SM, Tillisch K, Brody AL, London ED, Mandelkern MA, Mayer EA (2013). Diminished neurokinin-1 receptor availability in patients with two forms of chronic visceral pain. *Pain*. 154(7):987-96.
  - c. **Jarcho JM**, Chang L, Berman M, Suyenobu B, Naliboff BD, Lieberman MD, Ameen VZ, Mandelkern MA, Mayer EA (2008). Neural and psychological predictors of treatment response in irritable bowel syndrome patients with a 5-HT3 receptor antagonist: a pilot study. *Alimentary Pharmacology & Therapeutics*. 28(3):344-52.
  - d. Lieberman MD, **Jarcho JM**, Berman S, Naliboff BD, Suyenobu BY, Mandelkern M, Mayer EA (2004). The neural correlates of placebo effects: a disruption account. *NeuroImage*. 22(1):447-55.

**Complete List of Published Work in MyBibliography:**

<https://www.ncbi.nlm.nih.gov/myncbi/johanna.jarcho.2/bibliography/public/>

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

## Pending

### Ongoing Research Support

R03-DA046733

8/1/2019-7/31/2020

NIDA

Title: "Aberrant Reward Sensitivity: Mechanisms Underlying Substance Use"

Goal: This project examines how neural responses to social and nonsocial rewards are associated with reward sensitivity and substance use.

Role: Co-I (PI: Smith)

R21 HD093912

08/03/17-07/31/20

NICHD

Using Adolescent Nonverbal Behavior to Predict Aggression Against Bullies and Bystanders

This project uses computational modeling to predict aggression following peer rejection using gaze (attention), pupillary response (arousal), and facial expressions (affect) in adolescents at risk for aggressive behavior due to harsh parenting style.

Role: PI

R01 MH097767

09/01/17-03/31/21

NIH/NIMH

Trajectories of Reward Sensitivity and Depression across Adolescence

The goal of this project is to use a longitudinal multimethod neuroimaging (ERPs and fMRI) approach to examine trajectories of reward sensitivity across adolescence in relation to depression risk (maternal history and reward sensitivity, and adolescent stress) and the development of depressive symptoms and syndromes.

Role: Co-I (PI: Nelson)

### Completed Research Support

NARSAD

03/15/15-01/14/19

Young Investigator Award

The goal of this project is to determine whether neural circuits engaged during social interactions in inhibited youth predict subsequent expression of psychopathology in adolescence.

Role: PI

NIMH Wyatt Memorial Training Fellowship

02/01/14-02/01/16

Excellence in Translational Research

The goal of this project was to isolate neural circuits that distinguish anxious and non-anxious youth during distinct forms of social interactions.

Role: PI

**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: Michael L. Platt

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

POSITION TITLE: James S. Riepe University Professor, Depts. of Neuroscience, Psychology, and Marketing, University of Pennsylvania

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 <i>(if applicable)</i>	Completion Date MM/YYYY	FIELD OF STUDY
Yale University, New Haven, CT	B.A.	05/89	Biological Anthropology
University of Pennsylvania, Philadelphia, PA	Ph.D.	05/94	Biological Anthropology
New York University, New York, NY	Post-doc	2000	Neuroscience

**A. Personal Statement**

My lab studies the biological bases of cognition and behavior, how these mechanisms go awry in disorders like anxiety, addiction, and autism, and the development of new therapies to overcome these problems. We use a broad array of techniques, including computational modeling, functional imaging, pupillometry, eye-tracking, single neuron recordings, neuropharmacology, genomics, and brain stimulation to achieve these goals. We focus on the development of complex computational models in humans and rhesus macaques optimized for probing neural circuit function and its dissolution in problems in social cognition. We complement these studies through extensive collaborations with scientists using noninvasive neuroimaging and behavioral methods in human participants, and studies of attention and vigilance in other animals like birds. We have a strong track record in the development of novel and creative behavioral paradigms combined with high-end computation to probe cognitive function in humans and animals. Our lab pioneered the application of decision theory in neuroscience, and has made fundamental discoveries regarding the neurobiology of decision making. A current goal is leveraging computational models to identify mechanisms social processing deficits for a variety of disorders including anxiety disorders—a focus of Tessa's proposed project. Our lab also maintains the infrastructure for large-scale investigations of genetic, epigenetic, microbiome, and experiential contributions to naturally-occurring variation in behavior and cognition in a large free-ranging, freely-breeding population of rhesus macaques on Cayo Santiago Island, off the coast of Puerto Rico. We currently maintain a large database including deep observational phenotype information on >580 monkeys, DNA on >900 monkeys, experimental phenotype data on >750 monkeys, as well as pedigree and life-history data on the entire population of >1500 monkeys. We recently began work to characterize region specific transcriptomes and epigenomes for brain regions associated with social information processing and implicated in autism genetic models, including medial prefrontal cortex, superior temporal gyrus, striatum, and amygdala—regions implicated in Tessa's proposed project. I have authored over 120 peer-reviewed papers and over 50 review and opinion papers in leading journals including Science, Nature, Nature Neuroscience, Neuron, Biological Psychiatry, Current Biology, PNAS, Psychological Science, and the Journal of Neuroscience and my work has been cited over 12,000 times. My role on the project as Co-sponsor will allow me to lend my expertise in social behavior, computational modeling, and social neuroscience to Tessa's project. I have also served as PI on several multi-institution grants, Director of the Duke Institute for Brain Sciences, Director of the Duke Center for Cognitive Neuroscience, and currently serve as Director of the Wharton Neuroscience Initiative, thus lending considerable mentorship experience to Tessa's proposed project.

Full publication list in PubMed: <https://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/41482670/>

**B. Positions and Honors****Positions**

- 1992 Instructor, Department of Biological Anthropology, University of Pennsylvania  
 1992-1994 Research Scientist, Callitrichid Research Center, University of Nebraska

1994-1997	Individual NRSA Post-doctoral Fellow, Center for Neural Science, New York University
1998	Lab Coordinator, Behavioral and Integrative Neuroscience, New York University
1997-2000	Research Associate, Center for Neural Science, New York University
2000-2006	Assistant Professor, Department of Neurobiology, Duke University Medical Center
2000-present	Core Faculty, Center for Cognitive Neuroscience, Duke University
2001-2006	Assistant Professor, Dept. Biological Anthropology and Anatomy, Duke University
2005-2009	Co-Director, Center for Neuroeconomic Studies, Duke University
2006-2009	Associate Professor, Department of Neurobiology, Duke University Medical Center
2006-2009	Associate Professor, Dept. Evolutionary Anthropology, Duke University
2009-2015	Professor, Department of Neurobiology, Duke University Medical Center
2009-2015	Director, Center for Cognitive Neuroscience, Duke University
2011-2015	Director, Duke Institute for Brain Sciences
2015	Co-Director, Bass Connections Brain and Society Program, Duke University
2015-present	James S. Riepe University Professor, Departments of Neuroscience, Psychology, and Marketing, University of Pennsylvania
2016-present	Director, Wharton Neuroscience Initiative, the Wharton School of Business, University of Pennsylvania

### **Other Experience and Professional Memberships**

1995-	Member, Society for Neuroscience
2001-	Member, Society for Neuroeconomics
2005-2008	Board of Scientific Councilors, Society for Neuroeconomics
2011-2015	Academic Leadership Council (Provost's Cabinet), Duke University
2011-2015	Duke Health System Chancellor's Academic Cabinet, Duke University
2017-2018	Dean's Advisory Council, the Wharton School, University of Pennsylvania

### **Honors**

2018	Curricular Innovation Award, the Wharton School, University of Pennsylvania
2015	James S. Riepe University Professor, University of Pennsylvania
2015	Lawrence C. Katz Distinguished Professor of Neurobiology, Duke University
2013	Ruth and A. Morris Williams Faculty Research Prize, Duke University Medical School
2008-2009	President, Society for Neuroeconomics
2008	Master Teacher/Clinician Award, Duke University Medical School
2002-2005	Esther and Joseph Klingenstein Fellow
2002-2005	EJLB Foundation Scholar Award
2001-2003	Alfred P. Sloan Foundation Fellow

### **C. Contribution to Science**

1. *The neural basis of decision-making.* Decisions are made based on evidence and the relative value of each option. In my postdoctoral work, I showed that firing rates of neurons in posterior parietal cortex signal the expected value of an option. Thus, the neural processes that translate sensation into action do so by scaling the likelihood of generating a specific behavior by its value, as predicted by both economics and behavioral ecology. My subsequent independent work at Duke focused on using this approach to decipher how we make more complex decisions, the consequences of dysfunctional decision-making, and ways to improve decision-making and treat decision-making disorders. We made several fundamental discoveries that built upon and extended my earlier observations, including the neural mechanisms that compute outcomes of actions, learn from those outcomes, manage risk and uncertainty, choose when to abandon depleting options and search for something better, and evaluate opportunities to seek new information. We also identified neural signals that process counterfactual information about foregone rewards. Importantly, our studies provided biological foundation for understanding hemodynamic characterizations of decision mechanisms yielded by current neuroimaging studies in humans that comprise the cornerstone of neuroeconomics, and also provide a benchmark for understanding faulty decision-making in disorders like addiction, gambling, and schizophrenia.

- a. Hayden, B.Y., Pearson, J., and Platt, M.L. 2009. Fictive reward signals in anterior cingulate cortex. Science 324:948-50. PMCID: PMC3096846

- b. Hayden, B.Y., Pearson, J., and Platt, M.L. 2011. Neuronal basis of sequential foraging decisions in the macaque. *Nature Neuroscience*. Jul;14(7):933-9. PMCID: PMC3553855
  - c. McCoy, A.N. and Platt, M.L. 2005. Risk-sensitive neurons in macaque posterior cingulate cortex. *Nat. Neurosci.* 8:1220-1227.
  - d. Platt, M.L. and Glimcher, P.W. 1999. Neural correlates of decision variables in parietal cortex. *Nature* 400:233-238.
- 2. The neural basis of social motivation and attention.** To navigate our social worlds, we track the behavior of others and form models of intentions and emotional states, actively seek out and exchange information about others, and flexibly alter behavior in response to what we know about others. Like humans, rhesus macaques also live in large groups characterized by complex social interactions, offering an excellent animal model for social motivation and its dysfunction in disorders like autism. We discovered that both humans and monkeys find social stimuli intrinsically rewarding, and some social stimuli are more interesting and valuable than others. Moreover, we found decision and attention circuits treat social and nonsocial outcomes equivalently. Nevertheless, we also found the reward circuit that translates perceptual signals into value signals guiding decisions, including orbitofrontal cortex and striatum, contains populations of neurons specialized for encoding the type and importance of social information. This led us to hypothesize that the adaptive demands of social interaction favored the evolution of fast and accurate mechanisms for motivating appropriate behavior, leading to duplication and repurposing of general-purpose reward circuits to mediate social decisions.
- a. Klein, J., Deaner, R.O., and Platt, M.L. 2008. Social valuation signals in macaque parietal area LIP. *Current Biology* 18(6):419-24. PMCID: PMC2362498
  - b. Klein, J and Platt, ML (2013) Social information signaling by neurons in primate striatum. *Current Biology* Volume 23, Issue 8, 691-696. PMCID: PMC3654103
  - c. Shepherd, S.V., Klein, J., and Platt, M.L. 2009. Mirroring of attention by neurons in macaque parietal cortex. *PNAS* 106(23):9489-94. PMCID: PMC2685741
  - d. Watson, K.K., Werling, D., Zucker, N., and Platt, M.L. 2010. Altered social reward and attention in anorexia nervosa. *Frontiers in Psychopathology* 1, article 36. PMCID: PMC3157932
- 3. Neural mechanisms mediating empathy and prosocial behavior.** Empathetic behavior is at the root of cooperation and charity, and is severely compromised in neurodevelopmental disorders such as autism (ASD). Precisely how the brain develops representations of another individual's internal state, how such representations guide social decisions, and how these mechanisms can be disrupted or enhanced by a variety of interventions or manipulations remains unknown. This is a fundamental problem, of high therapeutic, economic, and philosophical interest, the complexity of which has frustrated mechanistic analysis due to the lack of a suitable animal model. To address this gap, we developed a paradigm enabling neurobiological investigation of live interactions between monkeys. Using this set-up, we recently showed male rhesus macaques prefer to donate rewards to another monkey over no one, but prefer to reward self over both monkeys. We probed the biology of this simple interaction in several ways. First we repurposed a pediatric nebulizer to deliver oxytocin (OT), a neuropeptide implicated in social bonding, intranasally. We demonstrated this method results in uptake of OT into the central nervous system and then showed OT increases prosocial behavior and social attention. We next showed intranasal OT reduces vigilance, permitting approach and social behavior. Building on these discoveries, we recently discovered specializations in frontal cortex for processing rewarding experiences in social contexts. Neurons in orbitofrontal cortex signaled self-rewards; neurons in dorsal anterior cingulate cortex signaled foregone rewards; and neurons in anterior cingulate gyrus (ACCg) signaled rewards experienced by another. These findings resonate with prior work showing activation of ACCg and medial PFC in humans associated with empathy and theory of mind. These observations suggest ACCg is a key nexus for computing shared experience, and may be specialized to support complex social decisions in primates.
- a. Chang, S., Winecoff, A., and Platt, M.L. 2011. Vicarious reinforcement in rhesus macaques (*Macaca mulatta*). *Frontiers in Decision Neuroscience*. 5:27. PMCID: PMC3080185
  - b. Chang SW, Barter JW, Ebitz RB, Watson KK and Platt ML (2012) Inhaled oxytocin amplifies both vicarious reinforcement and self-reinforcement in rhesus macaques (*Macaca mulatta*). *Proc Natl Acad Sci*, 109, 959–964. PMCID: PMC3271866
  - c. Chang SW, Gariepy JF, and Platt ML (2012) Neuronal reference frames for social decisions in primate frontal cortex. *Nature Neuroscience*. Dec 23;16(2):243-50. PMCID: PMC3557617

d. Ebitz RB, Watson KK, and Platt ML (2013) Oxytocin blunts social vigilance in the rhesus macaque. PNAS doi:10.1073/pnas.1305230110. PMCID: PMC3710816

**4. Genetic contributions to naturally-occurring variation in social function.** We are studying naturally-occurring variation in genes and behavior in the freely-breeding, free-ranging rhesus macaque population on Cayo Santiago Island off the coast of Puerto Rico. We have made several striking findings. Social skill and temperament are heritable, and thus have a genetic basis. Some of this variation is linked to polymorphisms in genes regulating serotonin signaling. For example, 5-HTTLPR contributes to removal of serotonin from the synapse and is polymorphic in rhesus and human; TPH2 codes for the rate-limiting enzyme in serotonin synthesis and is also polymorphic in both species. Monkeys with the minor allele of both genes are socially peripheral, making fewer allies than monkeys possessing a major allele. Genetic variation in TPH2 also contributes to variation in vigilance, which in turn is associated with social isolation. In the laboratory, we found that variation in 5-HTTLPR predicts elevated arousal and decreased social interest in laboratory assays of social attention. These findings suggest the potential of this population as a natural source of genetic and phenotypic variation or lab studies to determine neural mechanisms underlying these behavioral differences.

- a. Brent LJN, Heilbronner SR, Horvath JE, Gonzalez-Martinez J, Ruiz-Lambides AV, Robinson A, Skene JHP, Platt ML. (2013) Genetic origins of social networks in rhesus macaques. Nature Scientific Reports. 3:1042. PMCID: PMC3540398
- b. Brent LJN, Semple S, MacLarnon A, Ruiz-Lambides A, Gonzalez-Martinez J, and Platt ML (2014) Personality traits in rhesus macaques are heritable but do not predict reproductive output. Int. Journal Primatol. 35, no. 1 (February 2014): 188-209. PMCID: PMC3960078
- c. Watson, K.K., Ghodasra, J.H., and Platt, M.L. 2009. Serotonin transporter genotype modulates social reward and punishment in rhesus macaques. PLoS One 4(1):e4156. PMCID: PMC2612746
- d. Watson, KK, Li, D, Brent, LJN, Horvath, JE, Gonzalez-Martinez, J, Ruiz-Lambides, A, Robinson, AG, Skene, JHP, Platt, ML (2015). Genetic influences on social attention in free-ranging rhesus macaques. Anim. Behav., May 1;103:267–275. PMCID: PMC4448754.

## D. Research Support

### ACTIVE

**R37-MH109728** (Role: PI)

4/20/16 – 1/31/21

#### **Neural Circuit Mechanisms Mediating TMS and Oxytocin Effects on Social Cognition**

Intranasal oxytocin (OT) and transcranial magnetic stimulation (TMS) hold great promise as therapies for impaired social cognition, yet their neuronal bases, as well as safety and effectiveness, are poorly understood. We will address these questions by assessing the impact of focal repetitive TMS (rTMS) and inhaled OT on joint attention, social reward/empathy, and strategic social cognition, while monitoring concurrent neuronal activity in a circuit functionally implicated in social cognition.

**R01-MH108627** (Role: PI)

4/20/16 – 1/31/21

#### **Mechanisms Regulating Complex Social Behavior**

Our goal is to understand how the brain identifies social contexts, evaluates potential outcomes, and guides selection of appropriate behavior in order to provide insight into dysfunctional social behavior and help develop new treatments for neuropsychiatric disorders and disease states that change neural mechanisms involved in self-control. We will answer these questions through an integrated set of experiments conducted in humans and monkeys using similar tasks that manipulate the nature and quality of social contexts, involve both social and non-social reward outcomes, and provide complementary information from functional magnetic resonance imaging (fMRI) in humans, neurophysiological recordings in monkeys, and repetitive transcranial magnetic stimulation (rTMS) in both species including simultaneous neural recordings in monkeys.

**U19-MH108206** (PI: McPartland; Role: PI of Sub)      7/1/15 – 6/30/19

#### **Duke: 3/5 – The Autism Biomarkers Consortium Data Acquisition and Analysis Core (DAAC)**

The intent of the FOA is to qualify a set of measures, including eye-tracking, pupillometry and EEG, that can be used as stratification biomarkers and/or as sensitive and reliable objective measures of social impairment in ASD clinical trials.

**R01-NS088674** (PI: Sommer; Role: Co-I) 8/15/14 – 6/30/19

**Rational Design of TMS for Neuromodulation**

In this project we will vary TMS parameters while simultaneously recording from affected nerve cells in the brain and quantifying the results with computational models to produce a unique data set that will be a valuable resource for clinical researchers who seek to optimize TMS treatments.

**COMPLETED**

**R01 MH096875** (Role: PI) 6/15/12 – 2/28/18

NIH/NIMH

**Animal Model of Genetics and Social Behavior in Autism Spectrum Disorders**

The goal of this project is to develop a fully-realized biological model of the genetic contributions to social behavior phenotype in a natural population of nonhuman primates.

**K01 DA033347** (PI: Addicott; Role: Co-Mentor) 4/1/13 – 3/31/18

NIH/NIDA

**Acute and Chronic Nicotine Modulation of Reinforcement Learning**

This K01 includes a training plan for advancing Dr. Addicott's skills and knowledge in functional magnetic resonance imaging, neuroeconomic decision-making, and nicotine addiction. The goal of the study is to investigate the effects of acute and chronic nicotine on dopaminergic signaling in the mesocorticolimbic pathway.

**1650850** (Role: PI) 03/01/17-02/28/18

National Science Foundation

**Doctoral Dissertation Research: Epigenetic Signatures of Social Isolation in Free-Ranging Primates**

In this project we will examine the distribution of genome-wide DNA methylation (DNAm) through the affiliative networks of freely ranging, freely reproducing rhesus macaques. We will test for the over-representation of DNAm in behavior- and health- implication genetic pathways, including serotonergic signaling.

**SFARI 304935** (Role: PI) 9/1/14 – 8/31/17

Simons Foundation Autism Research Initiative

**Safety, Efficacy and Basis of Oxytocin and Brain Stimulation Therapy in ASD**

Contact PD/PI: Platt, Michael L.

Our goal is to determine the effectiveness, safety, and basis of both transcranial magnetic stimulation (TMS) -- a noninvasive form of brain stimulation -- and inhaled oxytocin (OT) to improve social function. We will answer these questions by measuring the impact of both TMS to the TPJ and inhaled OT on social anxiety, social learning, and prosocial behavior in rhesus macaques. Simultaneously, we will measure brain cell activity in TPJ and anterior cingulate cortex (ACC) as well as changes in brain structure and biomarkers of health.

**R01 MH095894** (Role: PI) 2/21/12 – 11/30/16

NIH/NIMH

**Neuronal Basis of Vicarious Reinforcement Dysfunction in Autism Spectrum Disorder**

Despite a broad continuum of phenotypic variation in behavior, individuals with autism spectrum disorders (ASD) share core deficits in social interaction. Here we propose that social dysfunction in ASD results, in part, from problems in deriving vicarious reward from others. We will use our new animal model of vicarious reward to discover how the brain signals vicarious reward, discover the impact of brain dysfunction on vicarious reward, and test how oxytocin, a potential therapy for ASD, might improve vicarious reward and brain function.

**R21 NS084176** (PI: Pearson; Role: Advisor) 4/15/14 – 3/31/16

NIH/NINDS

**Mechanisms of Parkinsonian Impulsivity in Human Subthalamic Nucleus**

We propose to characterize the patterns of neural activity underlying these failures of impulse control in an actual Parkinson's patient population undergoing surgery for the implantation of DBS electrodes. Such procedures offer a unique opportunity to collect data at the single neuron level in humans.

**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: David Victor Smith

ERA COMMONS USER NAME (credential, e.g., agency login): dvsmith84

POSITION TITLE: Assistant Professor of Psychology

**EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of South Carolina (Columbia, SC)	B.S.	05/2006	Experimental Psychology
Duke University (Durham, NC)	Ph.D.	05/2012	Cognitive Neuroscience
Rutgers University (Newark, NJ)	Postdoc	12/2016	Social Neuroscience

**A. Personal Statement**

My research to date has centered on characterizing the neurobiological mechanisms that construct our preferences and shape our choices. Over the course of my career, I have gained substantial experience in conceptual issues relating to cognitive and social neuroscience. For instance, my work has contributed to neuroscientific models of decision making and reward processing. In addition, I have also developed extensive analytical expertise in neuroimaging, particularly multivariate pattern analysis and brain connectivity approaches, such as dual-regression analyses, that examine brain-behavior relationships. These analytical approaches are crucial for understanding how the striatum and its connections with prefrontal cortex contribute to decision making and reward processing. My methodological and conceptual contributions are summarized and integrated with other work in my recent reviews and commentaries (see below). I have also recently initiated a collaboration with Dr. Jarcho on a pending grant application investigating aberrant reward sensitivity in substance use. Based on my expertise in brain connectivity analyses and current collaborations with Dr. Jarcho, Tessa's primary sponsor, I am well equipped to mentor Tessa Clarkson and her proposed application and training plan.

- a. **Smith DV** & Delgado MR (2015). Reward Processing. In A. W. Toga (Ed.), *Brain Mapping: An Encyclopedic Reference* (1st ed., pp. 361-366). Waltham, MA: Academic Press. PMCID: Not Available
- b. **Smith DV** & Delgado MR (2015). Social Nudges: Utility Conferred from Others. *Nature Neuroscience*, 18(6), 791-792. PMCID: PMC Journal - In Process
- c. **Smith DV** & Delgado MR (2017). Meta-Analysis of Psychophysiological Interactions: Revisiting Cluster-Level Thresholding and Sample Sizes. *Human Brain Mapping*, 38(1), 588-591. PMCID: PMC5148685
- d. Diehl MM, Lempert K, Parr AC, Ballard I, Steele VR, **Smith DV** (2018). Toward an Integrative Perspective on the Neural Mechanisms Underlying Persistent Maladaptive Behaviors. *European Journal of Neuroscience*, 48(3), 1870-1883. PMCID: PMC6113118

**B. Positions and Honors**Employment:

- |              |   |
|--------------|---|
| 2006-2012    | Graduate Student, Center for Cognitive Neuroscience, Duke University, Durham, NC.   |
| 2012-2016    | Postdoctoral Fellow, Department of Psychology, Rutgers University, Newark, NJ.      |
| 2017-present | Assistant Professor, Department of Psychology, Temple University, Philadelphia, PA. |

Other Experience and Professional Memberships:

- |              |   |
|--------------|---|
| 2004-present | Member, Cognitive Neuroscience Society  |
| 2007-present | Member, Society for Neuroscience  |
| 2007-present | Member, Organization for Human Brain Mapping  |
| 2008-present | Member, Society for Neuroeconomics  |
| 2011-present | Ad hoc manuscript reviewer for 38 journals (verified history: <a href="https://publons.com/a/1204254">https://publons.com/a/1204254</a> ) |

2015-present	Member, Social & Affective Neuroscience Society
2015	Ad hoc grant reviewer, Israel Science Foundation
2015-2017	Review Editor, <i>Frontiers in Neuroscience</i> ("Decision Neuroscience" section)
2016-present	Member, Association for Psychological Science
2017	Ad hoc grant reviewer, FWF Austrian Science Fund
2017	Ad hoc grant reviewer, Swiss National Science Foundation
2017	Ad hoc grant reviewer, Wellcome Trust
2018-present	Member, Society of Biological Psychiatry
2014 & 2018	Ad hoc grant reviewer, Scientific Research Network on Decision Neuroscience & Aging
2018-present	Academic Editor, <i>PLoS ONE</i> .

**Honors:**

2002	LIFE Scholarship, University of South Carolina.
2004	Baroody Scholar Award, University of South Carolina.
2004	<i>Phi Beta Kappa</i> Freshman Scholar Award, University of South Carolina.
2005	Fellow, NSF Summer Research Institute, University of South Carolina.
2005	<i>Phi Beta Kappa</i> , University of South Carolina.
2006	Roger Black Award for Psychological Research, University of South Carolina.
2007	Travel Award, Organization for Human Brain Mapping Conference.
2009	Fellow, Summer Institute in Cognitive Neuroscience, UC - Santa Barbara.
2009	Ruth L. Kirschstein Predoctoral National Research Service Award, NIMH.
2015	Merit Abstract Award, Organization for Human Brain Mapping.
2015	Ruth L. Kirschstein Postdoctoral National Research Service Award, NIMH.
2016	NIDA Director's Travel Award, The College on Problems of Drug Dependence.
2016	Young Investigator Travel Award, NIDA Symposium on Persistent Maladaptive Behaviors.
2016	Rising Star, Association for Psychological Science.
2017	Top Reviewer in the field of Neuroscience (Publons)
2018	Top Reviewer in the fields of Multidisciplinary and Neuroscience & Behavior (Publons)

**C. Contributions to Science**

\* Denotes shared first authorship

**1. Brain Systems Supporting Valuation.** Many of our decisions force us to compare a wide range of disparate rewards—from the economic incentive of money to the social incentive of praise from a peer. How do we compare distinct incentives and choose between them? Although economists have theorized that these decisions require each incentive to be transformed into a common currency, evidence for such signals in the brain have remained elusive. We addressed this problem in a series of experiments involving economic and social rewards. We provided the first evidence that a neural common currency signal was represented in a posterior region of ventromedial prefrontal cortex (VMPFC). Strikingly, VMPFC responses to economic and social rewards predicted individual differences in subjective value for those goods. In a follow up study, we strengthened the link between VMPFC and subjective value by demonstrating that changes in VMPFC responses following total sleep deprivation predicted concomitant changes in subjective value. My recent work extends these observations by quantifying how common currency signals within VMPFC rely on connectivity with other brain regions. Taken together, these studies illustrate how VMPFC plays a central role in choice, thus providing a foundation for understanding neurological diseases and psychopathologies characterized by aberrant decision making and reward processing.

- a. **Smith DV**, Hayden BY, Truong T-K, Song AW, Platt ML, Huettel SA (2010). Distinct Value Signals in Anterior and Posterior Ventromedial Prefrontal Cortex. *Journal of Neuroscience*, 30(7), 2490-2495. PMCID: PMC2856318
- b. Libedinsky C, **Smith DV**, Teng CS, Namburi P, Chen V, Huettel SA, Chee MLW (2011). Sleep Deprivation Alters Valuation Signals in the Ventromedial Prefrontal Cortex. *Frontiers in Behavioral Neuroscience*, 5:70. PMCID: PMC3199544
- c. **Smith DV**, Clithero JA, Boltuck SE, Huettel SA (2014). Functional Connectivity with Ventromedial Prefrontal Cortex Reflects Subjective Value for Social Rewards. *Social Cognitive and Affective Neuroscience*, 9(12), 2017-2025. PMCID: PMC4249475

**2. Brain Connectivity Patterns Underlying Decision Making and Reward Processing.** The striatum—which receives inputs from the prefrontal cortex and the midbrain—serves as a critical nexus for reward processing. Yet, understanding the link between striatum and reward presents a challenge because rewards are composed of multiple properties. Notably, affective properties modulate emotion while informative properties help obtain future rewards. Although both properties contribute to the reward response, understanding how each property is encoded remains a puzzle. We approached this problem by creating separate tasks emphasizing affective and informative reward properties. Although the striatum responded similarly to affective and informative reward properties, we found that striatal connectivity with ventrolateral prefrontal cortex (VLPFC) distinguished reward properties. Our recent work has quantified the consistency and specificity of the brain connectivity analysis approach used here and in our other papers: psychophysiological interaction (PPI) analysis. We performed a series of meta-analyses on 284 PPI studies. Our findings indicated that brain connectivity patterns revealed via PPI are reliable across studies and are specific to the process and neural system under investigation (e.g., reward and the striatum). In an exploratory analysis, we also identified a striatal-VLPFC pathway that was robust across studies, thus supporting our earlier findings and motivating efforts to understand corticostriatal interactions further in other grant submissions. We also have used neuroimaging data to refine popular psychological theories of decision making. For instance, we tested the standard interpretation of the gain-loss framing effect (i.e., a competition between reason and emotion) against alternative explanations that would predict different connectivity patterns. Our study concluded that the framing effect results from an unexpected source: differential cognitive engagement across frames. Finally, my lab has recently shown that reward-processing abnormalities in major depressive disorder are associated with blunted responses in the striatum and hyper responses in the orbitofrontal cortex, which we argue may be indicative of a dysregulated corticostriatal connectivity.

- a. **Smith DV**, Rigney AE, Delgado MR (2016). Distinct Reward Properties are Encoded via Corticostriatal Interactions. *Scientific Reports*, 6, 20093. PMCID: PMC4735713
- b. **Smith DV**, Gseir M, Speer ME, Delgado MR (2016). Toward a Cumulative Science of Functional Integration: a Meta-Analysis of Psychophysiological Interactions. *Human Brain Mapping*, 37(8), 2904-17. PMCID: PMC49454364.
- c. Li R\*, **Smith DV\***, Clithero JA, Venkatraman V, Carter RM, Huettel SA (2017). Reason's Enemy is Not Emotion: Engagement of Cognitive Control Networks Explain Biases in Gain/Loss Framing. *Journal of Neuroscience*, 37(13), 3588-3598. PMCID: PMC5373136
- d. Ng TH, Alloy LB, **Smith DV** (2018). Meta-analysis of Reward Processing in Major Depressive Disorder: Distinct Abnormalities within the Reward Circuit? *bioRxiv*. Link to preprint: <https://www.biorxiv.org/content/early/2018/05/29/332981>

**3. Methodological Innovations and Data Rigor in Neuroimaging.** Given the complexity of our decisions (and our behavior more generally), approaches to studying decision making should be a constant target of innovation. A large focus of my work has aimed to innovate analytical approaches in neuroimaging and provide tools for the community. We have identified critical differences between within- and cross-participant classification approaches—observations that should help guide researchers considering multivariate pattern analysis (MVPA). In addition, we pioneered efforts to apply MVPA to lesion mapping, which helps clinicians to overcome several issues that plague standard univariate analyses. Our other work extends this theme of examining how multiple brain regions contribute to behavior by improving functional connectivity analyses. We used independent component analysis (ICA) combined with dual-regression analysis to estimate connectivity with large-scale neural networks. Importantly, our study demonstrated that ICA combined with dual regression predicts individual differences (i.e., sex differences) better than canonical approaches that only consider specific nodes of a neural network. We also have used this approach to validate a probabilistic atlas of the midbrain, which we have made freely available to the community to help catalyze basic and clinical research focusing on the midbrain. Taken together, these studies advance analytical procedures within the neuroimaging community and provide models for enhancing data rigor and reproducibility (e.g., quantification of sex differences, large samples, and split-sample validations).

- a. Clithero JA, **Smith DV**, Carter RM, Huettel SA (2011). Within- and Cross-Participant Classifiers Reveal Different Neural Coding of Information. *NeuroImage*, 56(2), 699-708. PMCID: PMC2908207
- b. **Smith DV**, Clithero JA, Rorden C, Karnath H-O (2013). Decoding the Anatomical Network of Spatial Attention. *Proceedings of the National Academy of Sciences of the USA*, 110(4), 1518-1523. PMCID: PMC3557038

- c. **Smith DV**, Utevsky AV, Bland AR, Clement NJ, Clithero JA, Harsch AE, Carter RM, Huettel SA (2014). Characterizing Individual Differences in Functional Connectivity Using Dual-Regression and Seed-Based Approaches. *NeuroImage*, 95(1), 1-12. PMCID: PMC4074548
- d. Murty VP, Shermohammed M, **Smith DV**, Carter RM, Huettel SA, Adcock RA (2014). Resting State Networks Distinguish Human Ventral Tegmental Area from Substantia Nigra. *NeuroImage*, 100(1), 580-589. PMCID: PMC4370842

**4. Functional Significance of Large-Scale Neural Networks.** My recent work uses analytical innovations to address key issues in neuroscience, particularly those relating to the functional significance of large-scale neural networks. One such issue centers on the role of the precuneus in large-scale neural networks. We found that the precuneus is a functional core of the default-mode network, showing increased connectivity during rest states. Strikingly, however, the same portion of precuneus exhibited increased connectivity with a fronto-parietal network during task states. These results highlight the flexibility of precuneus and underscore the importance of considering how each brain region operates as part of a larger network depending on the processing state. In addition, we also have shown that reduced synchrony between large-scale networks contributes to variation in autistic traits, extending theories that autism is due to underconnectivity. Connectivity with large-scale networks also plays an important role in decision making and behavioral change following feedback. Whereas previous work indicates that the medial prefrontal cortex (MPFC) promotes behavioral change, it remains unclear whether these changes are due to the default-mode network or the executive control network because the MPFC is at the intersection of both networks. Our novel analytical approach—ICA combined with dual-regression—allowed us to separate these networks and examine how each contributes to behavioral changes. We found that behavioral changes were associated with distinct patterns of connectivity: MPFC increased connectivity with the default-mode network while the temporal-parietal junction decreased connectivity with the executive control network. Our most recent work integrates PPI with dual regression analysis—an approach we call network PPI (nPPI)—to further probe the functional significance of large-scale neural networks. Taken together, these studies highlight the importance of studying the brain as a system of interacting regions. Advancing models of brain connectivity and functional integration may lead to a better understanding of the neural systems that contribute to a host of psychiatric and neurological diseases.

- a. Utevsky AV, **Smith DV**, Huettel SA (2014). Precuneus is a Functional Core of the Default-Mode Network. *Journal of Neuroscience*, 34(3), 932-940. PMCID: PMC3891968
- b. Young JS\*, **Smith DV\***, Coutlee CG, Huettel SA (2015). Synchrony Between Sensory and Cognitive Networks is Associated with Subclinical Variation in Autistic Traits. *Frontiers in Human Neuroscience*, 9:146. PMCID: PMC4369640
- c. **Smith DV\***, Sip KE\*, Delgado MR (2015). Functional Connectivity with Distinct Neural Networks Tracks Fluctuations in Gain/Loss Framing Susceptibility. *Human Brain Mapping*, 36(7), 2743-55. PMCID: PMC4736507
- d. Utevsky AV, **Smith DV**, Young JS, Huettel SA (2017). Large-Scale Network Coupling with the Fusiform Cortex Future Social Motivation. *eNeuro*, 4(5), 1-12. PMCID: PMC5635486

**5. Linking Electrophysiology and Neurological Injury to Cognitive Processes.** Although much of my work has relied on neuroimaging (i.e., fMRI), my use of this tool has been informed by other neuroscientific approaches—e.g., electroencephalography (EEG), neuropsychology, and single-unit recordings. For example, we have shown that single-unit activity in posterior cingulate, a key node of the default-mode network, tracks trial-to-trial fluctuations in engagement and cognitive control. We also have used event-related-potentials and EEG to provide insight into how spatial attention circuits rapidly modulate specific aspects of sensory processing. In addition, my work has incorporated behavioral data from patients suffering from neurological injury (e.g., strokes and other brain lesions). Observing how neurological injuries cause specific deficits in behavior and cognition has highlighted the importance of incorporating causal techniques (e.g., noninvasive brain stimulation) into my work. Taken together, this diverse background has given me a unique perspective on my neuroimaging work and has helped me develop an integrative view of neuroscience.

- a. Hayden BY, **Smith DV**, Platt ML (2009). Electrophysiological Correlates of Default-Mode Processing in Macaque Posterior Cingulate Cortex. *Proceedings of the National Academy of Sciences of the USA*, 106(14), 5948-5953. PMCID: PMC2667004
- b. Hayden BY, **Smith DV**, Platt ML (2010). Cognitive Control Signals in Posterior Cingulate Cortex. *Frontiers in Human Neuroscience*, 4:223. PMCID: PMC3001991

- c. Appelbaum LG, **Smith DV**, Boehler CN, Wen C, Woldorff MG (2011). Rapid Modulation of Sensory Processing Induced by Stimulus Conflict. *Journal of Cognitive Neuroscience*, 23(9), 2620-2628. PMCID: PMC3096678
- d. Jelsone-Swain L, **Smith DV**, Baylis GC (2012). The Effect of Stimulus Duration and Motor Response in Hemispatial Neglect During a Visual Search Task. *PLoS ONE*, 7(5), e37369. PMCID: PMC3360686

Complete list of published work in My Bibliography (35 publications):

<http://www.ncbi.nlm.nih.gov/sites/myncbi/david.smith.5/bibliography/41143875/public>

Google Scholar *h*-index: 19 (i10-index: 24; total citations: 1487)

## D. Research Support

### ACTIVE

NIH R21-MH113917	(PI: Smith)	7/1/2017-4/30/2020
Title: "Remote Modulation of Reward Circuits with Noninvasive Brain Stimulation"		
Goal: This project integrates noninvasive brain stimulation with measures of brain connectivity during reward processing. The overarching goal is to determine whether stimulation applied to cortical regions results in downstream modulation of the striatum.		
Role: PI, with Co-I Krekelberg		
NIH R21-MH116422	(PI: Butler)	5/1/2018-3/31/2020
Title: "Social Reward Learning in Schizophrenia"		
Goal: The major goal of this grant is to assess social reward learning deficits in schizophrenia using behavioral paradigms and fMRI.		
Role: Consultant		
OVPR Small Grant Program Temple University	(PI: Smith)	1/1/2018-12/31/2019
Title: "Modulating Individual Differences in Reward Sensitivity with Transcranial Current Stimulation"		
Goal: This small grant examines associations between transcranial current stimulation and factors tied to behavioral reward sensitivity, including social and economic decision making.		
Role: PI		

### PENDING

NIH R03-DA046733	(PI: Smith)	8/1/2019-7/31/2020
Title: "Aberrant Reward Sensitivity: Mechanisms Underlying Substance Use"		
Goal: This project examines how neural responses to social and nonsocial rewards are associated with reward sensitivity and substance use.		
Role: PI, with Co-Is Alloy, Chein, Jarcho, and McCloskey		

### COMPLETED (last three years)

NIA/NIH	(PI: Smith)	10/1/2017-12/31/2018
Title: "Social Reward and Aging: Identifying the Neural Underpinnings of Peer Influences"		
Goal: In this pilot interdisciplinary grant, we aim to investigate the neural markers that underlie age-dependent changes in social reward processing, including decisions to trust peers relative to strangers.		
Role: Subaward PI (on Samanez-Larkin R24-AG054355)		
NIH F32-MH107175	(PI: Smith)	4/1/2015-12/31/2016
Title: "Parsing Reward: Identifying Distinct Neural Pathways for Specific Reward Properties"		
Goal: The primary research goal of this project is to study how corticostriatal systems contribute to affective and informative reward properties. Studying these reward properties provides training opportunities in high-resolution neuroimaging, physiological recordings of arousal, and multivariate analyses of neuroimaging data.		
Role: PI		

**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.**

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NAME: Philip C. Kendall, Ph.D., ABPP

---

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

---

POSITION TITLE: Distinguished University Professor and Laura H. Carnell Professor of Psychology Temple University; Director, Child and Adolescent Anxiety Disorders Clinic (CAADC)

**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 <i>(if applicable)</i>	Completion Date MM/YYYY	FIELD OF STUDY
Old Dominion University, Norfolk, VA	B.S.	1972	Psychology
Virginia Commonwealth Univ., Richmond, VA	PhD	1978	Clinical Psychology

**A. Personal Statement**

I have the clinical, research, treatment and mentoring experience to oversee the completion of the proposed project. Over the past 35 years I have developed psychosocial interventions for youth (including CBT programs for anxiety in youth) and I have completed and published reports of the outcomes of several randomized clinical trials that evaluated these interventions, including being a PI for one of the CAMS sites (a collaborative multi-site trial). The CBT that was implemented in CAMS was the Coping Cat program, and I developed and did some of the early evaluations of the program. Similarly, I developed the computer-assisted programs for the present project and was involved with their initial evaluations. I have been active in the conduct of treatment evaluation studies, the development of measures to assess treatment outcome and treatment fidelity, the provision of training and supervision of CBT for child anxiety, and I have examined the predictors, moderators, and mediators of treatment outcomes. I have also facilitated the dissemination and implementation of empirically supported treatments. NIMH / NICHD has supported the majority of this work. Publications related to this work are among those listed in this biosketch. I was PI on a recently completed NICHD-funded 3-site evaluation of approaches for the treatment of anxiety in children with ASD and I was PI on the NIMH-funded project entitled "Disseminating evidence-based practice to the schools: CBT for child anxiety." I have also recently initiated a collaboration with Dr. Jarcho, Tessa's primary sponsor; therefore, I am well-suited to mentor Tessa on the clinical aspects of her application and training plan as well as professional development.

**B. Positions and Honors****Positions**

- 1977; 1980-1981 Fellow, Center for Advanced Study in the Behavioral Sciences, Stanford, CA.  
 1983-1984. Full Professor and Director, Doctoral Program in Clinical Psychology, University of  
 1984-2001. Director, Doctoral Program in Clinical Psychology, Temple University  
 1985-96 Journal Editor: Cognitive Therapy and Research  
 1996-02 Journal Editor: Journal of Consulting and Clinical Psychology  
 2002-10 Journal Editor: Clinical Psychology: Science and Practice  
 2005 Research Recognition Award, from the ADAA (Anxiety Disorders Association of America).  
     Inaugural award for research contributions to advance the understanding of anxiety disorders  
     in children and teens

2006	Distinguished Scientific Contribution Award, from the Society of Clinical Psychology (Division 12) of the American Psychological Association
2007	Distinguished Career Research Award, from the Society of Clinical Child and Adolescent Psychology (Division 53) of the American Psychological Association
2014-2017	Associate Editor: <u>American Psychologist</u>
2014	Distinguished Scientist Award. Awarded by the Society for a Science of Clinical Psychology (SSCP) of the Association for Psychological Science (APS)
2016	Aaron T. Beck Award for Significant and Enduring Contributions to Cognitive Therapy. Awarded by the Academy of Cognitive Therapy, New York, October, 2016.

### C. Contribution to Science

One of the most common difficulties among youth is anxiety, with estimated prevalence rates ranging from 10 to 20% in community/clinical samples. Youth with anxiety experience difficulties in social and peer relations (Settipani & Kendall, 2013; Verduin & Kendall, 2008), and when left untreated, anxiety disorders can have a negative impact on family relations (Essau, Lewinsohn, Olaya, & Seeley, 2014; Ezpeleta, Keeler, Erkanli, Costello & Angold, 2001; Swan & Kendall, 2016) and quality of life (Mendlowicz & Stein, 2000). Fortunately, treatments such as cognitive behavioral therapy (CBT) and medications have been developed and evaluated, and are considered efficacious (Hollon & Beck, 2013). However, these treatments are not entirely successful and, therefore, need to be enhanced/improved.

#### My work (with illustrative citations provided) has...

**C1: evaluated treatments for anxiety in youth.** Several RCTs have been conducted and reported, including comparisons of treatment modalities.

Kendall, P. C., Cummings, C. ...& Albano, A. M. (2016). Mediators of change in the Child/Adolescent Anxiety Multimodal treatment Study. Journal of Consulting and Clinical Psychology, 84, 1-14.

Kendall, P. C., & Peterman, J. (2015). CBT for anxious adolescents: Mature yet still developing. American Journal of Psychiatry, 172, 519-530.

Peris, T., Compton, S., Kendall, P. C., Birmaher, B., ..., & Piacentini, J. (2015). Trajectories of change in youth anxiety during cognitive-behavior therapy. Journal of Consulting and Clinical Psychology, 83, 239-252.

Wolk, C. B., Kendall, P. C., & Beidas, R. (2015). Cognitive-behavioral therapy for child anxiety confers long-term protection from suicidality. Journal of the American Academy of Child and Adolescent Psychiatry, 54, 175–179.

#### **C2: considered parents and examined parent factors in treatment for anxious youth**

Manassis, K., ...Kendall, P. C., ...& Wood, J. (2014). Types of parental involvement in CBT with anxious youth: A preliminary meta-analysis. Journal of Consulting and Clinical Psychology, 82, 1163-1172.

Settipani, C. & Kendall, P. C. (2017). The effect of child distress on accommodation of anxiety: Relations with maternal beliefs, empathy, and anxiety. Journal of Clinical Child and Adolescent Psychology, 46, 810-823.

Kagan, E., Peterman, J. S., Carper, M. M., & Kendall, P. C. (2017). Accommodation and treatment of anxious youth. Depression and Anxiety, 24, 78-98.

Settipani, C., O'Neil, K., ...& Kendall, P. C. (2013). Youth anxiety and parent factors over time: Directionality of change among youth treated for anxiety. Journal of Clinical Child and Adolescent Psychology, 42, 9-21.

#### **C3: advanced theoretical understandings of the nature and development of anxiety in youth**

Cummings, C., Caporino, N., & Kendall, P. C. (2014). Comorbidity of anxiety and depression in children and adolescents: 20 years after. *Psychological Bulletin*, 140, 816-845.

Kendall, P. C., Swan, A., Carper, M., & Hoff, A. (2018). Anxiety disorders among children and adolescents. In J. N. Butcher and P. C. Kendall (Eds.). *APA handbook of psychopathology: Vol 2. Psychopathology of children and adolescents*. Washington DC: APA Books

Peterman, J., Carper, M., & Kendall, P. C. (2016). Testing the habituation-based model of exposures for child and adolescent anxiety. *Journal of Clinical Child and Adolescent Psychology*, 29, 1-11.

Kerns, C., Kendall, P. C., ...& Herrington, J. (2014). Traditional and atypical presentations of anxiety in youth with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, 44, 2851-2861.

#### **C4: facilitated the dissemination and implementation of empirically supported treatments**

Kendall, P. C. & Frank, H. (in press). Implementing evidence-based treatment protocols: Flexibility within fidelity. *Clinical Psychology: Science and Practice*, in press.

Kendall, P.C., Gosch, E., Furr, J., & Sood, E. (2008). Flexibility within fidelity. *Journal of the American Academy of Child and Adolescent Psychiatry*, 47, 987-993.

Kendall, P. C. & Beidas, R. (2007). Smoothing the trail for dissemination of evidence-based practices for youth: Flexibility within fidelity. *Professional Psychology: Research and Practice*, 38, 13-20.

McLeod, B., Jensen-Doss, A., ...Southam-Gerow, M., Weisz, J., & Kendall, P. C. (2016). The role of setting versus treatment type in alliance within youth therapy. *Journal of Consulting and Clinical Psychology*, in press

#### **C5: developed and evaluated computer-based programs related to youth with anxiety.** These computer programs facilitate dissemination and include a parent training program.

Khanna, M. & Kendall, P. C. (2010). Computer-assisted cognitive-behavioral therapy for child anxiety: Results of a randomized clinical trial. *Journal of Consulting and Clinical Psychology*, 78, 737-745.

Kendall, P. C., Carper, M., M., Khanna, M., S., & Harris, M. S. (2015). Computer technology and children's mental health, in *Emerging Trends in the Social and Behavioral Sciences* (eds.) Robert Scott and Stephen Kosslyn, Hoboken, NJ: John Wiley and Sons.

Khanna, M. & Kendall, P. C. (2015). Bringing technology to training: Web-based therapist training to promote competent cognitive-behavioral therapists. *Cognitive and Behavioral Practice*, 22, 291-301.

Pramana, G., Parmanto, B., Kendall, P. C., & Silk, J. (2014). The SmartCAT: An mHealth platform for Ecological Momentary Intervention in child anxiety treatment. *Telemedicine and E-Health*, 20, 419-427.

#### **D. Research Support**

Recently Completed:

NICHD "3/3 Treatment of Anxiety in Autism Spectrum Disorder

Period: February 2014 - January 2017. \$570,111.00

This three-site project was a randomized clinical trial examining approaches for the treatment of anxiety in youth ages 7-13 with ASD. This project was just completed and data analyses and manuscript preparation are well underway.

Recently Completed:

NIMH- "4/6 Child/Adolescent Anxiety Multimodal Extended Long-Term Study (CAMELS).

Period: 9/1/2010 – 8/31/2016; Total costs \$649,329.00

This project was a five-year naturalistic follow-up of patients who were part of the CAMS trial. This project included diagnostic and other evaluations' of participants at different times over the five-year period. The project was completed with the primary findings in press and secondary research reports in revision for publication.

**Recently Completed**

NIMH – Disseminating evidence-based practice to the schools: CBT for child anxiety

Period: 12/14/2010 – 11/30/2017; Total costs \$1,633,273.

This project involved gathering assessment data on child anxiety in schools, followed by a training phase (assessing and treating child anxiety), and a phase for the assessment of the sustainability. Systems measures, including measures of the school climate and features of the therapists, were gathered and examined as predictors of differential sustainability. A research report is under review.

**PHS Fellowship Supplemental Form****Introduction**

1. Introduction to Application  
(for Resubmission applications) Resubmission Introduction.pdf

**Fellowship Applicant Section**

2. Applicant's Background and Goals for Fellowship Training\* BackgroundTraining.pdf

**Research Training Plan Section**

3. Specific Aims\* Specific Aims.pdf  
 4. Research Strategy\* Research Strategy.pdf  
 5. Respective Contributions\* Respective Contributions.pdf  
 6. Selection of Sponsor and Institution\* Selection Sponsor\_Instit.pdf  
 7. Progress Report Publication List  
(for Renewal applications)  
 8. Training in the Responsible Conduct of Research\* Responsible Conduct.pdf

**Sponsor(s), Collaborator(s) and Consultant(s) Section**

9. Sponsor and Co-Sponsor Statements Sponsor Statement.pdf  
 10. Letters of Support from Collaborators, Contributors and Consultants Letters of Support\_Final.pdf

**Institutional Environment and Commitment to Training Section**

11. Description of Institutional Environment and Commitment to Training Institutional Environment.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 Animals Used?  Yes  No

12. 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

13. Vertebrate Animals

**PHS Fellowship Supplemental Form****Other Research Training Plan Information**

14. Select Agent Research

15. Resource Sharing Plan

16. Authentication of Key Biological and/or Chemical Resources

**Additional Information Section****17. Human Embryonic Stem Cells**Does the proposed project involve human embryonic stem cells?\*  Yes  No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s), using the registry information provided within the agency instructions. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

 Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s):


18. Alternate Phone Number:

19. Degree Sought During Proposed Award:

Degree:

If "other", indicate degree type:

Expected Completion Date (MM/YYYY):

PHD: Doctor of Philosophy

05/2022

20. Field of Training for Current Proposal\*:

600 Clinical Psychology

21. Current or Prior Kirschstein-NRSA Support?\*

 Yes  No*If yes, identify current and prior Kirschstein-NRSA support below:*

Level*	Type*	Start Date (if known)	End Date (if known)	Grant Number (if known)
.....	.....	.....	.....	.....
.....	.....	.....	.....	.....
.....	.....	.....	.....	.....

22. Applications for Concurrent Support?\*

 Yes  No*If yes, describe in an attached file:*

23. Citizenship\*

U.S. Citizen  U.S. Citizen or Non-Citizen National?  Yes  NoNon-U.S. Citizen  With a Permanent U.S. Resident Visa  
 With a Temporary U.S. VisaIf 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: 

Name of Former Institution:\*

24. Change of Sponsoring Institution

**PHS Fellowship Supplemental Form****Budget Section****All Fellowship Applicants:**

25. Tuition and Fees\*:

None Requested       Funds Requested

Year 1	\$5,358.00
Year 2	\$5,520.00
Year 3	\$0.00
Year 4	\$0.00
Year 5	\$0.00
Year 6 (when applicable)	\$0.00
<b>Total Funds Requested:</b>	<b>\$10,878.00</b>

**Senior Fellowship Applicants Only:**

26. Present Institutional Base Salary:	Amount	Academic Period	Number of Months
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27. Stipends/Salary During First Year of Proposed Fellowship:

a. Federal Stipend Requested:	Amount	Number of Months
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b. Supplementation from Other Sources:	Amount	Number of Months
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Type (e.g.,sabbatical leave, salary)

Source

**Appendix****28. Appendix**

## INTRODUCTION TO RESUBMITTED F31 APPLICATION

I thank the reviewers, who describe my mentorship team and I as “outstanding,” provide “high marks for overall impact and significance”, and note “excellent training potential” for my training plan and study. Primary concerns and additional issues raised by reviewers led to significant improvements, as described below.

### Responses To Primary Issues Raised By Multiple Reviewers

1. The social anxiety (SA) moderator was not described clearly and may be better specified by a confirmatory factor analysis (CFA). I agree that a CFA would be more appropriate for the SA moderator variable. Thus, will pre-specify a CFA model based on our recently published the exploratory factor analysis SA model<sup>1</sup>. Details about analytic technique have been added to the Research Strategy (C.1.8), and details regarding training plan have been added to the training goals and objectives (2).
2. Lack of neuroimaging pilot data. The LEARN task is variant of scanner-designed<sup>1,3</sup> task and an EEG task (Research Strategy C1.1.1 Fig. 3 A & B). However, to enhance confidence in the successful translation of the LEARN task, specifically, to fMRI and generating neural responses within our regions of interest (ROI), we conducted a pilot study that detected meaningful peer-type differences in our ROIs based on social learning; and these differences related to SA symptoms. Pilot results have added to the Research Strategy (C.1.1).
3. Relatively ambitious plan within two years. The proposed study and training plan are ambitious; however, my sponsors and I are confident in my ability to carry out all planned activities. This confidence is informed by my productivity in the last *two-year period*, in which I published or submitted 11 manuscripts (6 first author, 4 with primary sponsor), attended ~3 conferences a year at which I presented 4 symposia/talks (1 chaired) and 25 posters. Concurrently, I was trained and became reliable on administering the Autism Diagnostic Observation Schedule, attended AFNI bootcamp (fMRI analyses), and learned and applied factor-analytic methods in the context of a first-author publication<sup>1</sup>. Moreover, I was recognized for my exceptional achievements through a master’s thesis award, multiple travel awards, and was recently nominated to receive a departmental accommodation in recognition of excellence in all areas of training (i.e. research, academics, and clinical practice). While ambitious, we believe I will successfully achieve the proposed plan to publish 4 papers, attend 3 conferences a year, and learn 3 primary skills. To retain feasibility, I focus on building foundational skills, including having an in depth understanding of functional connectivity (FC) analyses as a primary training goal. In response to a minor concern of the relatively straightforward nature of FC analyses raised by reviewer 1, further clarification to the original training plan of the exploratory aim (*cutting-edge model-based dual regression*) and clearer emphasis on the proposed advanced neuroimaging analyses training (model-based fMRI analyses) have been more fully described in the training plan (see Training Goals and Objectives 3). Thus, my training plan is ambitious yet feasible as it is balanced between building foundational and advanced analyses skills.

### Response To Additional Issues Raised by Reviewer 1

1. Applicant's undergraduate grades and GRE scores demonstrate variability. While my undergraduate grades and GRE scores are variable, my achievements over the last three years demonstrate they do not accurately reflect my abilities and potential. An additional letter of recommendation from Dr. Adams (undergraduate professor) will also speak to the failure of these metrics to accurately capture my abilities.
2. Aim 2 may not provide valuable data for future grant applications. Despite our promising preliminary data, it is possible FC analyses will fail to yield significant results. To ensure Aim 2 yields valuable data in the event of null FC results, I will also explore *model-based* network FC analyses and conduct other model-based fMRI analyses (Research Strategy C1.1.1). Quantifying task-based effects on functional engagement, regardless of FC will yield important insights into relations of social learning and SA. Irrespective of outcome, the training potential for fMRI study design and analysis will provide me the skills needed to apply for future funding applications (see Training Goals and Objectives 1B and 3).

### Response To Additional Issues Raised by Reviewer 2

1. Lack of resource sharing plan. Though not required for F31s, a resource sharing plan is included (Research Strategy C.5).

### Response To Additional Issues Raised by Reviewer 3

1. Concern regarding junior faculty primary sponsor. Although Dr. Jarcho is a junior faculty, she is ideally suited to be my primary sponsor as she has extensive expertise in fMRI task design and imaging. Her long track record of success starts with her own F31, followed by two intramural grants awarded during her time at the NIMH, and a NARSAD young investigator award. She is currently the PI on an R21, and co-I on R03 and R01 awards. Critically, she has also successfully mentored an F31 recipient (Dr. Jackson) and has the support of both Drs. Platt and Kendall who have extensive experience mentoring F31 fellowships.

## DOCTORAL DISSERTATION AND RESEARCH EXPERIENCE

**Primary School and Undergraduate Research:** My devotion to empirical discovery began in the 4<sup>th</sup> grade, when my project on the heritability of eye color and fingerprint characteristics garnered me first prize at the state science fair. In high school I discovered my longstanding passion for understandings the neural mechanisms of behavior. I reviewed the neurophysiological effects of drug and alcohol on the brain and worked with administrators to implement a curriculum describing neuropsychosocial factors that influence substance use under social pressure.

At Boston University, I expressed my commitment to translating scientific research to real world social benefit as a Peer Health Exchange volunteer. I drew on my coursework and cardiology internship examining electrophysiological abnormalities of the pediatric heart to teach adolescents in underserved communities about the effects of stress, risky decision-making, and substance use on the body. Through these experiences I became interested in understanding how physiological activity in children and adolescents influence cognitive functioning and decision-making abilities to shape long-term quality of life.

**Post-Baccalaureate Research:** After graduating with a B.S. in human physiology, I became a research assistant with *Drs. Omar Khawaja & Walter E. Kaufmann* at Boston Children's Hospital/ Harvard Medical School (BCH/HMS). I worked on a randomized controlled trial (RCT) investigating the efficacy of insulin growth factor 1 in ameliorating symptoms in Rett Syndrome (RTT). RTT is a female predominant neurodevelopmental disorder characterized by a developmental regression resulting in impairments in motor, language, autonomic functioning. Such deficits result in challenges for assessing cognition and pain in RTT, which impact quality of life. I used electro-dermal activity (EDA) and brain activity via electroencephalography (EEG) to measure possible drug effects. This work lead to a coauthored publication using EDA as an objective index of pain in RTT, which could have broad impacts for measuring pain in disorders with similar motor and language deficits. This project piqued my interest in utilizing physiological techniques and behavioral measures to predict perceptions of pain, which, like social cognition, is perceived differently across individuals and contexts.

I continued to work on this and 2 additional projects developing assessments for girls with RTT in *Dr. Charles Nelson*'s lab. I assumed a leadership role in creating a developmental-cognitive assessment for girls with RTT. I utilized eye-gaze and eye-tracking technology to eliminate the need for fine motor control when assessing other developmental domains. This work led to 2 poster presentations and a first-author publication that was the first to isolate specific developmental impairments and preserved skills in RTT. I disseminated this work by training 5 staff members in administration and scoring procedures, and published the manualized protocol for others to utilize in clinical and research settings. This project solidified my belief in the utility of using multiple units of analysis to assess cognition across development.

During my time in Dr. Nelson's lab, I contributed to 4 additional projects identifying neurophysiological biomarkers for Autism Spectrum Disorder (ASD) in children at-risk for ASD due to Tuberous Sclerosis, 16p, or sibling ASD. I used EEG time-frequency (TF) and event-related potential (ERP) analysis, functional Near-Infrared Spectroscopy (fNIRS), and eye-tracking to monitor early social development. Through these projects I first became interested in the development of social cognitive impairments, and the use of neural indicators for examining changes in the brain that may precipitate long-term impairments in social skills.

When *Dr. Susan Faja* joined BCH/HMS I had the opportunity to help build her translational neuroscience lab. As lab manager, I worked with Dr. Faja to validate a battery of brain and behavioral measures that test for differences in executive functioning (EF) in children with and without ASD. The battery included multiple units of analysis, such as neural measures (EEG), subjective reports from multiple informants, and behavioral EF tasks, which we used to assess RCT-related changes in executive functioning (EF) in children with ASD. As a side project, I investigated mechanisms that could account for the variance we observed in our neural measures of EF. Specifically, I used phase-locked TF analysis to identify individual and group level differences in medial frontal theta contributions to EEG components implicated in error monitoring in volatile situations. In sum, this work lead to 9 poster presentations and 1 published second-author publication, and two coauthor publications currently under review. Importantly, this work kindled my interest in the role of prediction errors in social learning, and how these deficits might contribute to impairments in social skills in ASD.

My post baccalaureate training refined my interest in understanding how altered neural mechanisms related to learning may shape social experiences in clinical populations. I learned the merit in using multiple units of analysis to measure changes in cognition as a result of atypical development and after intervention. Together, these experiences culminated in my pursuit of a Ph.D. in clinical psychology to investigate neural mechanisms of social cognition in individuals with social anxiety (SA) disorder and ASD.

**Pre-Doctoral Research:** I gained admission to the clinical psychology Ph.D. program at Stony Brook University under the mentorship of Dr. Johanna Jarcho, an expert in social developmental neuroscience and fMRI, and Dr. Matthew Lerner, an expert in ASD, social skills intervention development, and EEG.

One of my first goals in graduate school was to better assess SA and social functioning. Although impairments in social communication and restricted, repetitive behaviors are core deficits in ASD, most individuals with ASD have complex symptom profiles that are similar to (or co-occur with) SA disorder. To disentangle these symptoms, I sought to isolate a brain-based index of SA in individuals with ASD. With Dr. Lerner's mentorship, I tested the relation of two candidate EEG-measures, the error-related negativity (ERN) and hemispheric asymmetry, with changes in anxiety symptoms in ASD. This project led to a co-first authored publication, highlighting the utility of these measures for assessing baseline, and treatment-related change in SA in ASD. Through this project I gained the advanced statistical skills needed to predict symptom change from brain function, and furthered my interest in examining neural mechanisms of prediction error in shaping SA symptoms. Additionally, I received training and became research reliable on the Autism Diagnostic Observation Schedule (ADOS-2), which assess for social impairments specific to ASD. This project inspired me to chair a symposium at the International Society for Autism Research conference discussing the utility of neural measures in assessing social functioning and predicting treatment response to various interventions in ASD.

In order to investigate mechanisms involved in social processing, I conducted a meta-analysis quantifying measures of social processing across RDoC units of analysis in children and adolescents (conditionally accepted). The results highlighted the importance of circuit-level units of analysis for examining the complex nature of social processing. These findings motivated my interest in using neuroimaging to determine how differences in brain function contribute to the formation of maladaptive social functioning in youth. Accordingly, in Dr. Jarcho's lab, for my master's thesis, I leveraged existing data collected in an on-going longitudinal project at the NIH and gained formal training in multivariate analysis to examine the neural mechanisms by which early childhood social reticence confers risk for SA during the transition from pre- to mid-adolescence. We found that among youth at risk for developing SA due to early childhood social reticence, dysregulated neural responses in the salience and reward networks during social interactions in preadolescence predicted more severe SA in mid-adolescence. My first author manuscript received the *Excellence in Research* award at Stony Brook University. This work shed light on the essential role changes in neural activation in the reward and salience networks have in the emergence of SA, however the mechanisms by which early risk and social environment influence dysregulation in these regions remains unclear.

To begin isolate specific mechanisms of dysregulated neural responses in SA, I initiated a multimodal fMRI/EEG study examining potential shared neural mechanisms between non-social and social contexts. Specifically, I tested the relations between a well-established biomarker for anxiety that indexes error processing, the error-related negativity (ERN), during a non-social EEG task and neural activation patterns during an ecologically valid social interaction fMRI-task and their relations to SA. To do this, I was trained to acquire fMRI data and attended AFNI bootcamp at the NIH to learn fMRI preprocessing and analysis skills. Final analysis and write-up of this study for publication are ongoing. Dovetailing this project, I designed an EEG study that tested the electrophysiological correlates of learning from social feedback that served as pilot data for this proposal (see C.1.1 of Research Strategy). The goal of this EEG project was to isolate potential behavioral and electrophysiological mechanisms of social learning in adolescents. This work was promising enough to motivate Dr. Lerner and I to conduct a follow-up study to isolate individual differences in social learning in youth with and without ASD. Additionally, this project has allowed me to gain rudimentary skills in assessing brain and behavioral changes during social learning. Specifically, I have been able to fit regression models to learning curves in order to estimate learning rates and their relations to electrophysiological responses. However, regression estimates are not well suited for modeling social learning curves, nor do they model parameters that may influence learning rates, such as the peer value, valence and volatility of social feedback. Moreover, electrophysiological responses are useful for examining timing of social learning processes, but are not well-suited to estimate impairments in neural circuit communication. Indeed, our preliminary EEG results suggests there are changes in mean amplitude of neural responses to peer feedback before and after learning. However, it is unclear if these changes are a result of greater neural network communication, or an increase in the salience of peer feedback over time. Such distinctions are better made by examining network-level communication during learning from social feedback. Thus, analyses on this EEG project has emphasized my need for advanced training in computational modeling designed to measure learning rates, and advanced neuroimaging training to estimate network-level mechanisms of social learning.

Together my experiences in graduate school have provided me with the foundation necessary for acquiring the skills proposed in my training plan, which will in turn, enable me to accomplish my research goals. Recently I relocated to Temple University with Dr. Jarcho's entire lab. Here I have the unique opportunity to work with my sponsors Drs. Jarcho and Michael Platt (U Penn), and my collaborators Drs. David Smith, and Phil Kendall to continue to grow my skill set. The proposed training plan includes mentorship in fMRI-study design, computational modeling, functional connectivity (FC) analyses, and clinical assessment. These skills are essential for expanding my research program to ask more sophisticated questions regarding the developmental mechanisms of social functioning in clinical populations.

**Doctoral Dissertation:** The proposed project is intended to serve as my doctoral dissertation; thus, data collection has not yet begun.

## TRAINING GOALS AND OBJECTIVES

The goal of this training plan is to prepare me to become an independent clinical social neuroscientist in an academic position researching the etiology of social impairments in clinical populations. Ultimately, I aim to leverage multimodal techniques to understand how neural mechanisms influence the emergence of social deficits. This aim corresponds with my long-term goal of elucidating underlying mechanisms of social dysfunction that can provide novel targets for interventions for at-risk youth.

My four training objectives are designed to enable me to achieve a career as an independent investigator who conducts social developmental neuroscience research in clinical populations. Specifically, I will obtain training in (1) fMRI-study design (2) computational model development and comparison, (3) FC analyses, and (4) professional development. To achieve these objectives, I selected mentors with expertise that complements that of my primary sponsor, and educational experiences that expand on the traditional requirements of my doctoral program. This training will facilitate my development as an independent clinical social neuroscientist, provide me with the necessary skills to successfully execute the proposed research, and enable me to make progress towards my long-term career and research goals.

### 1. fMRI-Study Design.

(A) Ecologically-valid fMRI task design. Ecologically-valid paradigms approximate real-world situations that elicit SA may uniquely identify targets for novel SA treatment. Thus, developing skills in ecological-valid fMRI paradigm design and data acquisition are essential for me to achieve my training and career goals. Dr. Jarcho (mentor), has considerable experience developing ecologically valid fMRI tasks to assess social functioning<sup>1</sup>. Through weekly meetings with Dr. Jarcho I will ensure the LEARN task (Research Strategy C.1.5) evokes SA in an ecologically valid context, while maximizing experimental control over valence, volatility, and social value of purported peers. Mentorship from Dr. Jarcho is intended to provide a strong conceptual and technical understanding of acquiring fMRI data while using ecologically-valid social tasks. Dr. Jarcho and I will work with physicists (Dr. Huiling Peng) in weekly meetings during the pilot-phase to select and optimize neuroimaging acquisition parameters for the proposed project (year 1). This training will maximize the generalizability and validity of my research, and provide me with a foundation for becoming the PI of a lab that performs fMRI-based research.

(B) Application of computational models to neuroimaging data. Computational modeling will permit me to isolate neural mechanisms of social learning that may promote SA. Training in cutting-edge methodologies in computational [model-based neuroimaging] will allow be to be at the forefront of the clinical social neuroscience field. I will consult with Dr. Platt to ensure the LEARN task is suitable for model-based neuroimaging. During meetings with Drs. Platt (bi-weekly) and Jarcho (weekly) I will utilize the best-fit computational models to localize learning-dependent changes in functional connectivity elicited by the LEARN task. Additionally, I will attend the Temple University Brain Imaging Center (TUBRIC) and Decision Neuroscience journal clubs lead by Dr. Smith and present articles on model-based imaging. To gain further exposure to cutting edge modeling techniques, I will attend the Organization of Human Brain Mapping (OHB) conference and participate in tutorials, workshops, and talks devoted to model-based imaging. After, I will discuss what I have learned with my sponsors and consultants so they can help me implement my new skills to my work. I will solidify what I have learned from these training experiences by leading a workshop on model-based imaging for my department and applying for presentations at the OHBM conference. I will prepare a first-author manuscript utilizing these methodologies with the data collected in my proposed study addressing aim 2 during Year 2 of this award.

**2. Model Development and Comparison of Behavioral Social Learning.** Model development and comparison skills are vital for allowing me to expand learning models to complex social neuroscience questions. [I will first learn to design and assess fit of a confirmatory factor analyses model to be used as a dimensional measure of SA.] Then, by learning to develop new models I can parameterize vital aspects of social interactions,

such as the valence and volatility of peer feedback, which may impact social learning. By achieving this training goal, I will successfully complete aim 1 and develop skills required to meet my career goals of determining mechanisms of social learning that may promote SA in youth. My co-sponsor, Dr. Platt is an internationally recognized expert in model development and comparison with 38 grants supporting this work and 120 published papers on these topics. Dr. Platt has used learning models to study how social connections are formed using measures of behavior, brain function, and physiology. As co-sponsor for the proposed project, he will (1) supervise model development and parameter optimization for data collected in the proposed study, (2) supervise model comparison and selection, (3) and provide guidance on how to incorporate modeling techniques I learn from his lab and through workshops into future grant applications to identify different factors that may influence social learning in clinical populations. He has agreed to meet with me bi-weekly throughout the project, with additional meetings as needed. I will also attend his lab meetings and seek additional supervision from post-doctoral and graduate students in his lab. To augment training with cutting-edge modeling skills and applications, I will attend the Reinforcement Learning and Decision Making (RLDM) conference and participate in tutorials, workshops, and talks devoted to modeling methods. At the conference, I will have the opportunity to expand my professional network across disciplines. With the help of Dr. Platt, I will apply my newly acquired modeling skills by preparing a first-author manuscript using previously collected pilot data (year 1) and data collected for this project addressing aim 1 (year 2).

**3. Functional Connectivity Analyses.** Though computational modeling of social learning is critical for understanding how social context modulate social learning and promote SA, isolating neural mechanisms of social learning within and between neural networks is paramount for developing novel treatment targets for SA. Under the mentorship of Dr. Jarcho, I will first learn to conduct FC analyses using psychophysiological interactions (PPI) analyses [*with social learning model-based regressors (M1-3 Research Strategy C see C.2.1 and Fig 4)*] in reward and salience networks to examine FC of social learning and its relations to SA. Most previous studies have only examined activation and FC with a single seed region, possibly missing important interactions between networks implicated in social learning. Thus, I will also gain skills in the application of [*cutting-edge model-based] dual regression analyses*, which will allow me to determine neural mechanisms of social learning within and between the reward and salience networks simultaneously, thereby estimating unique and interactive contributions of both networks in facilitating social learning. Unlike [*traditional FC*] analyses, this approach isolates spatial and temporal changes in networks of interest (salience and reward networks), rather than using predefined regions. Thus, dual-regression may better capture the dynamic and complex nature of social learning, [*particularly in hub regions such as the vmPFC*]. By achieving this training goal, I will successfully complete aim 2 in the research proposal. Dr. Smith is an expert in dual regression analyses and has published several papers using dual-regression analyses in decision making neuroimaging paradigms. Through regularly scheduled meetings with Dr. Smith, and participation in bi-weekly TUBRIC and Decision Neuroscience journal clubs on advanced neuroimaging methods lead by Dr. Smith, I will learn to apply these methodologies [*and other advanced computational model-based fMRI analyses*] to the fMRI data collected in the proposed project. To cement these skills, I will give a guest lecture in Dr. Smith's course advanced fMRI methods. Additionally, I will apply for the MIND summer institute program at Dartmouth college and the Kavli Summer Institute in cognitive neuroscience, which cover topics including computational modeling, experimental design, and their applications to social neuroscience. [*Regardless of the outcome of FC analyses, I will generate meaningful data that will allow for examination of task-effects and other computational and causal model-based analyses to broaden my neuroimaging skillset and inform future grant applications.*] In year 1 I will develop and refine the FC pipeline for my imaging data. Then, in year 2, I will analyze the data from the proposed study, present these findings at the FLUX conferences, and generate a first-authored manuscript (aim 2).

**4. Professional Development.** A principal training goal of the proposed project is to capitalize on opportunities generated by receiving a NRSA to develop my program of research, inform future grant applications, and assist in obtaining internship/postdoc experiences that will foster my career as an independent clinical scientist. Mentorship from my primary sponsor, Dr. Jarcho, who has had a prolific academic career (40 publications), will be a vital part of this training goal. We will use weekly one-on-one meetings to finalize first-authored manuscripts during years 1 & 2 from previously collected data and data collected in the proposed study. Using previously collected data, I will examine the shared neural mechanisms between the error-processing in non-social contexts and brain function during social interactions task, and their relations to SA. A second manuscript will describe learning rates in healthy adolescents using computational models on the pilot study data, which will inform model development for the proposed project. My co-sponsor, Dr. Platt, will provide additional modeling consultation on these projects, as needed. During Year 2, Dr. Jarcho and I will prepare

additional manuscripts contributing to my independent line of research on the neural mechanisms of social learning and the development of social impairments. One paper will examine differences in social learning rates, and parameters that modulate learning to fear social feedback in adolescents with varying degrees of SA (aim 1). Another will isolate social learning-dependent changes in FC in the brain and their relations to SA in adolescents (aim 2). Opportunities for involvement in additional research papers will be discussed with Dr. Jarcho. Finally, my mentorship team will provide guidance during both Years 1 and 2 on applying for F32 NRSA and K awards, building on results from the current proposal to begin to utilize neural mechanisms as predictors of treatment response to interventions for adolescents with SA. These experiences will be invaluable in helping to facilitate my growth as an independent researcher.

To develop my skills as a clinical scientist I will work Dr. Kendall to learn to assess and treat children and adolescents with SA disorder and other anxiety disorders. Dr. Kendall has had a prolific academic career (650+ publications, 35+ years of uninterrupted grant support) and is internationally recognized expert in research and cognitive behavior therapy for child anxiety disorders. The proposed project will function as an optional pre-treatment visit for patients who come into Dr. Kendall's Child and Adolescent Anxiety Disorders Clinic (CAADC). With Dr. Kendall's supervision, I will become reliable in administering the Anxiety and Related Disorders Interview Schedule for DSM-5 (ADIS-5) and will work in his clinic doing pre-treatment and post-treatment diagnostic assessments of anxiety disorders, including SA. Additionally, I will learn to deliver the empirically supported Coping Cat intervention to these patients. The training and mentorship provided by Dr. Kendall will allow me to gain critical clinical skills in assessing SA as well as knowledge of current treatments for SA, that can inform my research in elucidating underlying neural mechanisms of the etiology of SA.

#### **ACTIVITIES PLANNED UNDER THIS AWARD**

A comprehensive training plan has been designed in consultation with my mentorship team to develop my expertise in computational modeling methods, FC analysis, fMRI study design, and clinical assessment of SA. Activities planned under this award are outlined in Table 2 and detailed below.

**Research.** The proposed training plan includes mentorship from Drs. Jarcho and Platt and other experts in fields highly relevant to the proposed project. Dr. Jarcho will assess the overall progress of the research, data collection, and training activities during weekly meetings throughout years 1 and 2. In addition, we will review study design and scanning parameters during the piloting of the study with the TUBRIC physicist (Dr. Huiling Peng). Data collection will be conducted in year 1 and into year 2, along with analyses and manuscript preparation. I will meet with my co-sponsor Dr. Platt bi-weekly throughout the project while developing and refining my modeling skills. Dr. Smith (consultant) will meet with Dr. Jarcho and I regularly (e.g., bi-weekly) during stages of developing (year 1) and implementing (year 2) the FC pipelines on the fMRI data. Finally, funding from this fellowship will also allow me to attend and prepare presentations for annual conferences relevant to my development as a clinical social neuroscientist (e.g., RLDM, OHBM, & FLUX). In addition to keeping me aware of current advances in computational modeling and imaging approaches, attending these conferences will allow me to interact and communicate with top researchers in the field, participate in additional workshops on computational modeling, and present my own research.

**Courses.** I will guest lecture in Dr. Smith's course on advanced fMRI analyses in year 1. Through the consolation of my mentorship team, I will solidify my understanding of model-based imaging by leading a workshop for my department and delivering presentations for Temple-Penn journal clubs. I also will apply to an additional 9-day workshop at Dartmouth College and the Kavli Summer Institute in Cognitive Neuroscience in the summer of Year 1 to learn cutting-edge model-based imaging in social neuroscience.

**Clinical.** In line with program requirements and training goals, I will become reliable on the ADIS and begin to provide services at the Child and Adolescent Anxiety Disorders Clinic (CAADC).

#### **Specific Activities for Year 1 (08/2019-08/2020)**

**Research (75%).** Develop and compare computational models using pilot behavioral data via bi-weekly meeting with Drs. Platt; prepare and submit manuscripts and present findings at the RLDM conference. Pilot LEARN task and scan acquisition parameters with Dr. Jarcho and TUBRIC physicist (Dr. Huiling Peng). Begin data collection. Prepare and submit additional manuscripts using existing data with Dr. Jarcho on prediction error in SA disorder and social learning in adolescents.

**Courses (15%).** Guest lecture in advanced fMRI analyses course at Temple University; apply for MIND summer institute at Dartmouth College and Kavli Summer Institute. Attend bi-weekly TUBRIC and Decision Neuroscience journal clubs on advanced neuroimaging lead by Dr. Smith.

**Clinical (10%).** Practicum at Dr. Kendall's Child and Adolescent Anxiety Disorders Clinic (CAADC).

#### **Specific Activities for Year 2 (08/2020-08/2021)**

**Research (80%).** Continue to receive training and consultation on computational modeling and model-based imaging from Drs. Platt and Smith as needed; complete data collection; develop and implement FC pipelines with Drs. Jarcho and Smith. Present findings at FLUX conferences; prepare and submit manuscripts examining results from aim 1 and aim 2. Prepare and submit additional manuscripts with Dr. Jarcho.

**Courses (10%).** After consulting Drs. Jarcho, Platt and Smith, I will lead a workshop on model-based imaging at Temple. Attend bi-weekly TUBRIC and Decision Neuroscience journal clubs on advanced neuroimaging lead by Dr. Smith.

**Clinical (10%).** Practicum at Dr. Kendall's CAADC.

<b>Table 2. Proposed Activities: Training goals, mentorship, coursework, and research activities</b>				
<b>Year</b>	<b>Training Goals</b>	<b>Coursework/Activities</b>	<b>Training/Mentorship</b>	<b>Research Activities</b>
1	fMRI-study Design	-Task design and scan parameter piloting -initiate data collection - OHBM tutorials, workshops, and talks	- Dr. Platt: bi-weekly - Dr. Jarcho weekly - Dr. Huiling Peng (Physicist) weekly during pilot-phase	- OHBM conference
	Model Comparison and Development	-develop & compare computational models	- Dr. Platt: bi-weekly	- 1 first-author publication (using existing data) - RLDM conference
	Dual Regression Analyses	- MIND/Kavli training program -TUBRIC & Decision Neuroscience journal clubs -Guest lecture advanced fMRI course	- Dr. Smith: bi-weekly - Dr. Jarcho: weekly	- FLUX conference
	Professional Development	- Propose Dissertation - ADIS reliability training - Coping Cat training	- Dr. Jarcho: weekly - Dr. Platt: bi-weekly - Dr. Kendall: monthly - Diagnostic Meetings: weekly - Clinical Supervision: weekly	- 1 additional first-author publication (using existing data)
2	fMRI-study Design	- OHBM tutorials, workshops, and talks - Lead local workshop	- Dr. Platt: bi-weekly - Dr. Jarcho weekly	- 1 first-author publication (Aim 2 data) - OHBM conference
	Model Comparison and Development	- RLDM tutorials, workshops, and talks	- Dr. Platt: bi-weekly - Dr. Atlas as needed	- 1 first-author publication (Aim 1 data) - RLDM conference
	Dual Regression Analyses	-complete data collection -develop/apply dual regression pipeline - TUBRIC & Decision Neuroscience journal Club	- Dr. Smith: bi-weekly - Dr. Jarcho: weekly	- FLUX conference
	Professional Development	- Complete and Defend Dissertation - F32 submission - ADIS assessments -Coping Cat clinician	- Dr. Jarcho: weekly - Dr. Platt: bi-weekly - Dr. Kendall: monthly - Diagnostic Meetings: weekly - Clinical Supervision: weekly	- additional co-authored publications

## Specific Aims.

Social anxiety (SA) disorder is prevalent<sup>1</sup>, chronic<sup>2</sup>, and impairs quality of life<sup>3,4</sup>. Typical onset occurs in early adolescence<sup>2</sup>, and increases dramatically between 10-15 years of age<sup>5</sup>. During this time, social relationships become more salient and complex, thus difficulties learning from nuanced interactions may increase SA<sup>6-11</sup>. To successfully navigate this complex social landscape, adolescents must learn to make appropriate decisions about social behavior. One way they do this is by updating their predictions about peer feedback based on prior encounters<sup>11</sup>. Although SA is associated with suboptimal adaptive learning rates in non-social<sup>9-11</sup> and uncertain contexts,<sup>8,9</sup> little is known about relations between SA and learning from social feedback, which is central SA<sup>6,12-14</sup>. Moreover, in SA, social feedback is associated with dysregulated engagement of neural circuits implicated in salience and reward processing<sup>15-17</sup>, which are also critical for learning and decision-making<sup>9,10,18-21</sup>. Despite this overlap, the neural mechanisms that support learning from social feedback remain relatively unexplored in SA. Treating deficits in social learning may diminish acute SA before it becomes chronic thereby preventing the high costs of adult SA<sup>22</sup>. Progress towards this goal has been hindered by the limited application of well-established computational methods to social contexts. The proposed work addresses these limitations by combining computational modeling and fMRI to isolate the neural mechanisms by which peer feedback modulates social learning rates, and to determine the extent to which social learning influences SA in adolescents.

My long-term goal is to become an independent clinical social neuroscientist dedicated to examining etiopathogenic mechanisms of SA that can inform novel treatment targets. My training objectives are to gain skills in computational modeling and fMRI-study design and analysis. These goals coincide with my research objective, to apply computational models to fMRI data obtained with a social interaction task to elucidate mechanisms by which social learning may promote SA in adolescents. Specifically, I will quantify social learning while adolescents (N=60; 10-15 years) with varying degrees of SA complete my novel fMRI-based Learning from Evaluation And Recall of iNteractions (LEARN) task, which varies peer value, valence, and volatility parameters during real-time social interactions.

**Aim 1. A) Develop and compare models for social learning using the valence, peer value, and volatility of social feedback as parameters; B) Test relations between social learning rates and severity of SA.** Difficulty recalling and predicting positive<sup>-8</sup>, but not negative<sup>23,24</sup> peer feedback<sup>23-25</sup>, greater peer value<sup>26</sup>, and greater volatility of peer feedback<sup>9</sup> independently impair rates of learning in SA. Although valence, salience, and volatility of outcomes are common parameters in traditional learning models, they are rarely extended to the social domain. Reinforcement models estimate learning by computing the difference between predicted and expected valence of social feedback (prediction error) multiplied by a constant learning rate, not accounting for the salience (peer-value), or degree of certainty within a context<sup>27</sup>. Whereas, associative models adjust learning rates based on salience factors (i.e. peer value) and feedback valence, they do not account for degree of certainty within a context<sup>28</sup>. Combined approaches estimate learning rates that can adapt to volatile conditions, while modeling the valence of predictions and salience factors, and may thereby best capture complexities of the social-context<sup>11,16,17</sup>. I predict that A) the combined vs other models will optimally predict learning; B) more severe SA will correspond to suboptimal learning rates when interacting with high-value peers, when receiving uncertain positive feedback.

**Aim 2. Determine the extent to which within and between network functional connectivity (FC) evoked by social learning during social feedback relates to severity of SA.** Slower learning is associated with positive connectivity within the reward network<sup>29</sup> and negative connectivity in the salience network<sup>30</sup>. Although converging evidence also suggests the value<sup>29,31</sup>, valence<sup>32,33</sup>, and volatility<sup>30,33,34</sup> of social feedback evoke differential responses in reward and salience network in SA, little is known about how these parameters influence neural mechanisms implicated in social learning. Furthermore, neuroimaging studies examining value, valence, or uncertainty of social feedback typically measure activation or FC within either the salience<sup>30</sup> or reward<sup>29</sup> circuit, despite evidence that communication between circuits may facilitate learning<sup>15,16,35</sup>. Using FC analyses that integrate modeled learning rates, I will isolate neural mechanisms of social learning within and between the reward and salience networks and their relations to SA. I predict that more severe SA and suboptimal social learning rates will be associated with positive FC within the reward network<sup>29</sup> and negative FC in the salience network<sup>30</sup> during the receipt of positive peer feedback. Exploratory aim: I predict that more severe SA and suboptimal social learning rates will be associated with dysregulated FC between networks.

Given my prior training, promising preliminary data, expert mentorship team, and access to resources I am well positioned to undertake this work. By completing the proposed research, I will receive training in computational modeling and fMRI methods to establish the role of perturbed social learning in the etiology of SA. This will provide me with preliminary data for future grants and lay the foundation for my career as a clinical social neuroscientist.

## Research Strategy.

### A. Significance.

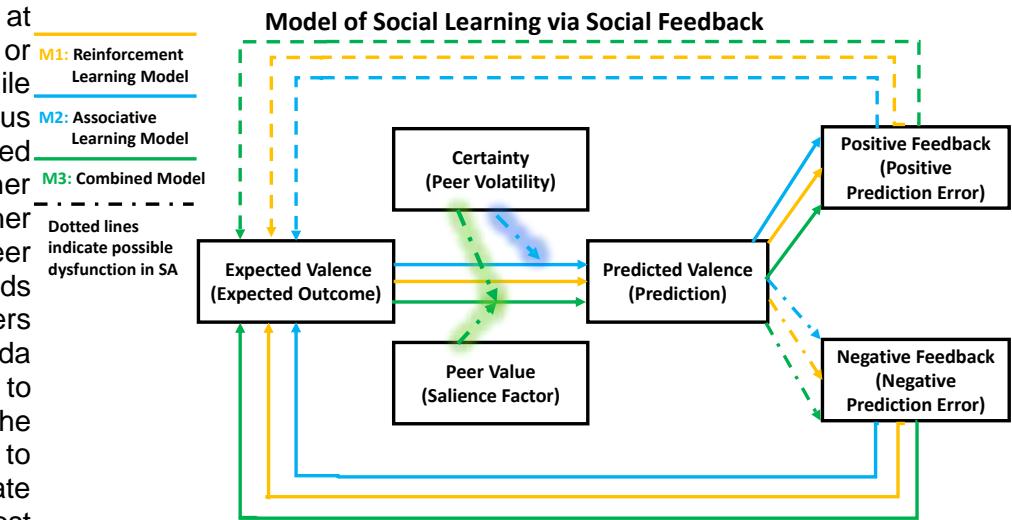
**A.1 Overview.** Social anxiety (SA) disorder is a chronic condition<sup>2</sup> that affects over 13% of the population<sup>1</sup>. Typical onset occurs in early adolescence<sup>2</sup> and peaks at 10-15 years of age,<sup>5</sup> when complexity of the social milieu and desire for social acceptance increase<sup>36</sup>. In the context of this increasing complexity, deficits in the capacity to learn about others may contribute to a core symptom of SA: fear of negative social feedback<sup>6,7</sup>. Adaptive learning in unpredictable social contexts may be crucial for youth to adjust to rapidly changing adolescent social contexts<sup>37</sup>. Because early onset SA is associated with more severe<sup>38-40</sup>, costly<sup>22</sup>, comorbid<sup>41</sup> and long-lasting symptoms<sup>42</sup>, isolating etiopathogenic mechanisms of SA is imperative<sup>1,40,43</sup>. While available SA treatment can reduce symptoms, they rarely result in full remission<sup>44,45</sup>. Targeting dysregulation in neural circuits of social learning may enhance treatment efficacy in SA<sup>11,46-48</sup>. An important first step toward developing such treatments is to isolate parameters of social interactions, such as peer value, or valence or (un)certainty of peer feedback, that may modulate neural mechanisms of social learning in SA. Progress towards this goal has been hindered by the limited use of computational methods in the context of social learning. The proposed study addresses this limitation by combining computational modeling and functional neuroimaging to establish how social contexts modulate learning rates in adolescents with a range of SA symptoms.

**A.2 Adolescent susceptibility for SA.** SA disorder is characterized by an intense fear of negative social feedback<sup>49</sup>. Symptoms are potentiated in uncertain or novel contexts<sup>7,8,50-52</sup> and when peer feedback has greater social value or importance<sup>53,54</sup>. Adolescence is a sensitive period for developing SA, likely due to an increased desire for peer acceptance<sup>36</sup> and the emergence of complex social relationships<sup>55</sup> that necessitate learning from more nuanced interactions. These changes coincide with fine-tuning of neural circuits implicated in reward and salience processing, which support social learning and decision making. Development of brain regions associated with social learning (ventral medial prefrontal cortex (vmPFC), insula, and dorsal anterior cingulate cortex (dACC) during adolescence are related to changes in neural responses to social experiences<sup>56-59</sup> and peer feedback<sup>60</sup>. Difficulty learning about others may promote fear of negative evaluation, a hallmark symptom of SA disorder<sup>61</sup>. Thus, early adolescence is a critical age for isolating maladaptive mechanisms of social learning, which may lay the foundation for severe and chronic SA.

**A.3 Computational models of learning and their neural correlates.** Well-established computational models utilize different parameters to estimate learning in the non-social domain. Reinforcement learning models (**M1; Fig 4**) estimate learning by computing prediction errors, such that positive errors reflect outcomes that were better than expected and negative errors reflect outcomes that were worse than expected. Learning is achieved by updating expectations in proportion to the prediction error and a constant learning rate<sup>27</sup>. Alternatively, associative learning models (**M2; Fig. 4**) estimate learning via the valence of prediction errors and the salience of the outcome, regardless of environmental uncertainty<sup>28</sup>. Recent studies have combined these approaches (**M3; Fig. 4**) to allow learning rates to be dynamically adjusted based on the valence of the prediction error, salience of the outcome, and level of (un)certainty in the environment<sup>11,16,17,62</sup>. Reinforcement and associative learning are encoded in brain regions shared by (vmPFC; C.3.2 Fig.5) and unique to the reward (striatum) and salience (insula, dACC, and amygdala) networks. In the reward network, the striatum encodes the perceived *value* of a stimulus<sup>63-65</sup> and varying degrees of perceived *(un)certainty* of the reward<sup>66,67</sup>. Specifically, larger positive prediction errors evince greater striatal activity, whereas larger negative prediction errors evince decreased striatal activation<sup>15,34,68,69</sup>. Similarly, in the salience network, the dACC and insula encode the perceived value of a stimulus<sup>16,70</sup>, as well as varying degrees of perceived *(un)certainty* in the environment<sup>11,17</sup>. Specifically, greater environmental uncertainty is associated with greater insula and dACC activity. Moreover, an overlapping region of the reward and salience network, the vmPFC<sup>71-73</sup>, is critical for learning based on past experiences<sup>15,16,35</sup>. Thus, learning may be best understood by probing inter-network relations. By extending and comparing different models of learning, I can isolate the parameters that most contribute to impaired social learning and dysregulated neural responses to social contexts.

**A.4 Extending learning models to SA.** While primarily implemented in non-social domains, the parameters of computational learning models (M1-3) can be leveraged to isolate the etiopathogenic mechanisms of SA. For example (Fig. 1), Sam is popular and Linda values becoming her friend (peer value), and may expect her to be nice (expected value). Their initial interaction is positive; thus, Linda predicts that their next interaction will be positive (predicted valence). However, during their next encounter Sam tells Linda how awful she looks (negative feedback). Linda may attribute the negative encounter to a bad mood (peer volatility), and since she still values Sam's friendship (peer value), she decides to approach her again. After several interactions, Linda determines that Sam is very unpredictable (peer volatility). Because of this, Linda may change her behavior or her thoughts about how nice Sam is prior to their next interaction (updated expected value). Learning to adapt to nuanced

social situations is therefore critical to social competence. Indeed, SA is associated with deficits in learning and recalling social rules<sup>74</sup>, updating predictions about social feedback<sup>33</sup>, and maladaptive behavioral responses to that feedback. Although limited research has probed the neural mechanisms of social learning in SA, emerging evidence suggests parameters critical to learning elicit altered neural response in the reward and salience networks during social feedback with highly-valued<sup>33,36</sup> volatile peers, particularly when they provide positive feedback<sup>12,14,33</sup>. Yet the extent to which seemingly critical parameters of the social context influence peer-based learning are largely unknown. To test this, (M1; Fig.1) reinforcement learning models consider Linda's expectations about Sam based on their prior interactions (expected value) and how accurate Linda is at predicting whether Sam was going to be nice or mean (prediction errors), irrespective of how much Linda values this feedback (peer value) or Sam's moodiness (peer volatility). Whereas, (M2; Fig.1) associative learning models consider how accurate Linda was at predicting whether Sam was going to be nice or mean (prediction errors), while considering all of her previous interactions with Sam (expected value), and how much she valued her feedback (peer value), regardless of her moodiness (peer volatility). Lastly, (M3; Fig.1) combined models consider how accurate Linda was at predicting whether Sam was nice or mean (prediction errors), while considering all of her previous interactions with Sam (expected value), how much she valued her feedback (peer value), and her degree of moodiness (peer volatility). Thus, each model adds additional contextual parameters that may influence how quickly Linda learns about Sam, and how to interact with her. By comparing the efficacy of different models to estimate social learning, I will isolate the contextual parameters that most contribute to impaired social learning in youth with varying degrees of SA.



**Fig. 1** Heuristic Model of mechanisms of social learning from peer feedback and social anxiety symptoms, dotted lines denoting possible impairments with the social learning process mechanism in SA. Highlighted regions indicate differences between models.

**A.5 Neural mechanisms that support social learning and SA overlap.** As in non-social learning, reward and salience networks are also implicated in social learning. In adolescents, faster social learning evinces stronger within reward-network coupling during negative-vs-positive feedback<sup>75</sup>. Activation within the salience network also varies as a function of the valence of peer feedback<sup>30,76</sup>, which may be a critical parameter of social learning. In social contexts, aspects of the reward network (striatum) may be involved in social reward processing and reinforcement learning while aspects of the salience network (dACC, insula, and amygdala) may enhance reward learning by boosting motivation or associative learning during social interactions<sup>77–79</sup>. These networks may function together to facilitate social learning<sup>80</sup>. Thus, maladaptive responses in either network and/or shared hubs, such as the vmPFC<sup>16</sup>, may underlie neurobiological susceptibility to SA in adolescence. Indeed, social interactions elicit dysregulated engagement in overlapping network hubs in SA<sup>30,81–84</sup>. We demonstrated that dysregulated neural responses in salience and reward networks during unpredictably positive social feedback in preadolescents at risk for SA disorder predicted more severe SA symptoms in mid-adolescence<sup>85</sup>. Thus, both social learning and SA are associated with highly convergent neural mechanisms.

**A.6 Dysregulated brain function is associated with impaired learning in SA.** Only two studies have investigated neural correlates of learning in adolescents with SA. Our previous work examined neural correlates of prediction errors, a parameter of learning models, to social feedback in adolescents with SA. We found prediction errors to unexpected positive feedback from high-value peers elicited heightened reward network activity and negative functional connectivity (FC) within the reward, salience, and overlapping network regions in anxious-vs-healthy adolescents<sup>33</sup>. The degree to which these regions exhibited negative FC predicted impaired recall for unexpected positive social feedback<sup>33</sup>. This suggests that dysregulated neural response to positive prediction errors (parameter of social learning) may negatively bias future expectations (expected value) about social feedback in SA<sup>61</sup>. However, this study did not examine whether social learning rates or parameters of the social context evince different patterns of FC in adolescents with SA. Another study examined relations of reinforcement, associative, and combined learning models during non-social learning and brain function. They found that a combined model best captured learning rates, such that impaired dynamic learning of emotionally

salient stimuli in SA were associated with dysregulated activation in the salience network<sup>11</sup>. This study suggests that associative factors that dynamically change learning are associated with dysregulated salience network activation in SA in uncertain contexts. Yet, they did not examine learning in a social context, which typically engages reward circuits given the rewarding nature of social feedback, nor did they examine patterns of FC.

### B. Innovation.

The proposed study addresses prior limitations by using computational modeling and functional neuroimaging to establish mechanisms of social learning that relate to SA in adolescents. Using the novel Learning from Evaluation And Recall of iNteractions (LEARN) task, I will manipulate the valence and predictability of purported peer feedback, while obtaining peer value ratings over the course of iterative social interactions. These data will be used to derive computational models of social learning in adolescents with varying severity of SA. I will also determine how brain mechanisms of social learning relate to SA symptoms. To do this, I will use psychophysiological interaction (PPI) analyses and a cutting-edge dual-regression analyses to quantify within and between reward and salience network perturbations. Results will help isolate etiopathogenic mechanisms of impaired social learning promote SA, thereby providing novel prevention/treatment targets.

### C. Approach.

#### C.1 Research Design and Methods.

**C.1.1 Preliminary studies.** Typical non-social tasks require a large number of trials to demonstrate learning. We utilized a variant of the LEARN task<sup>30</sup> to demonstrate that adolescents learn about peers through a relatively small number of social interactions. In this study, a Control group (N=30) of adolescents ( $M_{age} = 12.11$ ) learned the reputation of peers prior to their interactions. A Learn group (N=30) learned that peers were mean, nice, or unpredictable solely through interactions. For the Control group (Fig. 3A), average learning curves showed that participants learned reputations prior to interactions and reputation ratings were consistent across interactions. For the Learning group (Fig. 3B) average learning curves showed that participants were naïve to reputations prior to their interactions (unsure ratings for all peers), differentiated peers (orange dotted line) after 8 interactions, and exhibited similar ratings to the control group (black dotted line) after 16 interactions. Rate of deception was 100%. Thus, the LEARN task elicits social learning in adolescents with even a limited numbers of trials. [Additionally, pilot fMRI data obtained using a similar variant of the LEARN task<sup>30</sup> (N=4) revealed learning-related changes in neural activation in critical regions of interest (ROIs: dACC – Fig. 3C; insula, amygdala, vmPFC, and striatum, not shown) varied depending on SA symptoms (Fig. 3D). Greater activation in early (pre-learning) vs late (post-learning) social interactions was associated with more SA symptoms. Given similar patterns emerged across all ROIs, this suggests the proposed study with methods optimized to detect differential neural responses to social learning will likely differ by SA symptoms.]

**C.1.2 Protocol.** At visit 1 ( $\leq 150$  mins) participants undergo diagnostic screening and a mock scan to acclimate to the fMRI environment. At Visit 2 (90 mins), participants complete the LEARN task while undergoing fMRI. **C.1.3 Power Estimates.** This work is the first to use LEARN to quantify neural mechanisms of social learning in relation to SA. Thus, power calculations are informed by three sources. The first source, Jarcho (2015), examined relations of FC to recall of unexpected (prediction error) positive (valence) social feedback in anxious youth (N=22,  $f=.63$ ). The second source, Jarcho (2016) used a variant of the LEARN task<sup>30</sup> in adolescents at high-risk for SA and examined FC between the insula and vmPFC during certain (volatility) positive (valence) interactions (N=30,  $f=.73$ ). The third source, Piray (2019) used similar computational learning models as proposed here to examine relations between dACC activation and SA (N=22,  $f=.46$ ). Estimations ( $g^*$ power) for multiple regression with at least 5 predictors (peer value, valence, volatility, learning rate, and SA) determined a sample size of 49 is adequate ( $\beta > 0.80$ ) to detect small-to-medium ( $f \geq 0.30$ ) effects. Thus, we will study 60 participants, factoring in data loss due to fMRI acquisition (~10%) or lack of deception (~3%).

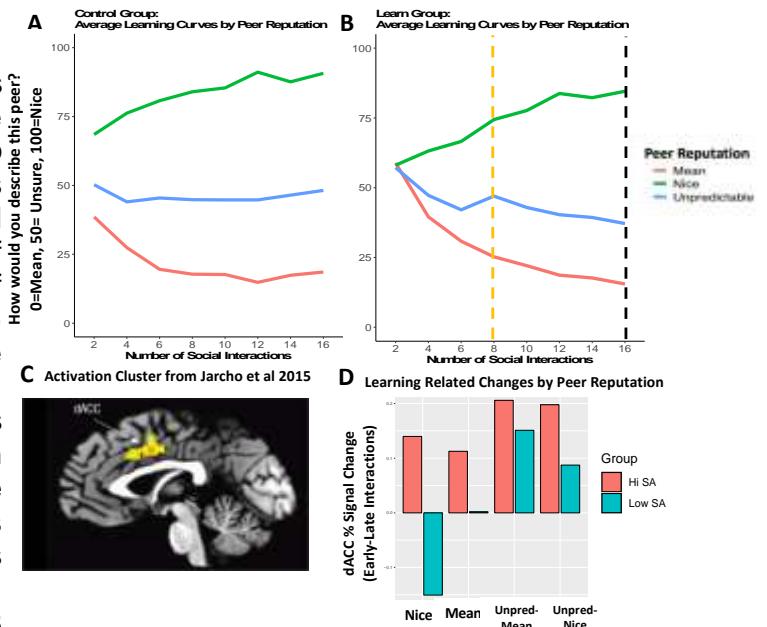
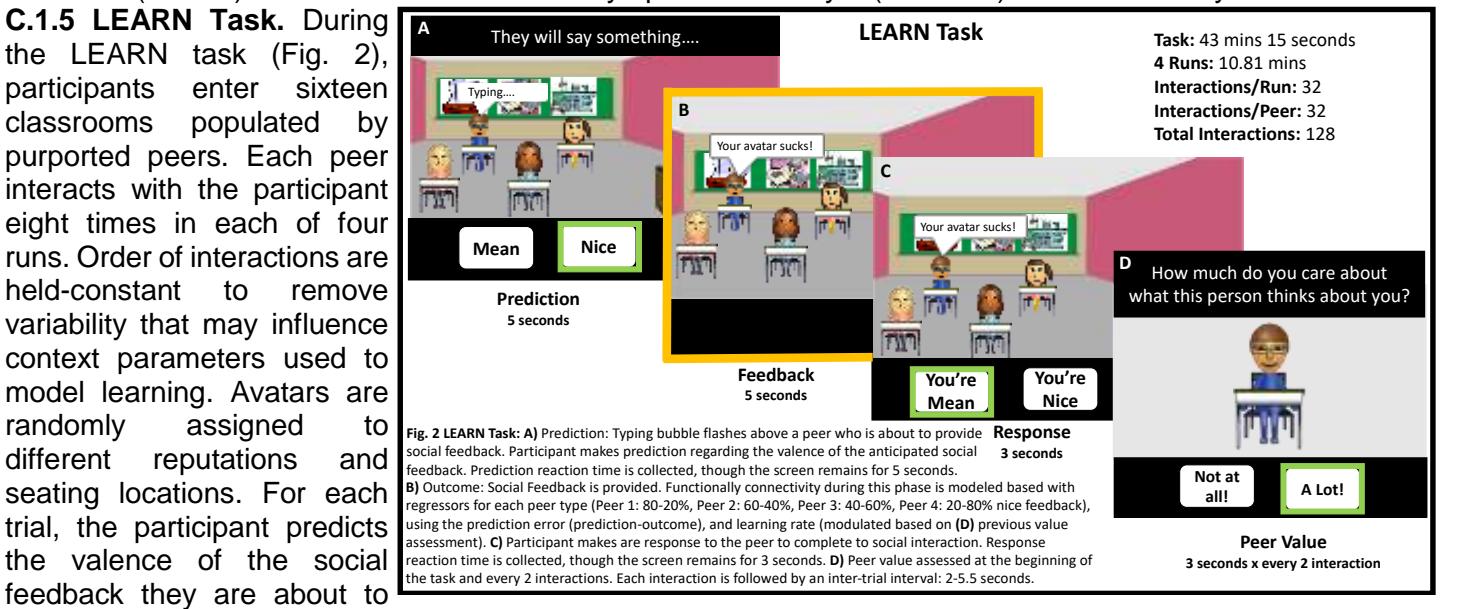


Fig. 3 Learning curves of reputation ratings for mean (100% negative), nice (100% positive), and unpredictable (50-50% negative/positive) peer types during a variant of the LEARN task for the control (A) and the learn (B) group. Using (C) previously identified dACC region of interest there was a (D) change in dACC engagement for late (post-learning: last 4 interactions) vs. early (pre-learning: first 4 interactions) interactions varies by peer type depending on social anxiety (SA) symptom severity.

**C.1.4 Participants.** Participants (N=60; 50% female) will be English-speaking adolescents recruited during the peak age of onset for SA (10-15 years of age), who exhibit a range of SA symptoms. Demographics will reflect the greater Philadelphia area and patients at the Child and Adolescent Anxiety Disorders Clinic (CAADC; see Human Subjects B.1). Participants will be recruited from the community using well-established recruitment methods (Jarcho) and from the CAADC (Kendall), located across the hall from Temple's neuroimaging facility. The CAADC performs clinical assessments and delivers treatment to 20-30 adolescents with SA symptoms in the 10-15 year range each year. Exclusionary criteria include contraindications for fMRI, neurological, or physical impairment, other primary psychiatric diagnoses, head injuries with loss of consciousness or unstable medication (<3 months; see Human Subjects A.1.3). Diagnoses will be assessed with the Anxiety Disorders Interview Schedule (ADIS<sup>86</sup>) and the Child Adolescent Symptom Inventory 5 (CASI-5<sup>87</sup>) and reviewed by Dr. Kendall.



Next the participant receives social feedback (Fig. 2B), which will confirm their prediction or result in a prediction error. Primary neuroimaging analyses focus on the Feedback phase, given this is the point in the interaction during which learning is most likely to occur. Then, participants make a response to complete the social interaction (Fig 2C). Peer value ratings are acquired prior to the LEARN task, and after each classroom (Fig. 2D). All choices are binary in order to ensure model parameters can be estimated within a unit range. The most recent value assessments are used as associative factors in M2 and M3 (see C.2.1 and Fig 4). After completing the task, deception is assessed, and participants are debriefed.

**C.1.6 fMRI data acquisition.** After mock scanning, neuroimaging data will be acquired with a 3-Tesla Siemens MAGNETOM Prisma MRI (64-channel head coil). For each participant, 340 functional image volumes with 35 contiguous axial 3mm slices (in-plane resolution = 2.5x2.5mm) will be acquired using a T2\*-weighted echo-planar sequence (TR/TE= 2300/25ms, flip=50°; FOV=240 mm, matrix=96x96). To facilitate anatomical localization and coregistration of functional data, a high-resolution structural scan will be acquired (axial plane) with a T1-weighted magnetization-prepared spoiled gradient-recalled echo sequence (TE/TI= min full/725ms, flip=6°; FOV=220mm, matrix=256x256, in-plane resolution, 0.86x0.86mm). The LEARN task (Eprime 2.0; PST Inc, Pittsburgh, PA) will be projected onto a screen and viewed via a head coil-mounted mirror. Responses will be provided via fMRI-compatible button box.

**C.1.7 Questionnaires.** In addition to diagnostic screening, SA will be assessed dimensionally using questionnaires: Screen for Childhood Anxiety Related Emotional Disorders<sup>88</sup> and the Brief Fear of Negative Evaluation Scale<sup>89</sup> [*and the Social Anxiety Scales*<sup>13</sup>]. Social competence, puberty<sup>55,90,91</sup>, peer victimization<sup>92-94</sup>, and depression<sup>95-97</sup> can influence SA symptoms and brain function and may be used as covariates and/or in exploratory analyses. Measure will include: Social Responsiveness Scale-2<sup>98</sup>, Peer Victimization Questionnaire<sup>99</sup>, child/parent Child Depression Inventory<sup>100</sup>, puberty<sup>101,102</sup>, and demographics questions.

**C.1.8 Social anxiety composite.** SA will be derived from a composite of [SA subscales (see C.1.7), using an confirmatory factor analyses (CFA) based on our recently published exploratory factor analysis<sup>85</sup> SA model. The CFA model will be pre-specified (i.e. factor structure, error, and cross-loadings), and compared using standard fit indices<sup>103-105</sup> in Mplus 8.1.5(<http://www.statmodel.com/>). Latent factor scores will be extracted] for analyses.

**C.2 Aim 1** **A)** Develop and compare models for social learning using the valence, peer value, and predictability of social feedback as parameters; **B)** Test relations between social learning rates and

**severity of SA.** I will use computational models and composite SA symptoms to test my working hypothesis that A) relative to other models, the combined model will optimally predict learning; B) more severe SA will correspond to suboptimal learning rates when interacting with high-value peers who provide uncertain positive feedback. When completed, I expect to identify the contextual parameters of social learning most closely linked to SA. These findings will provide treatment targets for ameliorating social learning impairments that may prevent chronic SA.

**C.2.1 Computational modeling.** To determine how the valence, peer value, and degree of certainty influence social learning, three models will be constructed and compared (Fig 4). Models will be optimized by iteratively adjusting the free model parameters and  $\tau$  (softmax temperature) to test the likelihood the model parameters fit the observed data<sup>106</sup>. Model comparison will be performed using goodness-of-fit parameters<sup>107</sup>. Relations between learning rates for all models and SA will be examined.

**Model 1: Reinforcement Learning Model:**  $S_t$  is the feedback presented on trial t,  $C_t$  is the prediction and  $O_t$  is the received outcome,  $\delta_t = O_t - X_t(S_t, C_t)$   
 $\delta_t$  is the prediction error on trial t and  $\alpha$  is the learning rate representing the degree to which the prediction error influences the current expected value  $X_t(S_t, C_t)$ .

$$X_{t+1}(S_t, C_t) = X_t(S_t, C_t) + \alpha_t \delta_t$$

**Model 2: Valence-Specific Associative Learning Model:**  $w$  is the valence weighted-parameter of outcome,  $K_t$  is a weighted combination of a constant- and a dynamic- component according to  $w$  and  $A_t$  salience factor (2a).  $A_t$  gets updated via random diffusion (2b) and the squared prediction error times the value of the peer  $\lambda$ .  
(2)  $\alpha_t = \kappa K_t$     (2a)  $K_t = w A_t + (1-w)$     (2b)  $A_t = \lambda A_t^{\text{post}}$     (2c)  $A_{t+1}^{\text{post}} = A_t + (1-\lambda) \delta_t^2$

**Model 3: Combined Learning Model:** This model is the same as model 2, except that the learning learning rate  $\alpha$  is a dynamic component and the associability is updated according to the absolute value of previous prediction error (instead squared prediction error) and  $\mu$  and  $\kappa$  are free parameters (peer value) which determine the step-size for updating associability & scale of the learning rate.  $\alpha_t = \kappa A_t$

Table: Comparing Resulting Learning Rates From Learning Models

Peer 1	Peer 2	Peer 3	Peer 4	Social Context Parameter
% Nice-vs-Mean 80-20	60-40	40-60	20-80	
M1	$\alpha_1$	$\alpha_1$	$\alpha_2$	$\alpha_2$
M2	$\alpha_1(A_1)$	$\alpha_1(A_2)$	$\alpha_2(A_3)$	$\alpha_2(A_4)$
M3	$\alpha_1(A_1)$	$\alpha_2(A_2)$	$\alpha_3(A_3)$	$\alpha_4(A_4)$

Fig. 4 Each peer (1-4) has a distinct probability of giving nice/mean social feedback. The table depicts the learning rate ( $\alpha$ ) and the salience factor ( $A$ ) for each type of peer for each model. M1 The learning rate for the two mostly nice peers is different than the two mostly mean peers. This model tests whether valence of social feedback is an important modulator of social learning. M2 The learning rates are the

same as model 1, however the salience factors may vary for each peer, as they are based on how much the participant values a peer's feedback. This model tests whether valence of social feedback and peer-value are important modulators of social learning. M3 The learning rates is different for each peer type because they vary based on valence (as in model 1) and degree of certainty of the peer's valenced feedback. As in model 2, the salience factor may vary for each peer, as it is based on how much the participant values that peer's feedback. This model tests whether valence of social feedback, peer-value, and degree of certainty of peer feedback are important modulators of social learning.

**C.2.2 Primary data analyses.** Aim 1A) Models M1-3 will be compared to determine best fit of social learning. Aim 1B) Social learning rates from each model (Fig. 4; M1-3) will be correlated with composite SA scores to determine which model best explains variance in SA symptoms. Covariates (e.g., gender, race, age) will be included in analyses when significantly correlated with the dependent variable. Exploratory data analyses. Social competence, puberty<sup>55,90,91</sup>, experience of peer victimization<sup>92-94</sup>, and suppressor effects of depression<sup>95-97</sup> are also known to influence SA. Exploratory analyses will also test for, and covary significant relations between, these factors when correlating social learning to SA using questionnaire data (see C.1.7).

**C.2.3 Expected Outcomes.** Our working hypothesis is that social learning impairments in SA will be best estimated using the combined model, implying that the valence, volatility, and value of peer feedback are each essential modulators of social learning in SA. These results could inform treatment strategies for SA.

**C.3 Aim 2 Determine the extent to which within and between network FC evoked by social learning during social feedback relates to severity of SA symptoms.** To attain this goal, I will use FC analyses convolved at the individual level with learning rates from the best fitting social learning model (Aim 1) and their relations with composite SA at the group level. My working hypothesis is that more severe SA and suboptimal social learning rates will be associated with positive FC within the reward network<sup>29</sup> and negative FC in the salience network<sup>30</sup> during the receipt of positive peer feedback. When completed, I expect to delineate neural network mechanisms related to impaired social learning in SA.

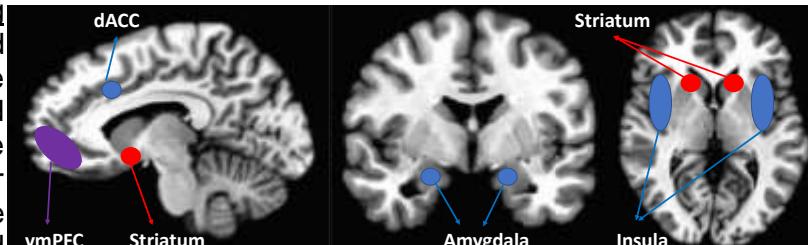


Fig. 5 The reward network and possible seed regions for the PPI analyses are depicted in red. The salience network and possible seed regions are depicted in blue, and overlapping regions that could serve as seed regions are depicted in purple.

**C.3.1 fMRI data preprocessing and first level analyses.** AFNI (Analysis of Functional and Neural Images<sup>108</sup>) and FSL (FMRIB's Software Library, Oxford,UK; [www.fmrib.ox.ac.uk/fsl](http://www.fmrib.ox.ac.uk/fsl)) will be used. For each participant, functional data will be slice-time corrected, co-registered to a high-resolution structural scan, smoothed, spatially normalized to standard space, and resampled. Preprocessed data will be analyzed using multiple regression including learning rates to create model-derived time series. Each trial will be categorized by peer type (Fig 4;

Table) and feedback valence. Trial-by-trial learning rate for each peer will then be used as a parametric regressor. Task-level events of no interest (prediction, response) and 6 motion parameters will also be included as regressors. TRs exceeding total motion >1mm will be removed.

**C.3.2 Functional Connectivity Analyses.** To examine perturbations in FC between and within reward and salience networks after the receipt of social feedback [*in relation to trial-level social learning rates from M1-3*], I will perform psychophysiological interaction (PPI) analyses, which estimates changes in FC between a region of interest (seed) and each other prespecified region within the salience and reward networks. Each region will act as a seed and as part of the network of ROIs (Fig. 5). Peer contrasts will compare effects of valence [(*Mostly Nice 1&2 vs Mostly Mean 3&4 Peers*), value (Peer rated as high vs low value), and volatility (*Volitale1&4 vs Stable 2&3 Peers*) *on learning in relation to FC*] (familywise error corrections).

**C.3.3 Primary data analyses.** To isolate patterns of FC that relate to social learning, FC between each set of specified regions in the reward and salience network will be convolved with learning rates and extracted for each peer-type. Then, contrasts examining significant patterns of FC during social learning for each peer-contrast (see C.3.2) will be correlated with composite SA (see C.1.8). Covariates (e.g., gender, race, age) will be included in analyses when significantly correlated with the composite SA<sup>109</sup>. **Exploratory data analyses.** While PPI is effective for examining FC, multiple comparisons are needed to test for patterns of FC between networks of interests, [*resulting in challenges resolving overlapping FC between networks hubs, such as the vmPFC<sup>110</sup>*]. To address this limitation and achieve my training goals, I will also use a [*cutting-edge model-based*] dual-regression analyses to test for within and between network FC. Dual-regression analysis includes spatial and temporal regressions. In the spatial-regression step, spatial maps of the reward and salience networks are regressed onto each participant's fMRI data, resulting in time × components beta coefficients that differentiate temporal dynamics for each spatial network. Then the spatial beta coefficients for the reward and salience networks are entered into a single analysis to determine patterns of FC that relate to social learning within and between reward and salience networks and SA.

**C.3.4 Expected Outcomes.** Our working hypothesis is that suboptimal social learning rates will be associated with positive connectivity within the reward network<sup>29</sup> and negative connectivity within the salience network<sup>30</sup> during the receipt of positive peer feedback in those with more severe SA. We expect the dual regression analyses to replicate intra-network findings from the PPI analyses and extend these results by providing information about inter-network FC.

**C.4 Potential problems and alternative strategies.** While the proposed study addresses many gaps in the literature, it is not without limitations. To balance ecological validity and simulate real-time social interactions in the context of fMRI, the LEARN task has a fewer trials than typical learning studies. However, our preliminary data suggests learning occurs in as few as 8 interactions; the LEARN task includes 32 trials for each peer-type. Additionally, we expect that social learning impairments will relate to dimensionally assessed SA. If subclinical symptoms show weak relations to our models of social learning, we will perform categorical analyses based on clinical cutoffs provided by the ADIS (see C.1.4). We also hypothesize that more severe SA and suboptimal social learning rates will be associated with dysregulated FC. If FC is not related to social learning in SA, we will determine task effects of neural activation for the novel LEARN task, and their relations to SA, which could provide valuable insights into the etiology of SA. [*We will also investigate other computational and causal model-based analyses model-based approaches<sup>111</sup>*].

**C.5 Resource sharing plan.** If results from the proposed work are promising, then Dr. Jarcho (sponsor) will facilitate distribution of the LEARN task. Following collection, data will be tagged with a unique identifier to preserve anonymity of private health information (PHI). Anonymized data and relevant documentation will be made available upon request following publication.

**C.6 Rigor and Reproducibility.** All primary hypotheses and analyses will be pre-registered (e.g., [AsPredicted.org](https://AsPredicted.org)) to minimize researcher degrees of freedom. In addition to controlling for biological variables, we will enhance rigor and reproducibility by sharing all exploratory analyses with the broader community. This will increase transparency and improve future meta-analytic efforts (see C.5).

**C.7 Future Directions.** As additional exploratory analyses, given that part of this sample will be collected as part of a research-based treatment clinic, we can examine whether differences in social learning and FC could provide hints for predicting treatment outcomes. This sample will also be uniquely diverse and could therefore provide hints as to whether race, ethnicity, socioeconomic status, and lifetime history of trauma may moderate relations between social learning and SA. Despite being underpowered, gender will also be explored, as gender differences in mechanisms of social learning may help explain observed gender differences in SA. In sum, this study provides a foundation for many future studies that could potentially lead to novel treatment targets for SA, and offers essential research training that I would otherwise not receive in my current predoctoral program.

## **RESPECTIVE CONTRIBUTIONS**

The current research proposal was developed, designed, and written by the applicant. However, the applicant's sponsors and consultant have provided guidance and support throughout. Over the past several months, the applicant has met with her primary sponsor, Dr. Jarcho, regularly to refine theoretical and methodological aspects of the study and to develop an appropriate training plan that would allow the applicant to achieve the goals both for the proposed study and for her future career. Dr. Platt has provided consultation regarding implementation and selection of computational models appropriate for quantifying social learning. Additionally, Dr. Platt has also consulted on LEARN task development to ensure appropriate parameters for modeling analyses are included. Dr. Smith has provided consultation regarding implementation of functional connectivity analyses methods. The applicant has also worked closely with her consultant, Dr. Kendall, who has provided additional guidance on diagnostic assessment training and access to the Child and Adolescent Anxiety Disorder Clinic (CAADC) enrollment records that were needed to determine the feasibility of the proposed study sample size. All members of the research team have reviewed components of the current application, and provided feedback that has been invaluable in shaping the final proposal. Dr. Jarcho has reviewed multiple drafts of the entire research plan and application and provided feedback that has been incorporated into the final submitted proposal.

The applicant has received additional consultation beyond her research team. Dr. Michael McCloskey, the Director of Clinical Training for the Ph.D. Program in Clinical Psychology at Temple University, contributed information for the Description of Institutional Environment and Commitment to Training sections. Several of Temple's previously successful applicants for predoctoral NRSA funding provided feedback on the proposed study methods.

## SELECTION OF SPONSOR AND INSTITUTION

**Dr. Johanna M Jarcho** (Primary Sponsor): Dr. Jarcho is an expert in conducting clinically relevant social neuroscience research, and has extensive experience using fMRI to elucidate the neural mechanisms of pediatric anxiety disorders. As an Assistant Professor of the Brain & Cognitive Sciences and Social Areas in Temple University's Department of Psychology she has developed numerous ecologically valid behavioral and fMRI-based social interaction tasks. She has successfully led interdisciplinary teams and obtained competitive extramural and intramural funding from the NICHD, NIMH, and private foundations for her work investigating trajectories and risk factors of adolescence anxiety and bullying. She serves on the editorial board of 2 journals, has published more than 40 papers (> 3,600 citations; H-index 23). Dr. Jarcho has an impressive track record of mentorship, and has demonstrated her commitment to aiding me in developing a strong foundation in clinically-focused social neuroscience and neuroimaging methods over the past 3 years. She is regularly available to discuss research ideas and methodologies or offer guidance on professional development. Her commitment to my successful development as a clinical social neuroscientist and her significant expertise make her an ideal sponsor for my proposed project and training plan. Dr. Jarcho has a strong working relationship with my proposed co-sponsor and consultants.

**Dr. Michael Platt** (Co-Sponsor): Dr. Platt is an expert in using cutting-edge computational methods to probe the neurobiology of social cognition in human and non-human primates. As a distinguished professor with an endowed chair in the University of Pennsylvania's Depts. of Neuroscience, Psychology, and Marketing, he studies the biological bases of altered cognition and behavior in anxiety disorders and develops therapies that target these problems. Dr. Platt is PI of single- and multi-institution grants that have provided continuous funding for over 19 years. He has sponsored numerous pre- and post-doctoral NRSA and National Science Foundation fellows who have, consistent with my ultimate goal, obtained academic positions at research institutions. Dr. Platt directs the Wharton Neuroscience Initiative and serves on multiple editorial and advisory boards for journals and scientific centers. Dr. Platt has authored over 170 papers in journals including Science, Nature, PNAS, and Psychological Science (>13,000 citations; H-index 58). As a co-sponsor, Dr. Platt will provide me with the training I need to develop a strong foundation in computational modeling while providing a unique perspective on social behavior and neurobiology. Dr. Platt has been readily available throughout the grant application process to consult on analyses, and has developed a strong working relationship with Drs. Jarcho, Smith, Kendall and myself. Drs. Jarcho and Platt provide complementary expertise that will significantly enhance my career development and training.

**Dr. David V. Smith** (consultant): Dr. Smith has extensive expertise in brain connectivity analysis approaches. As an Assistant Professor of Psychology in the of the Brain & Cognitive Sciences area at Temple University, he uses fMRI to study social decision-making in the context of neuroeconomics. Dr. Smith has completed two NIMH training grants, and received awards from the NIH and other private foundations. He has published more than 20 articles (> 1,400 citations; H-index 19). Dr. Smith has provided mentorship on functional connectivity analyses, and given his dedication to open science, will also provide guidance on my resource and data sharing plan for publication in top-tier journals.

**Dr. Philip Kendall** (consultant): Dr. Kendall is an internationally recognized expert in the study, assessment, and treatment of pediatric anxiety. He is a distinguished University Professor, a Laura H. Carnell Professor of Psychology, and Director of the Child and Adolescent Anxiety Disorders Clinic (CAADC), at Temple University. He has over 30 years of uninterrupted grant support as PI of several NIH-funded, multi-site treatment development and outcome studies. Dr. Kendall has successfully sponsored multiple F31 and K awardees, and mentored many students who have obtained prestigious academic positions. Dr. Kendall has over 700 publications and is one of the most highly cited individuals in the social and medical sciences (H-index 123). In the last year, Dr. Kendall, has been available to regularly discuss research ideas or offer guidance on career development. His commitment to my success along with his significant expertise in youth anxiety assessment make him the ideal consultant for the clinical aspects of the project.

**Temple University.** Temple is the ideal institution for my proposed research and training. Its clinical psychology PhD program is accredited by the American Psychological Association and the Academy of Psychological Clinical Science. The Psychology Department is home to several distinguished faculty who have consistently demonstrated a strong commitment to mentorship and developed highly skilled clinical scientists. Its location in the Philadelphia area, home to a number of graduate programs in clinical psychology and related fields, will help me to expand my professional network. Additionally, Temple has the Temple University Brain Imaging Center (TUBRIC), located directly across the hall from the CAADC, which is exclusively dedicated to research. Overall, my mentorship team and training environment provide the necessary framework to complete the proposed project and develop into an independent clinical social neuroscientist.

## TRAINING IN THE RESPONSIBLE CONDUCT OF RESEARCH

There are several mechanisms through which I have and will continue to enhance my knowledge of the protection of human subjects in research. Together, these experiences will provide me with a strong knowledge regarding the responsible conduct of research with human subjects. This ethical training will be invaluable to me as I move forward in my career conducting research with human subjects.

**Format:** I will meet with Dr. Jarcho regularly to discuss ethical issues surrounding conducting neuroimaging studies, as well as broader ethical issues regarding data collection and management, human subject protection, deception, and confidentiality. I have *completed* the Collaborative Institutional Training Initiative (CITI) training program administered by the Institutional Review Board (IRB) at Temple University, and *will* complete this training again during the funding period. The CITI training program focuses on the ethical and responsible conduct of research with human subjects, and includes extensive information about current ethical guidelines. The majority of my coursework in the Clinical Psychology Doctoral Program at Temple University and Stony Brook University, which I have *completed*, incorporates discussion of ethical issues in human subjects' research, including (1) a one-semester course Ethics and Professional Issues (2) a two-semester course on assessment and (3) a one-semester course on multicultural issues in clinical psychology. In addition, I *will* conduct research in accordance with Temple University's manual on the protection of research subjects. Thus, all study protocols for the proposed study *will* be submitted to the Temple University IRB. Finally, Temple hosts mandatory monthly clinical area talks led by graduate students, faculty members, and visiting scholars, which often cover topics relevant to the ethical conduct of research. At least one meeting per year is devoted entirely to ethical issues.

**Subject Matter:** As discussed above, I *will* complete CITI training on the ethical and responsible conduct of research with human subjects. Modules covered in this training include: History and Ethical Principles, Assessing Risk in Social and Behavioral Sciences, Conflicts of Interest in Research Involving Human Subjects, Informed Consent, Internet Research, Privacy and Confidentiality, Research and HIPAA Privacy Protections, Research in Public Elementary and Secondary Schools, Research with Children, Research with Prisoners, Students in Research, and Workers as Research Subjects. At the end of each module, participants are asked to complete a quiz on the material in order to ensure comprehension of ethical principles and ability to apply these principles in hypothetical scenarios. I have *completed*, Stony Brook's course on Ethics and Professional Issues mentioned above, in which we covered the American Psychological Association's (APA) Ethical Principles of Psychologists and Code of Conduct, including ethical principles and standards related to beneficence and nonmaleficence, integrity, resolving ethical issues, competence, privacy and confidentiality, education and training, research and publication, assessment and therapy. We read APA ethical guidelines and spent considerable time discussing and role-playing hypothetical case examples. These examples included potential ethical "gray areas" not fully addressed in the guidelines in order to facilitate an even deeper understanding of ethical principles. I also *completed* Stony Brook's course on assessment incorporated discussions of ethical considerations related to conducting testing, providing testing results, reporting abuse, monitoring suicidality, and ensuring confidentiality. I [also *completed*] Temple's course on multicultural issues in clinical psychology provided me with additional ethical training related to issues of cultural, religious, sexual orientation, socio-economic status, and ethnic diversity. Finally, I *will* attend the Temple's mandatory monthly clinical area talks meeting is devoted entirely to ethical issues, including management of conflicts of interest and dual relationships, maintenance of research participant safety, and maintaining privacy and confidentiality. At these meetings, students are able to pose ethical questions that have come up in their work as researchers/clinicians for group discussion and feedback.

**Faculty Participation:** Meetings with Drs. Jarcho, Platt, Smith, and Kendall *will* include discussions of responsible conduct of research. At least two weekly meetings per semester with Dr. Jarcho will be devoted entirely to ethical issues. Interaction with faculty members and peers will also occur informally and during clinical area talks on ethical principles and practices.

**Duration of Instruction:** Instruction *will* be approximately 15 hours: two clinical area talks (1.5 hours each), CITI certification (2 hours), and regular meetings with members of my mentorship team (10 hours).

**Frequency of Instruction:** Throughout the period of fellowship, the applicant will meet regularly with members of the mentorship team: weekly with the primary sponsor (Dr. Jarcho) and bi-weekly with the co-sponsor (Dr. Platt) and consultants (Drs. Smith and Kendall). These meetings will incorporate discussions of ethical principles related to the proposed project, particularly issues related to deception, data sharing, and aggregation. Dr. Jarcho will be available for additional consultation for any emergent ethical issues.

**SPONSOR AND CO-SPONSOR STATEMENT****RESEARCH SUPPORT AVAILABLE**

In addition to support described below, funds for participant recruitment/payment and fMRI will come from Dr. Jarcho's startup funds (\$175,000 earmarked for fMRI) as a new faculty member at Temple University.

**Table 1. Current and Pending Research and Research Training Support**

Source	ID number	Title	PD/PI	Dates	Amount(\$)
NIH	R03- DA046733	Aberrant Reward Sensitivity: Mechanisms Underlying Substance Use	Smith Co-I Jarcho	08/19- 7/20	~225,000
NICHD	R21 HD 093912-02	Using Adolescent nonverbal behavior to predict aggression against bullies and bystanders.	Jarcho	08/18 – 08/20	232,781
NIMH	R01 MH 108627-04	Mechanisms regulating complex social behaviors	Platt	04/16 – 01/21	655,759
NIMH	R37 MH 109728-04	Neural circuit mechanisms mediation TMS and oxytocin effects on social cognition	Platt	04/16 – 01/21	570,254

**Coordination among Sponsors and Co-sponsors.** Drs. Jarcho and Platt are committed to fostering interdisciplinary, collaborative research, and have developed a strong working relationship while providing joint feedback on the applicant's proposed project. As a team, the applicant and Drs. Jarcho and Platt have agreed on clearly defined roles to ensure that the applicant is able to develop a strong understanding of computational modeling and functional connectivity analyses, and achieve her overarching career objectives. Dr. Jarcho will be the primary sponsor and will provide guidance and support during weekly meetings. Specifically, she will facilitate utilization of co-sponsor and consultant expertise, provide training on neuroimaging study design, fMRI acquisition, and analyses, and mentor the applicant in generating several first-author manuscripts relevant to her independent line of research. Dr. Platt will supplement Dr. Jarcho's mentorship by providing her with a strong conceptual and methodological understanding of computational modeling via bi-weekly meetings. Dr. Platt is also committed to helping the applicant develop as an independent researcher, and will provide guidance on how best to use the proposed project as a foundation for future grant applications that implement novel computational models applied to social neuroscience questions. Both Drs. Jarcho and Platt reside within the greater Philadelphia area, see each other at monthly Temple/Penn meetings on social neuroeconomics and are available for joint mentorship team meetings to ensure optimal coordination, quarterly.

**SPONSOR'S/CO-SPONSOR'S PREVIOUS FELLOWS/TRAINEES.**

Dr. Jarcho is an F31 fellowship recipient and has consulted on a previous successful F31 award: Felicia Jackson, Ph.D. (now at McClean Hospital). Dr. Jarcho has had an impressive track record mentoring graduate level students who have gone onto impressive faculty positions, clinical internships, and doctoral programs: A list of five representative students appears below:

- (1) Felicia Jackson, Ph.D., McClean Hospital Clinical Psychology Intern.
- (2) Adrienne L. Romer, M.A., Duke University, PhD. Student.
- (3) Erin Gardner, M.A. University of Albany, PhD. Student.
- (4) Brady Rainville, M.A., Northern Vermont University, Adjunct Professor of Psychology
- (5) Hannah Grossman, M.A., University of Buffalo, Counseling Psychology PhD. Student.

Dr. Platt has sponsored 11 predoctoral F31 awards: e.g., Sarah Heilbronner (now faculty at U. Minnesota), 5 postdoctoral F32 awards: e.g., Jamie Roitman, Ph.D. (now faculty at U. of Illinois at Chicago), 4 K awards: e.g., Ben Hayden, Ph.D., (now faculty at U. Minnesota) and Steve Chang, Ph.D. (now faculty at Yale University), and R21 awards: John Pearson, Ph.D., (now faculty at Duke University). Dr. Platt has mentored over 18 Ph.D. students, most of whom have gone on to academic/research careers. A list of five representative students appears below:

- (1) Sarah Heilbronner, Ph.D. Duke University, faculty at U. Minnesota
- (2) David Barack, Ph.D. Columbia University, Presidential Scholar, Science and Society Program
- (3) Heather Dean, Ph.D. policy expert, FDA
- (4) Alli McCoy, MD/PhD., oculoplastic surgeon, San Diego, CA
- (5) Becket R. Ebitz, Ph.D. Princeton University, Post-doctoral Fellow

**TRAINING PLAN, ENVIRONMENT, RESEARCH FACILITIES**

**Primary Sponsor: Dr. Jarcho.** I am delighted to serve as primary sponsor on Tessa Clarkson's proposed research and training plan [(4/2020 to 4/2022)]. Tessa's proposal uses computational modeling and fMRI to determine the underlying mechanisms of how the social environment modulates neural processes of social

learning to promote socially anxiety (SA) in youth. Through her post baccalaureate and graduate work, Tessa has received basic training in research design, clinical assessment, statistics, psychopathology and use of neuroimaging to investigate social cognition in youth. Her training plan clearly broadens her existing skills and supplements training she will receive at Temple. Through the support of an NRSA, her training plan and research will provide her with the opportunity to develop expertise in model-based neuroimaging, computational modeling, and functional connectivity analyses. Tessa's proposal is comprehensive; it was a plan designed by Tessa, myself, her co-sponsor (Dr. Platt), and consultants (Drs. Smith and Kendall) to both address her research and learning goals and promote her professional development. Building these competencies will be critical for her development as an independent researcher. Her experience working on the proposed project will ultimately help her pursue future grant applications using results from the current study to inform the development of novel treatment targets for youth with SA. Tessa has four primary training goals she would like to accomplish through her NRSA.

**1. fMRI-study design.** This goal will be accomplished in several ways. I will take primary responsibility for over-seeing Tessa's training in task design, neuroimaging sequence selection, and data collection. In my role as primary sponsor, I will meet with Tessa on a weekly basis and prepare directed readings in both ecologically-valid neuroimaging task design and neuroimaging methods. Additionally, I will work directly with Tessa to pilot test the Learning from Evaluation And Recall of iNteractions (LEARN) task and implement stringent quality control procedures. In the LEARN task, participants learn about four "peers" who provide social feedback (Peer 1: 80-20; Peer 2: 60-40; Peer 3: 40-60; Peer 4: 20-80 positive/negative) over iterative social interactions. Participants make predictions about the valence of social feedback they are about to receive. They also rate how much they value each peer. In this way, the LEARN task is able to examine how peer value, valence and volatility of social feedback impact the rate at which participants learn about each peer. This approach will be useful for determining how parameters of social contexts modulate neural responses to social learning to promote SA—an area that is surprisingly under-studied. [Tessa has created and tested an initial version of her LEARN task in a sample of normative youth—results provide promising preliminary data for ascertaining learning curves (see Research Strategy C.1.1).]

I will attend Tessa's meetings with the Temple University Brain Imaging Center (TUBRIC) physicist (Dr. Huiling Peng) to help her learn how to select scan acquisition parameters that will maximize signal associated with task effects in brain regions of interest. Beyond hands on learning, I will support Tessa's attendance at the Organization for Human Brain Mapping (OHB) conference, where she will present her findings and attend workshops and symposia on emerging neuroimaging methods. I will also support her application to summer programs such as the MIND and Kavli Summer training programs for neuroimaging study design and methodology. Tessa will have the opportunity to practice her teaching skills via- presentations in my lab meetings and as guest lecturer for Dr. Smith's advanced neuroimaging course. Tessa's exposure to a broad range of neuroimaging study design and analysis methods will allow her to achieve her long-term career goals of running her own neuroimaging lab at an academic institute. I can provide excellent theoretical and hands-on training in fMRI methods for investigating neural mechanisms of social neuroscience questions. [Despite being a junior faculty member, my lab (3 years at Stony Brook University and 1 year at Temple University) has extensive experience developing new neuroimaging paradigms, especially related to social development in adolescents, Tessa will receive training that will prepare her to establish an independent line of research.

**2. Model development and comparison of behavioral social learning.** This goal will be accomplished under the supervision of myself, and Tessa's co-sponsor (Dr. Platt). Dr. Platt is a renowned expert in the use of computational models in social neuroscience, and can provide excellent training that will help Tessa achieve her second goal. As her primary sponsor, I will facilitate collaboration with Tessa and Dr. Platt, and her attendance of Platt lab meetings as well as joint Penn-Temple social neuroeconomics meetings. I will provide Tessa with additional support in her attendance of the Reinforcement Learning and Decision-Making (RLDM) conference where she can present findings, and attend workshops and talks related to computational model development and comparison. Then, Tessa, with the consultation of myself and Dr. Platt, will lead a workshop on computational modeling at Temple to reinforce and disseminate her skills. Tessa and I will also discuss directed readings, to ensure that she is fluent in topics in the existent literature. In particular, our discussions will focus on ways to bridge her areas of interests—learning, neuroscience, and social competence. Importantly, this will help Tessa achieve her career goal of understanding and modeling mechanisms that contribute to psychopathology in youth. Through the support of the NRSA, Tessa will gain skills and have opportunities to work with Dr. Platt and his group that she would not otherwise have through her graduate training. Specifically, she will become proficient in applying computational models to complex social interactions to determine the etiology of social deficits. Application of these cutting-edge methods are rarely

used in the field of social neuroscience and provide Tessa with the unique opportunity to become a leader in her field.

**3. Functional connectivity analyses.** Tessa ultimately would like to run her own neuroimaging lab and examine circuit-level dysfunction associated with impairments in social processing. To achieve this long-term goal, Tessa will need to acquire skills in functional connectivity analyses techniques. As a leading expert in the field of social neuroscience and the use of neuroimaging to investigate mechanisms of social dysfunction in youth, I am well-positioned to train Tessa on a variety of neuroimaging techniques. I will teach Tessa to implement psychophysiological interaction (PPI) analyses in a hands-on fashion. [As a junior faculty member, I am able to provide Tessa with hands on training that will] refine her ability to write data analysis scripts and implement quality-control methods. This will directly allow her to address aim 2 of her research proposal.

I will meet with Tessa weekly to discuss directed readings on functional connectivity analyses and review her analyses on several of my existing data sets as well as data collected under her proposed project. In addition to my direct mentorship, I will facilitate her collaboration with Dr. Smith to learn cutting-edge functionally connectivity techniques, such as dual-regression analysis, which she will use as exploratory analyses for her proposed project. I will ensure that Dr. Smith and Tessa meet bi-weekly to develop, test, and assess the quality of her dual regression pipeline. To facilitate her training, Dr. Smith will provide Tessa hands-on instruction and an opportunity to work in his lab to get regular feedback on her pipelines. I will also confirm that Tessa has access to existing scripts for functional connectivity analyses in both my lab and Dr. Smith's lab and the computational resources necessary to conduct analyses on her data. In order to cement her functional connectivity analyses skills, Dr. Smith has agreed to let Tessa guest lecture in his advanced fMRI course at Temple. I will assist Tessa in preparing this lecture and work with her to practice teaching complex neuroimaging to undergraduate and graduate level students. Tessa's hands-on training will also be supplemented by her participation in the TUBRIC and decision-neuroscience journal clubs, and summer fMRI programs (see goal 1). Thus, Tessa's proposed training plan and research project are well-designed to build upon her existing skill set and supplement the training available through Temple and my lab. Obtaining cutting edge, advanced neuroimaging skills will allow Tessa to emerge as a leader of her field and while generating preliminary data for future grant applications. Additionally, she will have the opportunity to gain skills in teaching and course development, which will aid her in acquiring and academic position.

**4. Professional development.** This will be addressed in weekly meetings with myself and Tessa, where we will review data collection progress and plans for manuscripts that describe data collected on existing projects in my lab, her preliminary studies, and the proposed research project. Tessa will benefit from the vibrant research environment in my lab and in the Penn-Temple community more broadly. I will ensure that Tessa attends workshops and seminars on issues of publication, professional collaboration, and ethical responsibilities regularly offered at Temple. Tessa is also the most senior graduate student in my lab (*going into her 4th year*), and she will contribute to the supervision of junior graduate and undergraduate students as part of her professional development. I will also facilitate her collaboration with Dr. Kendall who will provide clinical supervision to help Tessa attain her clinical assessment and therapy training goals in the Child and Adolescent Anxiety Disorders Clinic (CAADC). Finally, toward the end of her training period, Dr. Platt and I will provide mentorship as Tessa prepares applications for grants, faculty, and postdoctoral positions at major research institutions. Thus, the overall scope of Tessa's training plan is to broaden and deepen her research program through didactic and experiential activities, and help enhance her growing set of skills. Tessa's research training will primarily take place at the Social Developmental Neuroscience Laboratory (SDN lab) within Temple's Department of Psychology. As the director of the lab, I can assure that Tessa will have access to the recruitment resources, consultants, space, and equipment that are necessary to follow her proposed project through to completion. Throughout the award period, Tessa will benefit from a rich intellectual training environment, including close interactions with Dr. Smith—an expert on functional connectivity analyses, Dr. Kendall—an expert in child and adolescent anxiety disorders, and interactions with other graduate students and research assistants. My office and lab space are in the same building as TUBRIC and the CAADC, all of which I can ensure Tessa will have access to in order to conduct her research project.

As Tessa's sponsor, I will help her implement her research plan, oversee her research training, and coordinate with her co-sponsor (Dr. Platt) and consultants (Drs. Smith and Kendall). I am very much invested in Tessa's training and will be actively engaged in all phases. Broadly, my research uses fMRI, EEG, eye-tracking, and behavior to isolate the neurocognitive mechanisms that support social cognition across development in youth with or at risk for psychopathology. Thus, my experience, methodological expertise, and research interests make me an ideal sponsor for Tessa's project and training goals. I will provide Tessa with the scientific and logistical input she needs to complete her research plan. As Tessa's primary sponsor, I will

meet with her weekly to discuss research design issues, data analysis and interpretation, and manuscript preparation. During these meetings, Tessa and I will also discuss issues related to responsible conduct of research, including studies involving deception, ensuring confidentiality of data management, authorship concerns and collaboration, and issues of conflict of interest. *I will coordinate training and activities with her co-sponsor and consultants to ensure that Tessa is exposed to the extant literature on computational modeling, functional connectivity analyses, and SA disorder – and that she applies this knowledge to the proposed project. It is my expectation that Tessa will submit at least two abstracts for presentation at professional meetings each year, and be first author on 1-2 publications per year, as well as secondary author on at least one other paper each year.* Tessa's own previous publication history, suggests that this is realistic and achievable. After completing her training, Tessa will have gained in-depth knowledge of theoretical and practical issues, and she will be well-equipped to pursue her ultimate goals of becoming faculty at a research institution. Overall, this plan will provide Tessa with extensive training including individualized didactics, in-depth guided readings from experts in the field, workshops, and visits to other laboratories. An NRSA fellowship would provide her with the time and resources necessary to gain expertise in computational modeling and advanced neuroimaging, and the utilization of these measures to examine the development of SA using her own novel paradigm to assess social learning. Importantly, this training plan will allow her to develop expertise in integrating multiple methodologies well beyond what she would be able to learn as a graduate student in my lab alone.

**Co-Sponsor: Dr. Platt.** Based on conversations with Tessa and Dr. Jarcho, I understand that my role in the proposed project will be to mentor Tessa on 3 of her training goals: fMRI-study design, computational modeling and professional development. Through the support of an NRSA, her training plan and research study will allow her to develop the expertise needed to achieve her long-term career goal of becoming a clinical social neuroscientist at an academic institution. Her experience conducting the proposed project will provide her with data to support future grant applications and help her build a unique program of research.

**fMRI study design.** Along with Dr. Jarcho, I will help mentor Tessa's Learning from Evaluation And Recall of iNteractions (LEARN) task design ensure it is optimized for modeling social learning. In particular, I will work directly with Tessa to guide her in making methodological decisions that may impact outcomes, including trial structure and timing, response selection, and interval of measuring peer value. I will hold bi-weekly meetings with Tessa that include directed readings in both learning task design and neuroimaging methods. I believe her LEARN task will be useful for understanding the role of social learning in promoting SA. By using computational modeling, she can estimate the specific mechanisms by which aspects of the social interaction modulate neural processes of social learning. I will help her develop her own program of research for which she can continue to develop and adapt learning tasks to answer clinically relevant social neuroscience questions. My team and I have extensive experience developing and using learning tasks in neuroimaging to understand social development.

**Model development and comparison of behavioral social learning.** As a social neuroscience expert who has extensive experience with computational modeling, I can provide excellent training that will help Tessa achieve her second goal. I will provide Tessa with hands-on training in computational model development and optimization through our bi-weekly meetings and as needed meeting with my post-doctoral students. Our lab uses a variety of modeling techniques and have existing scripts that Tessa will be able to work from in order to adapt her models for her LEARN task. Additionally, I have invited Tessa to attend our lab meetings, where she will be able to present her models and get feedback from our lab on ways to improve and optimize their application to her task. I will help Tessa prepare her work to present at the Reinforcement Learning and Decision-Making Conference, where she can present findings from the proposed study as well as her pilot study. I will also assist Tessa in the preparation of a workshop that she will help run at Temple on computational model development and optimization to strengthen and teach her skills. Tessa and I will also discuss readings from the literature to provide her with a solid theoretical foundation for her modeling skills. Our discussions will focus on methods as well as ways to bridge the learning, neuroscience, and SA literatures. Through the support of the NRSA and her training plan she will gain skills and have opportunities to work with my lab and expand her training outside of her clinical psychology program at Temple University. Tessa's goal of applying computational models to social neuroscience questions to understand psychopathology will give her the skills needed to become a leader of her field.

**Professional development.** This goal will be accomplished through our bi-weekly meetings in which we will review progress on manuscripts on computational modeling. Tessa will also benefit from working directly with my team of graduate students and post-doctoral student who can provide valuable mentorship and guidance on future grant applications, job talks and post-doctoral opportunities. I will also serve on Tessa's

dissertation committee and assist her in preparing for her dissertation proposal and defense based of the proposed project. I am uniquely poised to help Tessa network within the fields of learning and computational modeling that extends her current training and networking opportunities within her primary lab and University. Finally, both Dr. Jarcho and I will provide mentorship as Tessa prepares applications for grants, faculty, and postdoctoral positions at major research institutions. Tessa's primary training in computational modeling will take place in my lab. As the director of the lab, I can guarantee that Tessa will have access to the resources and consultation needed to fulfill her research proposal and training plan.

It is my expectation that Tessa will submit at least two abstracts for presentation at professional meetings, and a first author publication utilizing computational modeling on data collected as part of her NRSA project. Based on my lab's track record and Tessa's publication record this is a feasible goal. Through her proposed training plan and research proposal I strongly believe Tessa will gain the knowledge and skills necessary to pursue her ultimate goals of becoming faculty at a research institution.

#### **NUMBER OF FELLOWS/TRAINEES TO BE SUPERVISED DURING THE FELLOWSHIP.**

Dr. Jarcho will supervise 3 predoctoral trainees (including Tessa). Dr. Platt will supervise 4 predoctoral trainees (including Tessa), and 11 post-doctoral trainees.

#### **APPLICANT'S QUALIFICATIONS AND POTENTIAL FOR A RESEARCH CAREER**

**Sponsor: Dr. Johanna Jarcho.** Working with Tessa for the last 3 years has been an extremely gratifying experience—I am thrilled about her NRSA research and training plan, in large part because of her obvious passion about her proposal. She is exactly the type of student who will make the most of this opportunity and is highly deserving of the NRSA award. Tessa graduated from Boston University with a BS in Human Physiology, which provided her a strong foundation in neuroanatomy, physiology, and pathology. After graduating, she worked as a full-time research assistant for Charles Nelson and a lab manager for Susan Faja at Boston Children's Hospital/Harvard Medical School. I still recall the glowing recommendation letters I received from Drs. Nelson and Faja. Indeed, Tessa had two publications and one first-author publication under review (now published) when she applied to graduate school and had presented several posters at conferences. My own experience working with Tessa has been outstanding—she is on a stellar trajectory already. Her CV actually speaks for itself: although she is [going into her 4<sup>th</sup> year] of our demanding clinical program, Tessa lists 11 papers (4 first-authored) that are published or under editorial review in high-quality journals such as *Journal of Clinical Child and Adolescent Psychology*, *Biological Psychology*, *Depression and Anxiety*, and *Journal of Child Psychology and Psychiatry*—and another 2 first-author in preparation.

During her first two years at Stony Brook University, Tessa laid the foundation for her present proposal. First, she led a study that tested relations between brain function, measured by fMRI and EEG during social and non-social contexts, and SA. Through this project, Tessa quickly learned to scan adolescents and preprocess fMRI data while implementing strict quality control procedures. The results of this project, on which she is currently preparing a manuscript, sparked her interest in the use of neuroimaging to isolate region-specific network activation implicated in SA. However, this study left Tessa with more questions regarding the role of dysregulated brain function in SA.

To address these questions, Tessa took an interest in understanding role that dysregulated brain function plays in the etiology of SA in at risk youth. Using a longitudinal data set, she performed analyses that utilized level of early childhood social reticence, brain function during a social interaction task and SA in preadolescence, to predict subsequent expression of SA in mid-adolescence. Her results demonstrate complex relations between brain and behavior that shed light on why it is that only some socially reticent youth go on to become anxious adolescents. Tessa independently devised the analytic strategy and performed exploratory factor analysis (EFA) to create a composite measure of SA that was used to quantify symptoms during preadolescence and adolescence. While Tessa did not collect these data, the amount of effort she put into wrangling 10 + years of multimodal longitudinal data collected at two different sites was nothing short of herculean. This paired with the fact that she was using new statistical methods and working with neuroimaging data for the first time make the outcome of this project all the more impressive. In fact, her manuscript, [recently accepted] at the *Journal of Depression and Anxiety*, won her an *Excellence in Research Award* at Stony Brook University. Thus, her ability to rapidly and skillfully learn to both collect and analyze neuroimaging data gives me complete confidence that Tessa will be capitalize on the opportunity for advancing her neuroimaging and computational modeling skills in her training plan and proposed study.

After recognizing the important role social experience and dysregulated brain function plays in promoting SA, Tessa and I began to discuss her ideas regarding the current NRSA. Tessa's key insight was the notion that social experiences shape future social behaviors, and despite the fact that most adolescents

experience negative social feedback from peers, many do not develop SA. One reason may be that individuals with SA have difficulties learning from social experiences. Over the next few weeks, we discussed developing a novel paradigm that would allow her to test the role of social learning via social interactions in SA. The paradigm is called the Learning from Evaluation And Recall of iNteractions (LEARN) task, and I firmly believe that this paradigm is poised to make a substantive contribution to the field. It is particularly exciting that she will be examining neural responses to social interactions and predictions about future interactions because it will provide novel insights into how negative biases are formed in SA. Moreover, Tessa will be measuring peer value ratings throughout the task, which will provide her with information about how participant value-judgments effect social experiences. Her proposed study will shed light on how circuit-level functioning may relate to negatively biased predictions about social interactions observed in SA. In our conversations about how to analyze the data, Tessa came up with the idea to apply computational modeling, often used to study learning in non-social contexts, to the social domain. This is another example of Tessa's star quality – very few [*rising 4<sup>th</sup>*] year graduate students are able to independently, take a broader view of multiple fields of research and build a bridge between them. Simultaneously, Tessa began reading about techniques she could use to map functional connectivity between neural circuits that likely support social learning, and identified dual-regression analysis as a possible method for doing so. She then set about building a team of experts to provide her with the training and input needed to successfully bring this project to fruition. The enthusiasm with which Dr.'s Platt (co-sponsor), Smith (consultant), and Kendall (consultant) each agreed to serve in this role are a testament to the quality of the proposed research, and Tessa's capacity to build and lead an interdisciplinary team. Tessa's ability to design the proposed project, outline the analytic strategy, and reach out to mentors exemplifies her ambitious, dedicated and hard-working nature, which will serve her well in completing her training plan.

Given Tessa's obvious intelligence and dedication to clinical research, I believe that her proposed research has a high likelihood of success, and will produce results that will be important for the field, *so much so that I am enthusiastically financing the project*. More importantly, I think the training aspect of the proposal will be crucial for Tessa's scientific development—I am confident that Tessa will be a rising star with unparalleled expertise in advanced neuroimaging and computational modeling skills; she will have the ability to use and combine these methods to answer clinically meaningful questions in relation to SA in adolescence. I have been fortunate to have worked with an impressive group of students at various training levels and I would rank Tessa among the most promising. She is a highly talented young scientist with the ability, skills, and determination to become a successful clinical social neuroscientist. She continues to exceed my high expectations. I give Tessa my highest recommendation and will provide her with the mentorship and financial support she needs to accomplish her goals. Tessa has made the most out of every opportunity that has come her way; I expect the same will hold true with this NRSA.

**Co-Sponsor: Dr. Michael Platt.** I am extremely excited to serve as a co-sponsor for Tessa in the proposed project. While preparing her grant for submission, Tessa approached me to advise on computational modeling and learning task design. During this initial discussion, Tessa was well prepared and answered any questions I had about the project in a manner that demonstrated a strong understanding of the literature and analytic methods. I was impressed with her initiative in reaching out to me, and her clear appreciation of the importance of collaboration in successful science. In my numerous follow-up discussions with her about the project, I continued to be impressed with her intelligence, independence, curiosity, and creative approach to social neuroscience questions. She is clearly the type of student who is highly deserving of and would benefit from an F31 Fellowship. I am very excited to collaborate with her on this project, and to be involved in an interdisciplinary collaboration across departments at Temple.

From our discussions, it is clear that Tessa's proposal represents a perfect supplement to her current training at Temple University and aligns well with her stated research interests. Tessa has assembled a team of interdisciplinary mentors that will ensure that she receives the training needed to complete the proposed project and develop as an independent scientist. Her training plan is strong, and the role of each member of the mentorship team is clearly defined. I understand that my role will involve considerable mentorship on computational modeling methods, and implementation of these methods in multiple manuscripts and future grant proposals. I am happy to meet with Tessa bi-weekly during the funding period, and help her to build her understanding of novel analytic methods. Tessa's research proposal reflects an already sound grasp of computational modeling methods, and the untapped potential role of this analytic method in identifying neural mechanisms of social learning and their role in prompting SA. Her project is novel, exciting, and has potential for important public health impact. I recommend her in the strongest possible terms.



Michael Platt, Ph.D.  
Director, Wharton Neuroscience Initiative  
James S. Riepe University Professor  
Department of Neuroscience, Perelman School of Medicine  
Department of Psychology, School of Arts and Sciences  
Marketing Department, the Wharton School  
University of Pennsylvania  
[mplatt@mail.med.upenn.edu](mailto:mplatt@mail.med.upenn.edu)



July 3, 2019

Dear Tessa,

I am thrilled to serve as a consultant on your proposed project, "Learning to fear social interactions: Dysregulated neural mechanisms of social learning in adolescent social anxiety." I firmly believe that you have the potential to become an expert in social neuroscience and the application of computational modeling to your work. Your proposed project is ideal for helping you to achieve your career-goals as it isolates mechanisms of how the social environment modulates social learning to promote social anxiety symptoms through computational modeling and functional neuroimaging.

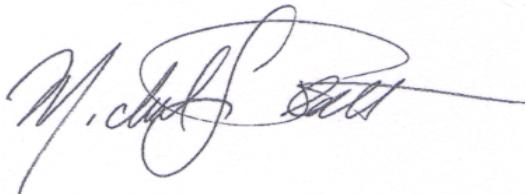
I am excited to serve as a consultant on your dissertation project. Your thoughtfully developed novel task models social interactions in real-time in an ecologically valid context, which allows participants to make trial-by-trial predictions about future social interactions and value judgements about how a peer's feedback matters to them while in the scanner. The design and questions raised by this project showcase your ability to bridge multiple disciplines to ask critical questions in social neuroscience and leverage cutting-edge methodologies to disentangle complex social questions. As an expert in social neuroscience and computational modeling analyses, I am strongly qualified to mentor the study design and computational modeling analyses for your proposed project. Additionally, I have supervised many PhD students and post-docs with NRSA awards to great success. My trainees have gone on to attain academic positions at universities and research institutes and to compete successfully for their own grant funding. Thus, I am highly-qualified to ensure your proposed project and training plan can be successfully conducted and your findings disseminated to the scientific community.

I am eager to join your mentoring team, which is led by a rising star in social cognitive neuroscience Johanna Jarcho. Though more junior than myself, Johanna is not only brilliant but she is clearly committed to providing a superb environment for your training and, based on my experience, she will be an able and involved mentor. It is my understanding that my role on your project will be to mentor the computational model development and optimization in order to compare multiple models of social learning. I will also mentor you on the application of model-based approaches to neuroimaging data. My lab will provide support with example code and I will meet with you every other week for an hour to mentor these analyses. Additionally, you will attend my weekly lab meetings and meet with my team to

discuss and present your analytic strategies and findings from your proposed project. You will also attend our joint Penn-Temple neuroeconomics journal club to learn from and present your proposed project and results.

I believe you are a remarkable graduate student, and your proposed project and training goals have the potential to provide you with the training and skills required to become a leader in your field. Funding from an NIH NRSA would be an ideal way for us to work together on this project and allow you to access the resources and expertise of my lab. It is with great eagerness that I serve as a consultant on your application and professional development.

Best wishes,

A handwritten signature in blue ink, appearing to read "Michael L. Platt".

Michael L. Platt, Ph.D.  
James S. Riepe University Professor  
University of Pennsylvania



David V. Smith, Ph.D.  
Assistant Professor  
Department of Psychology  
Temple University  
[david.v.smith@temple.edu](mailto:david.v.smith@temple.edu)

825 Weiss Hall  
1701 North 13th Street  
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March 20<sup>th</sup>, 2019

Dear Tessa,

I am delighted to serve as a consultant on your proposed project, "**Learning to fear social interactions: Dysregulated neural mechanisms of social learning in adolescent social anxiety.**" I believe that you have the potential to not only thrive as an independent researcher, but to become an expert in social neuroscience, decision and learning modeling, and clinical psychology. Your proposed project, which examines computational and neural mechanisms of how the social environment modulates social learning to promote social anxiety symptoms, will help you achieve these goals.

Though I have only recently begun working with you, I am thrilled to be serving as a consultant on your dissertation project. I believe your ambitious and carefully thought out study design uniquely leverages a clinical sample of socially anxious youth to measure the formation of maladaptive behavioral and neural mechanisms that contribute to core symptoms of social anxiety. As an expert in decision neuroscience and neuroimaging methods and analyses, I am uniquely qualified mentor the study design and neuroimaging analyses for your proposed project. Specifically, I understand that I will be providing mentorship on psychophysiological interaction (PPI) analyses and dual-regression analyses. I also believe that your previous training and research background have prepared you well for undertaking your training goals of learning these analyses.

Through our recent conversations, it is my understanding that my primary role will be to supervise the model-based task decision for ensuring your task will be able to measure social learning curves and social environmental factors. As well, I will be mentoring you on the development of your PPI and dual-regression pipelines in Year 1, and the application of these pipelines in Year 2 of your grant. My lab will provide support with example scripts and pipeline and I will meet with you every other week for an hour to mentor these analyses. Additionally, you will be attending my neuroimaging journal club, as well as the Penn-Temple neuroeconomics and decision-neuroscience journal clubs. During these meetings you will be presenting the techniques you are learning and your results from your project. You will also be invited to present project updates in my lab meetings each term.

I believe you are an exceptional graduate student who has the potential to become a leader in your field. Funding from the NRSA would be an excellent way for you to further cultivate the skills you need to address the gaps in your training that would help you not only complete your dissertation proposal, but also aide you in developing skills required to for achieving your long-term career goals. It is with great enthusiasm that I serve as a consultant on your application and professional development. Best of wishes with your grant application!

Sincerely,

A handwritten signature in blue ink that reads "David V. Smith".

David V. Smith, Ph.D.  
Assistant Professor of Psychology



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**Distinguished University Professor**  
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Director: Child and Adolescent Anxiety Disorders Clinic

Telephone: 215 204 1558  
Clinic phone: 215 204 7165  
Fax: 215 204 5539

July 8, 2019

Dear Tessa:

This letter expresses my excitement and commitment to work with you on your proposed project, "Learning to fear social interactions: Dysregulated neural mechanisms of social learning in adolescent social anxiety." I understand that your project involves computational modeling and functional neuroimaging to study how the social environment modulates learning and social anxiety symptoms. Your project is very innovative and could have meaningful implications for developing and improving treatments for youth with social anxiety. Because my research addresses the treatment of anxiety in youth, I feel well-suited to provide expertise, access to participants, and professional development. I have supervised several NRSA student awards and have aided them in attaining further grant funding and positions at academic institutes. I already collaborate with your advisor, Dr. Jarcho, and my research and clinical expertise are well-suited for your proposed project.

Based on our several conversations and our shared interests, I am happy to serve as a consultant. I understand my primary role on the proposed study will be to supervise the diagnostics of youth with social anxiety. I also understand that we will be integrating your study into my Child and Adolescent Anxiety Disorders Clinic (CAADC) as part of participants' initial intake visits and first session of therapy. Specifically, we will use an opt-in procedure for participants with social anxiety (structured diagnostic interview for DSM-5). Should CAADC participants be interested and eligible, you can work with CAADC staff to schedule your study visits (prior to treatment). In addition to supporting your clinical training and recruitment of CAADC participants, I agree to meet with you every other week for an hour as well as during our regularly scheduled weekly lab meetings. I will also continue to collaborate with Dr. Jarcho and can be available for mentoring. We can discuss practical applications of your proposed study, study enrollment, and overall professional development. During lab meetings we will review the diagnoses of your participants.

I believe the NRSA is an ideal way for you to receive the training and mentorship required to fill the current gaps needed for achieving your long-term career goals. Dr. Jarcho is an active mentor and very knowledgeable. It is with great excitement that I serve as a consultant on your application.

If we can be of any further assistance, or provide you with any further information, please do not hesitate to contact us at 215-204-7165 or [pkendall@temple.edu](mailto:pkendall@temple.edu).

A handwritten signature in black ink, appearing to read "Philip C. Kendall".

## **DESCRIPTION OF INSTITUTIONAL ENVIRONMENT AND COMMITMENT TO TRAINING**

Temple University provides an ideal institutional environment to carry out the proposed training plan and research project. Temple is an R1 university with over 29,000 undergraduate and 10,000 graduate students. The university is home to a diverse range of internationally-renowned research centers and institutes. Within Temple University, the Department of Psychology is a vibrant and stimulating academic environment that is home to distinguished faculty members that have and continue to make substantial contributions to psychological science. The Department of Psychology is the largest doctoral program within the College of Liberal Arts and offers concentrations in Clinical Psychology, Developmental Psychology, Brain and Cognitive Sciences, and Social Psychology. Graduate students are individually mentored by faculty advisors; however, collaboration frequently occurs across faculty labs. The department actively promotes graduate research through the provision of departmental funds to attend conferences and through active sponsorship of departmental colloquia and talks from internationally-acclaimed researchers. Further, there are active journal clubs and seminar series, such as the Decision Neuroscience and Temple University Brain Imaging Center clubs, that span multiple areas of interest and examine cross-cutting themes (e.g., computational modeling and imaging) through the lens of psychology and cognitive behavioral neuroscience.

**The Clinical Psychology Doctoral Program.** Temple University's Department of Psychology's Doctoral Program in Clinical Psychology is accredited by the Psychological Clinical Science Accreditation System, American Psychological Association, and the Academy of Psychological Clinical Science and is one of the leading clinical psychology programs in the country. Its overarching goal is to train competent, innovative clinical scientists who make an impactful contribution to psychological science within academic and medical research settings. The doctoral program is also designed to provide the necessary research and clinical experiences that students need to build a solid foundation of clinical skills. Doctoral students are taught how to effectively research, assess, and treat individuals with psychological, emotional and behavioral disorders. The psychology department is home to internationally renowned faculty who are actively engaged in cutting-edge research actively funded by the NIMH, such as the applicant's sponsor, Dr. Johanna Jarcho and consultant's Drs. Philip C. Kendall and David Smith. The program cultivates a collaborative environment where faculty members are consistently available to graduate students to offer consultation, mentorship, and research support – the applicant has found her mentorship team to be extraordinarily knowledgeable and generous with their time.

**Temple University Brain Research and Imaging Center (TUBRIC).** The scanner is housed within the Temple University Brain Research and Imaging Center (TUBRIC), a 3400sf, multi-modal, research imaging center serving the neuroimaging research community on Temple's main campus. TUBRIC is a research-dedicated facility with immediately adjacent participant preparation, testing, and interview space, furnished with a range of integrated and supplemental research instruments to complement basic imaging work. Integrated tools include MRI compatible stimulus delivery (e.g., visual projection, audio, liquid delivery, electric shock delivery), response collection, physiological monitoring, and eye-tracking devices. The center also houses brain electrophysiology (EEG) and brain stimulation (tDCs) equipment. The facility is staffed by a director (Dr. Jason Chein), MRI physicist (Dr. Huijing Peng), neuroimaging supervisor, and administrative and IT support.

**The Child and Adolescent Anxiety Disorders Clinic (CAADC).** The CAADC, directed by Dr. Kendall, is a productive research clinic investigating the efficacy of cognitive behavioral therapy for anxious youth. Dr. Kendall mentors 15 graduate students (applicant included) and cultivates an active and collaborative research environment, whereby graduate students present research and receive feedback from colleagues at weekly.

### **Requirements for a Ph.D. in Clinical Psychology: American Psychological Association (APA)**

**Breadth Requirements.** APA requires that clinical psychology doctoral students have a substantial understanding of and competence in: the breadth of scientific psychology, the history of thought and development within the field, its research methods, and its applications; the scientific, methodological, and theoretical foundations of practice in the substantive area(s) of professional psychology in which the doctoral program emphasizes training; diagnosing or defining problems through psychological assessment and measurement and formulating and implementing intervention strategies (including training in empirically supported procedures); questions of cultural and individual diversity that are relevant to all of the above; and attitudes essential for lifelong learning, scholarly inquiry, and professional problem-solving as psychologists in the context of an evolving body of scientific knowledge. The vast majority, but not all, of APA requirements are satisfied by the curriculum outlined below, since the curriculum is flexible to allow students choice in deciding how some requirements are met and elective courses. Additionally, non-classroom specialized individual activities (e.g., independent readings) in specific areas may also satisfy these requirements.

**Specific Breadth Requirements to be Completed within the First Six Semesters.** Five breadth courses

are required: Biological Bases of Behavior (e.g., Behavioral Neuroscience), Cognitive Bases of Behavior (e.g., Cognitive Psychology), Social Bases of Behavior (e.g., Social Psychology), Affective Bases of Behavior (e.g. Affective Psychology), and Human Development (e.g., Developmental Psychology). The History and Systems requirement is satisfied by completing the courses where History and Systems content is sufficiently covered.

**Required Courses for the Clinical Psychology Program.** Clinical psychology doctoral students must complete the following courses: Introduction to Clinical Psychology, Research Methods in Clinical Psychology, Psychopathology, Psychological Assessment I, Psychological Assessment II, Cognitive and Behavioral Therapies and Empirically-Supported Treatments, and Multicultural Issues in Clinical Psychology.

**Clinical Psychology Topical Seminars.** Requirements include two clinical psychology topical seminars selected from offerings that vary from semester to semester (e.g., Developmental Psychopathology).

**Clinical Psychology Area Talks.** All doctoral students are required to attend clinical psychology area talks during their first four years. The talks fulfill multiple program functions, including dissemination of cutting-edge research by invited speakers, training in empirically-supported treatments, facilitating discussions between the Director of Clinical Training/Clinical Faculty and the graduate student body, and discussion of ethical, multicultural, and diversity issues of relevance to researchers and clinicians.

**Professional Development Seminar.** All students are required to take the Professional Development Seminar during the fall semester of their first year. The Professional Development Seminar covers challenges and opportunities students may encounter following graduation as well as approaches that will help students excel in their graduate careers. The Professional Development Seminar covers topics that include: ethics; mentoring; managing research assistantships; developing an independent line of research; applying for research grants, scholarships and fellowships; publishing empirical journal articles; diversity in academia; career opportunities after graduate school; and the hiring process in academia.

**Departmental Electives.** Doctoral students are required to take two elective courses offered by the Department of Psychology, outside of the Clinical Psychology Area. The applicant has met all course-requirements via transfer credits from Stony Brook University and coursework at Temple University.

**Clinic Teams.** Doctoral students are enrolled on a clinic team, which serves as an in-house practicum experience, during each semester of their second and third academic years. Clinic teams provide doctoral students with training and experience in the assessment and psychological treatment of clients at the Department of Psychology's Psychological Services Center. During a student's fourth and fifth years, students may apply for time-limited practicum experiences in a community setting. The applicant has applied to work in the CAADC for a practicum experience commensurate with her training goal.

**Master's Research Paper.** Due on April 15th of the student's second year in the program, the student defends their Master's paper before a committee of three members of the Department of Psychology Clinical Area faculty. The applicant's Master's research paper was successfully defended at both Stony Brook and Temple Universities and received an *Excellence in Research Award*.

**Preliminary Examination.** Students are required to write a critical review and synthesis of the literature on their special area of interest that is defined through consultation with the student's mentor and be substantively related to the student's dissertation. Students must pass an oral examination by a committee of Department of Psychology faculty members. The manuscript must be completed before June 1 and the oral examination must be passed by September 1 in Year 4. The applicant successfully passed her oral examination.

**Dissertation Proposal.** Students must submit a written proposal of their dissertation research to their Doctoral Advisory Committee. The Dissertation Proposal must be successfully completed by June (completed), and defended by September 1 in Year 5 for students to apply for an internship placement the following year.

**Internship.** A 2,000-hour predoctoral internship is completed in the fifth or sixth year. The internship site supplies a mid-year and end-of-year evaluation of the student, which becomes part of the student's graduate record. The doctoral program requires that all eligible internships be accredited by the APA.

**Time to Completion.** Temple University requires that students complete all degree requirements, including their predoctoral internship, within 7 years (Mean = 6.3 years).

**Evaluation of Progress.** Evaluation of student performance occurs through course grades, evaluative feedback from faculty mentors, and via clinical student evaluation meetings, which take place at the end of each fall and spring semester. Clinical student evaluation meetings consist of a review of each student's progress in coursework, research activities, clinical practicum performance, and collegiality/general professional demeanor. Progress toward timely completion of program requirements is also discussed. The overall evaluation is recorded by the student's mentor, who provides written and verbal feedback to the student. The applicant is on track for meeting all degree requirements and has received faculty commendations for excellence for all semester evaluations at Stony Brook and Temple Universities.

## PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

Are Human Subjects Involved	<input checked="" type="radio"/> Yes	<input type="radio"/> No
Is the Project Exempt from Federal regulations?	<input type="radio"/> Yes	<input checked="" type="radio"/> No
Exemption Number	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5 <input type="checkbox"/> 6 <input type="checkbox"/> 7 <input type="checkbox"/> 8	
Other Requested Information		

**Human Subject Studies**

<b>Study#</b>	<b>Study Title</b>	<b>Clinical Trial?</b>
1	Learning to fear social interactions: Dysregulated neural mechanisms of social learning in adolescent social anxiety	No

## Section 1 - Basic Information (Study 1)

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

### 1.1. Study Title \*

Learning to fear social interactions: Dysregulated neural mechanisms of social learning in adolescent social anxiety

### 1.2. Is this study exempt from Federal Regulations \*

Yes       No

### 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       No

1.4.b. Are the participants prospectively assigned to an intervention?       Yes       No

1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?       Yes       No

1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?       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

- Pediatric social anxiety
- Social Learning
- Computational Modeling
- Functional Neuroimaging

### 2.2. Eligibility Criteria

Eligibility Criteria. Aged 10-15; Capability of performing the experimental tasks (e.g., can read, able to cooperate with MRI data collection); Fluent or native speaker of English; and Informed assent and consent from legal guardian.

Exclusion Criteria. Younger than 10 years, older than 15 years; Problems seeing (not including colorblindness or vision that is corrected with glasses); History of neurological, psychiatric or medical diseases (currently or in the past 3 months of screening) that may interfere with the completion of specific experimental tasks; Head injury with the loss of consciousness greater than 60 seconds; for MRI examination: metal in body or prior history of working with metal fragments (i.e., as a machinist) or any other contraindications for MRI examination (i.e., pacemakers, specific types of braces, surgical aneurysm clips, or known metal fragments embedded in the body); Pregnancy; severe claustrophobia. Youth with current threat of harm to self or others, intellectual impairment, neurological diseases, psychotic disorders, other primary psychiatric diagnoses, significant medical disability, or individuals who have not been stable on a medication for at least 3 months will be excluded from participation.

2.3. Age Limits	Min Age: 10 Years	Max Age: 15 Years
2.4. Inclusion of Women, Minorities, and Children	Inclusion of Women, Minorities, and Children.pdf	
2.5. Recruitment and Retention Plan	Recruitment and Retention Plan.pdf	
2.6. Recruitment Status	Not yet recruiting	
2.7. Study Timeline	Study Timeline.pdf	
2.8. Enrollment of First Subject	05/01/2020	Anticipated

## B.1 Inclusion of Women, Minorities and Children.

**Inclusion of Women and Minorities.** Participants will include males and females ages 10 to 15. There are no proposed exclusion criteria related to sex/gender or racial/ethnic background. There were no exclusion criteria related to sex/gender or racial/ethnic background for the proposed study. None of the hypotheses proposed in the current study are based on sex/gender or ethnic/racial differences. However, demographic differences will be examined as covariates in exploratory analyses given previous studies have shown age, puberty, gender and socioeconomic status effect both social learning and SA.

Participant demographics will reflect both the greater Philadelphia area (35.3% White/Caucasian; 42.9% Black/African American; 12.4% Hispanic/Latino; 6.9% Asian; 2.6% Other/Mixed race) and the Child and Adolescent Anxiety Disorder Clinic (CAADC) patients (based on intakes conducted in the clinic between 2005 and 2018, it is expected that 45% of the sample will be female, 80% White/Caucasian, 10% Black/African American, 10% Hispanic/Latino and 10% Asian). The CAADC recruits from the diverse Philadelphia area. Of note, the CAADC offers treatment on a sliding scale so that individuals from lower socioeconomic backgrounds are able to participate in treatment and research.

Racial Categories	Ethnic Categories				
	Not Hispanic or Latino		Hispanic or Latino		Total
	Female	Male	Female	Male	
American Indian/Alaska Native	0	0	0	0	0
Asian	2	3	0	0	5
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	8	8	0	0	16
White	15	16	3	4	38
More than One Race	1	0	0	0	1
<b>Total</b>	<b>26</b>	<b>27</b>	<b>3</b>	<b>4</b>	<b>60</b>

**Inclusion of Children.** Participants in the current study include adolescents ages 10 to 15 with varying degrees of social anxiety symptoms. Thus, children and adolescents will be included as participants in the present study. The Social Developmental Neuroscience (SDN) lab focuses on neuroimaging research in children and adolescent populations and provides trainees with extensive training and skills in conducting neuroimaging research with children and adolescents, including ethical considerations for scanning, deceiving, and debriefing children and adolescents after their visits. The Child and Adolescent Anxiety Disorders Clinic (CAADC) at Temple University is an outpatient treatment facility specializing in the treatment of anxious youth. CAADC provides trainees with extensive training and experience regarding the ethical conduct of research with children. To supplement this training, all graduate clinicians, including the applicant, at the CAADC receive weekly supervision from licensed clinical psychologists with specialization in treatment of children/adolescents. These supervisors are available for supervision regarding emergent ethical issues during all parts of the proposed study, as needed.

This research will include individuals who are not yet adults (i.e., children and teenagers). The study will pose no more than minimal risk to the participants. We will also obtain permission from the child's legal guardian as well as individual child assent for these participants to protect their rights and welfare.

The proposed research focuses specifically on dysregulated patterns of functional connectivity in social learning that relates to SA. SA typically manifests in early adolescence (~13yrs), and the neural mechanisms that promote SA in early adolescence may differ from the mechanisms that maintain SA during later adolescence and adulthood (16yrs+). Therefore, to limit potential variability associated with maturational changes in brain function, only early adolescents between 10-15 years of age will be studied.

## **Recruitment and Retention Plan**

All recruitment procedures will be carried out by the Jarcho lab staff and managed by Dr. Jarcho. Potential participants will be recruited with: (1) flyers posted and/or handed out around the campus at Temple University and around the Greater Philadelphia community with, (2) the CAADC during their initial assessment visit, (3) purchased commercial mailing lists that include participants in the age bands of interest, (4) telephone calls, emails, letters and/or brochures explaining the study sent to individuals homes, and/or (5) posting advertisements online with information about our study on platforms such as Craigslist, Reddit, Nextdoor, Community listservs, and Facebook. Flyers and on-line postings will target a specific age range based on the audience that is being targeted.

Potential participants recruited from the community will be screened for eligibility via a telephone/in-person screening, with the prospective participant's parent or legal guardian. During screening, potential participants will be assessed to determine if they meet inclusionary or exclusionary criteria. With their verbal permission, they will be asked questions regarding inclusion and exclusion criteria.

To increase the likelihood of obtaining a sample that also includes high levels of SA, individuals will also be recruited during their diagnostic intake assessment (ADIS; Anxiety Disorders Interview Schedule) at the CAADC at Temple University. All CAADC clients will be asked if they would be interested in participating the proposed study prior to their ADIS. Eligible (see A.1.2) and willing participants, will be escorted across the hall to TUBRIC to complete an additional 30 minutes of consent, behavioral tasks, and a stimulated scan. The CAADC receives referrals from a variety of sources, including pediatricians, school guidance counselors, and psychologists. Based on CAADC data (~80 intakes per year), recruitment of 20-30 SA youth is feasible within the project timeline. To allow for attrition, we will begin recruitment at the beginning of Year 1. If recruitment is unexpectedly low (which is very unlikely), additional efforts of recruitment and other community youth anxiety clinics and schools will be made.

Subjects participating in-person will be paid from \$20 per hour for participation. For every eligible participant that a former participant refers to the study, that former participant will receive \$10. Participants would be made aware prior to the session how they would be compensated (e.g., cash or pre-paid gift card). Subjects who withdraw before they complete their participation will receive the prorated expense rate.

### **Study Timeline**

Year 1. Month 1-2: Initial study setup and piloting of the LEARN task and scan acquisition parameters. Month 2: Data collection will begin. Months 2-12: scripts for computational learning models will be developed and tested using existing data; fMRI preprocessing and first level analyses will be conducted directly after data collection of each participant to ensure usability and to inform recruitment. Functional connectivity (FC) analysis pipelines will be developed. Year 2. Months 1-6: Data collection completed. Months 6-12: Final group-level computational modeling and FC analyses and statistical analyses addressing aims 1-2 will be completed. Final manuscripts and dissertation defense completed.

**Inclusion Enrollment Reports**

IER ID#	Enrollment Location Type	Enrollment Location
Study 1, IER 1	Domestic	

**Inclusion Enrollment Report 1**Using an Existing Dataset or Resource\*:  Yes  NoEnrollment Location Type\*:  Domestic  Foreign

Enrollment Country(ies): USA: UNITED STATES

Enrollment Location(s):

Comments:

**Planned**

Racial Categories	Ethnic Categories					Total	
	Not Hispanic or Latino		Hispanic or Latino				
	Female	Male	Female	Male			
American Indian/ Alaska Native	0	0	0	0	0	0	
Asian	2	3	0	0	0	5	
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	
Black or African American	8	8	0	0	0	16	
White	15	16	3	4	0	38	
More than One Race	1	0	0	0	0	1	
<b>Total</b>	26	27	3	4	0	60	

**Cumulative (Actual)**

Racial Categories	Ethnic Categories									Total	
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity				
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported		
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0	
Asian	0	0	0	0	0	0	0	0	0	0	
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0	
Black or African American	0	0	0	0	0	0	0	0	0	0	
White	0	0	0	0	0	0	0	0	0	0	
More than One Race	0	0	0	0	0	0	0	0	0	0	
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0	
<b>Total</b>	0	0	0	0	0	0	0	0	0	0	

### Section 3 - Protection and Monitoring Plans (Study 1)

- 3.1. Protection of Human Subjects PROTECTION OF HUMAN SUBJECTS.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?  Yes  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?  Yes  No
- 3.5. Overall structure of the study team

## PROTECTION OF HUMAN SUBJECTS

### D.1 Human Subjects Involvement, Characteristics, and Design.

The proposed research includes an fMRI study using the LEARN task (see Research Strategy C.1.5) to assess relations between patterns in FC of social learning and their relations to SA. The study will include a screening visit to obtain IRB-approved informed assent/consent and determine eligibility via a diagnostic assessment of SA (ADIS), undergo simulated MRI scanning, and an fMRI visit to complete the LEARN task. This study will be completed on the Temple University campus.

The study will use computational models of social learning to detect patterns of FC during social interactions and their relations to SA in 60 adolescents (10-15 years of age). This work will focus specifically on how factors of the social environment such as peer value and valance and volatility of peer feedback modulate neural mechanisms of social learning to promote SA. SA disorder typically manifests in adolescence, and the neural mechanisms that promote SA in early adolescence may differ from the mechanisms that maintain SA disorder during adulthood. Therefore, to limit potential variability associated with maturational changes in brain function, only early adolescents will be studied. The study will recruitment a clinically-elevated SA sample through the CAADC and the community.

Inclusion Criteria. (see A.1.2)

Exclusion Criteria: (see A.1.3)

Rationale for Inclusion and Exclusion Criteria. Participant inclusion/exclusion criteria were selected based on minimizing risk for SA youth and their families. Additionally, the age range of early adolescences was chosen in order to leverage increases in onset and susceptibility to SA in this populations, which minimizes confounds of neural development if a larger age range were included.

### D.2 Study Procedures, Materials, and Potential Risks.

**D.2.1 Procedures.** After providing parental consent and assent, participants will engage in two study visits. At the first visit (<150mins), the initial diagnostic assessment will be completed along with a simulated fMRI scan, behavioral tasks, and minimal questionnaires. At the second visit (90mins), the participants will undergo a scan (structural MRI and fMRI) while completing the LEARN task. They will also complete a series of questionnaires designed to measure individual differences in social anxiety, social competence, puberty, depression, and other demographics, and a debriefing interview. Parents will complete questionnaires about their child (see Research Strategy C.1.7).

**D.2.2 Materials.** Research material will be obtained from participants enrolled in the study, and will include diagnostic interview, questionnaire, behavioral, and structural and functional MRI data. All data will be identified using alphanumeric codes, and no individually identifiable private information about participants will be attached to data records. A list matching participant names with the numeric codes will be saved in a password-protected computer file, which will be stored on a password-protected server that is behind the Temple University firewall. The only people with access to this password-protected computer file will be the applicant, mentor, and well-trained staff members who must access these data for scheduling purposes.

**D.2.1 Potential Risks.** The studies proposed in this application involve collection of: 1) diagnostic interview and questionnaire data related to current and past mental health status; 2) behavioral data collected during the LEARN task; and 3) structural and functional MRI data. A risk assessment for each type of data collection is presented below.

**D.2.2 Diagnostic interview and collection of questionnaire data.** The diagnostic interview and questionnaires that will be used in this research assess personally sensitive topics, including current and past mental health status, substance abuse and dependence, and current and past psychiatric diagnoses. It is possible that some participants may find questions about these topics distressing. Two steps will be taken to address this possibility. First, during the informed assent/consent process, participants will be told that their responses will be kept confidential, with one exception: the staff is obligated to report significant distress or intent to harm self or others. Second, participants will be told that they may choose not to respond to questions that they find too upsetting. They will also be informed that choosing not to answer certain questions during the diagnostic interview may prevent them from participating in the study, if inclusion/exclusion criteria cannot be adequately assessed. Finally, a plan is in place for assessing and managing immediate risks associated in all participants (described below D.3.2 & D.3.7.1).

**D.2.3 LEARN task.** The LEARN task involves deception, such that participants are told that peers who they interact with will evaluate them. In fact, no peers participate in the study. Some of the peer feedback is negative (e.g., You're boring!). It is possible that some participants may be upset by the negative feedback, or by having been deceived in the course of the study. Steps will be taken to address this possibility. After the study has concluded, participants are debriefed about the use of deception (see D.3.3). Extra care is taken to

ensure that subjects and their guardians understand the concept of deception. Additionally, subjects are reminded that they may choose to discontinue the LEARN task at any time, and that payment is not contingent on their decision to discontinue their participation. Finally, in the unlikely event that the subject expresses distress after debriefing, clinical staff members are available for immediate consultation. Dr. Jarcho's lab has conducted a series of fMRI studies that involve deception in several hundred healthy and anxious children without incident. This includes preliminary work with LEARN, led by the applicant (see Research Strategy, C.1.1).

**D.2.3 MRI scanning.** fMRI scanning is safe, but involves greater risk than behavioral testing. Consequently, standard safety procedures have been established to address relevant risks. These risks include:

- Clinical Hazards. The confining conditions of the MR bore can precipitate claustrophobia. Although participants will be screened for claustrophobia, if a participant becomes uncomfortable during scanning, they will simply be removed from the scanner (notified via squeeze ball). Payment is not contingent on completion of scanning; thus, participants should not be motivated to suppress disclosure of discomfort;
- Collision Hazard. The scanner's magnetic field can cause ferromagnetic objects to become projectiles. Research staff and participants are carefully screened for metallic objects to prevent this hazard;
- Implants/Prostheses. The magnetic field of the scanner can cause a ferromagnetic implant or prostheses to heat up or be displaced and cause injury or death. Individuals with these devices will be excluded from research;
- Neurostimulation. Some subjects have experienced minor neurostimulation effects with fMRI, such as muscle twitches and "tingling" sensations. There are no known risks associated with these effects;
- Pregnancy. The safety of MRI for imaging embryos/fetuses has not been clearly established. Therefore, women who are pregnant or who suspect that they may become pregnant will be excluded;
- Incidental Findings: The MRI portion of the study is done for research purposes rather than diagnosis. The brain images collected will not be routinely examined by health professionals for potential structural and functional clinical abnormalities. However, in the event an abnormality is detected by the investigator or the MRI technician, Dr. Jarcho will be notified immediately and the brain images will be further examined by a radiologist and the investigator may encourage participants' family to consult their child's physician.

### **D.3 Adequacy of Protection against Risks**

**D.3.1 Compensation.** Participants will be paid \$20/hr for completing the study. This is consistent with payment participants this age range receive in studies conducted by the sponsor, Dr. Jarcho. Participants will be paid the full amount even if they withdraw before completion, thus there will be no incentive for distressed participants to continue in order to receive full payment. This rate of compensation is commensurate with standard rates paid for adolescent research at Temple University.

**D.3.2 Collection of questionnaire data and maltreatment reporting protocol.** Questionnaire data will not be shared. The exception involves evidence of maltreatment, which will be reported to Child Protective Services, as required by law. All research staff will complete Pennsylvania State's Mandated Reporter Training. If, during the course of assessment procedures, clinical or research staff identifies a condition that should require immediate clinical intervention or official reporting (e.g., homicidality/suicidality, child abuse), all necessary steps will be taken. If the staff member believes that the child is at significant risk, or poses significant self or other-destructive behavior, the applicant, the sponsor (Dr. Jarcho), and clinically trained consultant (Dr. Kendall and clinicians in the CAADC) will be notified immediately. The team will review the information provided, and inform the participant's parent and any mental health or professional persons currently treating the child and family (with permission from the guardian), so they can determine the appropriate treatment steps (e.g., hospitalization, referral to a care provider, etc.). During the assent/consent process, guardians will be advised that the law requires reporting of child abuse. When appropriate these reports will be made as soon as possible, but no later than 24 hours after the visit.

**D.3.3 LEARN task.** The clinical staff who obtains informed consent will make a concerted effort to use simple and easy-to-understand language to ensure that the subject understands what this means. The LEARN task will be completed in the fMRI scanner. In addition to being reminded that they may discontinue the scan at any time, subjects will be constantly monitored visually and via a 2-way intercom system. A staff member will communicate with the subject before and after each of the 4 scan runs to assess how they are doing. If the subject expresses significant distress, or asks to discontinue the scan, they will be removed from the scanner. Additionally, the subject will have a squeeze ball (see below), that they can use at any time to discontinue the scan. After the study has concluded, participants are probed for deception, and debriefed about the use of

deception in the study. A process debriefing technique is used in order to:

- probe for the precise nature of participant suspicions by starting with broad questions about their experience in the study, followed by increasingly narrow questions specific to deception;
- explain the nature and purpose of deception, and to do so in a gradual and considerate manner;
- explain the true purpose of the study, and the relationship between procedures and the hypotheses being tested.

This debriefing is designed to ensure that participants:

- are informed of all deceptive elements of the study;
- understand the occasional need for deception in some research;
- leave the study with a better understanding of research and a positive regard for research participation.

All efforts will be made to ensure the subjects (and guardians) are not upset or disturbed by the use of deception. To minimize the potential for any negative effects related to the deception, this debriefing will be performed promptly after task completion. Additionally, subjects and their guardians will be provided with the opportunity to remove their data after deception is revealed. Finally, in the event that the subject expresses being upset after debriefing, clinical staff will be available for immediate consultation.

**D.3.4 MRI scanning.** Several steps will be taken to minimize risks associated with fMRI scanning. In addition to those outlined above (D.2.3), participants will be constantly monitored visually and via a 2-way intercom system during fMRI scans. Participant status will be assessed before and after each scan and during breaks in the tasks, and any adjustments required to facilitate participant comfort will be made. MRI sessions can be discontinued at any time at the participant's request, as outlined during the informed consent procedure. During MRI scanning, participants will hold a squeeze ball and will be taught to use it to communicate with the experimenters and inform them if they wish to stop the scan and be removed from the magnet. In addition, as described previously, careful screening for contraindications will be conducted prior to participation. Subjects will wear earplugs and have padding on either side of their head to minimize the noise of the scanner.

**D.3.5 Confidentiality.** To minimize any legal or social risks and to ensure confidentiality, participants will be assigned an alphanumeric code upon arriving for their screening visit. This code will be used to identify interview, questionnaire, behavioral, and MRI data, and will be kept separate from any personally identifying material. Identifying material will be kept separate from the data in a password-protected computer file stored on a password and firewall-protected server at Temple University.

**D.3.6 Vulnerable Subjects.** This proposed research requires the involvement of children, who are defined as a vulnerable population. The proposed research focuses specifically on dysregulated patterns of functional connectivity in social learning that relates to SA. SA typically manifests in adolescence, and the neural mechanisms that promote SA in early adolescence may differ from the mechanisms that maintain SA during later adolescence and adulthood. Therefore, to limit potential variability associated with maturational changes in brain function, only early adolescents will be studied. See B.1 & D.3.7 for specific measures taken to ensure the protection of this population.

**D.3.7 Additional protections for children.** While the proposed research involves no greater than minimal risk, any form of research with children, and particularly those with or at risk for psychopathology, requires careful attention to issues of protection and tolerability. A series of procedures will therefore be used to minimize risk for distress in the early adolescents who participate in the proposed research.

**D.3.7.1 Diagnostic interview and collection of questionnaire data.** To reduce participant fatigue, the screening and assessment procedures may be spread over additional visits, with breaks interspersed to reduce any discomfort. If a subject becomes distraught in the course of the assessment procedures, or at any other point during the study, staff will pursue steps for appropriate intervention (see D.3.2). If, in the opinion of the research staff, the subject, or the subject's guardian, the assessment procedures or study participation is adversely affecting the subject's emotional well-being, clinical circumstances will be reviewed to determine what additional steps should be taken.

**D.3.7.2 LEARN task and MRI scanning.** A member of the research staff will assess subjects immediately before and after each aspect of the proposed research. For the fMRI visit associated with the LEARN task, the applicant will conduct this assessment, under the supervision of a credentialed clinician (Dr. Kendall). In the event that any level of distress is experienced or reported by the subject, the clinical staff will perform an immediate evaluation. Hence, any problems that stem from these procedures will be detected immediately. All subjects will be debriefed regarding deception following the study. Subjects will have ready access to the applicant who will be present at the scan, should they experience any problems. During scanning, the subject can be seen and heard at all times by research staff. The subject can communicate with the control room

personnel via an intercom at the operating console. The subject can be removed immediately from the scanner if necessary. Subjects will wear earplugs to minimize exposure to excessively loud noises and the length of each MR study will not exceed 90 minutes. If the subject expresses being upset at any point during the scan, while completing the task, or at debriefing, the applicant, and Dr. Kendall are available for immediate consultation. Additionally, prior to scanning, the subject will have the opportunity to habituate to the MRI environment with an fMRI simulator. The proposed research has been approved by the IRB for Temple University.

**Potential Benefits of the Proposed Research to Human Subjects and Others.** Careful consideration was given to minimize the risks and maximize the benefits associated with participating in this study. There are no direct benefits to my research subjects from their participation in the proposed study.

Indirect benefits may include greater understanding of research procedures and satisfaction from contribution to scientific studies. The risks in these studies are comparable to having a routine MRI like that performed in hospitals throughout the world. Functional MRI sessions are performed many hundreds of times a year at Temple alone, and many tens of thousands of times each year throughout the world. The risks associated with this study are reasonable, given that they are very minimal and that significant society benefits in understanding the development of SA and providing novel treatment targets for SA.

**Importance of the Knowledge to be Gained.** The information gained from these studies will not be of benefit to the volunteer subject, but will help further our knowledge of the role of social learning in SA. As social learning is impaired in many neurological and psychiatric diseases, the results from these studies may be of value in future clinical work. The risks associated with this study are reasonable, given that they are very minimal and that significant knowledge will be gained.

**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?**

N/A

**Will a data safety and monitoring board be appointed for this study?**

N/A

**Overall structure of the study team**

N/A

## Section 4 - Protocol Synopsis (Study 1)

### 4.1. Brief Summary

### 4.2. Study Design

#### 4.2.a. Narrative Study Description

#### 4.2.b. Primary Purpose

#### 4.2.c. Interventions

Type	Name	Description

#### 4.2.d. Study Phase

Is this an NIH-defined Phase III Clinical Trial?  Yes  No

#### 4.2.e. Intervention Model

4.2.f. Masking  Yes  No

Participant  Care Provider  Investigator  Outcomes Assessor

#### 4.2.g. Allocation

### 4.3. Outcome Measures

Type	Name	Time Frame	Brief Description

### 4.4. Statistical Design and Power

### 4.5. Subject Participation Duration

4.6. Will the study use an FDA-regulated intervention?  Yes  No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/Investigational Device Exemption (IDE) status

### 4.7. Dissemination Plan

**Delayed Onset Studies**

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