Advancing integrative systems neuroscience education in Northwest Arkansas

The University of Arkansas is investing heavily in neuroscience research and education. In the past 5 years, the university made 10 faculty hires who direct neuroscience labs. These faculty banded together with existing faculty to form an Integrative Systems Neuroscience group, and applied recently to become a Center at the university. In lock step with the Center designation, the university created an institute for interdisciplinary research in neuroscience and is additionally constructing a building that will house modern neuroimaging and wet lab facilities. The building will open in 2024 thanks to philanthropic support from the Walton Family Foundation. Thus, the enthusiasm for neuroscience is shared across many university departments and colleges, and extends outside the university to companies in Northwest Arkansas. An R25 neuroscience education grant from the National Institutes of Health (NIH) can scaffold these developments and build momentum toward the neuroscience institute.

Integrative neuroscience efforts at the university are manifold and beyond infrastructure. These efforts include monthly seminars with external researchers, a neuroscience summit, and interdisciplinary courses, all of which attract students and faculty spanning the departments of psychology, biology, computer science, engineering, and physics. Collaborations between the faculty in these departments have also generated grants, for example, an R21 submission from the Co-PIs on this proposal (Lamm, Westerman, and Zhan), and ABI equipment grants to Westerman, Shew, Nakanishi, and Ceballos. Whereas neuroscience activities on campus are growing in size and frequency, the faculty can lay additional foundation to advance neuroscience research and education.

The R25 grant would fund a neuroscience education program for doctoral students. The program will assemble an interdisciplinary cohort of fellows and provide supplemental summer stipends for 3 years. Students at the end of the second year of their doctoral studies will apply to the program. The program fellows will have completed many requirements in their home department, and so the program supplements years 3-5 of their research. The program includes project-based courses in human and animal neuroscience, workshops in research methodology, research and teaching opportunities outside the fellows' home department, and individualized mentorship. These activities broaden the fellows' scope beyond the training in their home department, and enhance their competitiveness for postdoctoral positions in an increasingly interdisciplinary field.

The program unifies and augments ongoing neuroscience activities at the university, and builds momentum toward the completion of the i3r institute in 2024, in which neuroscience is strongly represented among other University foci. At that point, the faculty will formalize a doctoral degree program in neuroscience and then apply for a T32 grant to support the doctoral program. The R25 bridges current developments to future plans. A neuroscience program provides access to research and education in an ethnically and socioeconomically diverse region with no such program. Neuroscience requires a unique synthesis of skills, for example, deep consideration of space and time in experimental design, statistical analysis, and clear communication. These skills poise students to compete in job markets that emerging technologies will change in unpredictable ways. The outflow of students from the program will form a web of connections in the midwestern and southern United States, thus increasing the ethnic, gender, and geographical diversity of researchers in neuroscience.

Program Activities
The program is designed to broaden the fellows' scope in neuroscience research. The activities are tabulated to show the timeline and then described below.

	Year 1	**Year 2**	**Year 3**
Research and education activities	Attend integrative neuroscience course Attend workshops (MRI, EEG, wet lab, research computing, grant writing) Research rotation	Present research at campus seminar Teaching assistantship for course outside home department Present research at national conference	Dissertation / grant writing group Teach introduction to neuroscience course Host neuroscience summit

Integrative Neuroscience Course. This year-long course will be team-taught by the program faculty. The course surveys the evolution and development of nervous system structure and function, neuroimaging and stimulation methods in humans, physiological techniques in animals, emerging synergies between human and animal neuroscience, and translations of basic science to the clinic. The course also provides instruction on the responsible conduct of research in humans and animals. The fellows will complete a project on real behavioral and neural data with resources that increase the transparency and reproducibility of research (e.g., preregistration, code review, and cloud-computing). The fellows will present their projects to the broader research community on campus.

Workshops
Computing resources (Zhan). The workshop teaches how to use computing resources (e.g., campus clusters and cloud computers) to deploy novel analyses on large datasets, and practices for increasing the transparency and reproducibility of analyses.
EEG research methods (Lamm & Zabelina). The workshop teaches EEG analyses of brain electrical activity (e.g., spectral analyses and event-related potentials).
Grant writing (Behrend & Westerman). The workshop teaches skills to develop and write proposals for student training fellowships (e.g., F31/F32).
MRI research methods (Leong). The workshop teaches MRI analyses of human brain structure, white-matter connectivity, and functional activity.
Rodent research methods (Shew). The workshop introduces students to invasive physiological methods in rodents and combining the neural measurements with naturalistic behaviors (e.g., motion and video recordings in free-moving animals).
Wet lab research methods (Nakanishi). The workshop teaches methods for studying invertebrate nervous systems (e.g., CRISPR/Cas-9, immunohistochemistry, RNASeq).

Teaching opportunities. The fellows will serve as a team of teaching assistants and lecturers for an undergraduate course on introduction to neuroscience under the direction of the program faculty. The fellows will also assist one course outside their home department. The student evaluations of these courses build the fellows' teaching portfolio for future applications to postdoctoral and faculty positions.

Mentorship. Fellows will complete an Individual Development Plan (IDP) with their primary advisor every year in the program. The IDP helps fellows to meet and exceed advisors' expectations, facilitate communication with colleagues, and improve specific skills. The fellow will also be matched with a program faculty outside their home department for additional mentorship. A research rotation will be completed with this secondary advisor or a researcher at another institution. A writing group will gather in the final year of the program to provide guidance and accountability for completing the dissertation and/or a postdoctoral training grant (e.g., F32).

Networking. The fellow will conduct a research project in a laboratory outside of their primary appointment. The research rotation can be completed with a researcher at another institution. This opportunity allows the fellow to learn complementary skills, and will help build the fellows' network for future postdoctoral research positions. Alternatively, fellows can complete an internship at a private company if they intend to work in industry after graduation. The fellows will present their research at seminars, which provides practice for job talks and can also grow their professional network. The fellows will also present their research at a national conference in the final year of the program. Finally, the fellows will organize and host a neuroscience summit in the last year of their participation in the program. The experience will help the fellows build a network with researchers at distant institutions.

Budget. The grant proposal requests funding for 5 years (see **Budget Excel** and **Budget Justification**). Briefly, the program budget will fund supplemental summer stipends (7 fellows in each cohort; 3 cohorts over the course of the grant, 2021-2024, 2022-2025, 2023-2026). Funds will also be provided for fellows to present their research at a national conference. A fraction of summer salary is budgeted for the faculty to develop the curriculum and maintain the program. Funds are also requested to pay for the logistics of hosting the workshops and neuroscience summit. External consultants will be paid modestly to advise the program faculty on not only the R25, but also the university's advancement toward a formal neuroscience doctoral program.

The final grant application to the NIH will expand on the text in this internal application to describe plans for Diversity Recruitment, Instruction in the Responsible Conduct of Research, Evaluation, and Dissemination, as required by the funding opportunity. The final application will also include letters of support from university administration, department heads, and external consultants (e.g., director of the Laureate Institute for Brain Research in Tulsa, Oklahoma; clinical and research directors at University of Arkansas Medical Sciences; collaborating faculty with experience in mentoring student researchers and building interdisciplinary neuroscience programs from Stanford University, University of Alabama, and The University of Texas at Austin).

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: **Leong, Josiah**

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

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 *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California at Berkeley, CA	BA	05/2010	Psychology
University of California at San Francisco, CA	Postbacc	07/2013	Neurology
Stanford University, Stanford, CA	PhD	06/2019	Psychology
Indiana University, Bloomington, IN	Postdoc	07/2020	Psychological & Brain Sciences

A. Personal Statement

Emotions can sway what humans see and do. One framework that can link human emotions to perception and behavior is along the axes of affective valence and arousal. Positive arousal and negative arousal are specifically linked to neuromodulatory systems that innervate not only the subcortical circuits that drive behavioral choices, but also the cortical circuits that process visual stimuli. My research builds tools to measure the structure and function of these circuits, and my current scientific aim is to understand the influence of affect on perception and choice. I have additional expertise with cloud-computing resources, which helps me to train my research team to conduct innovative and reproducible analyses – even in cases where the trainees may not yet have acquired computer programming skills.

My research program originates from the doctoral research that I conducted with Dr. Brian Knutson at Stanford University. I studied how humans can sometimes inhibit their impulses in the face of high stakes, such as money. The functional neuroimaging literatures on incentive anticipation and response inhibition guided me to investigate specific circuits involving the nucleus accumbens, anterior insula, and ventrolateral prefrontal cortex. Inspired by the animal neuroanatomy literature, which established monosynaptic axons between the brain regions, I was the first researcher to use diffusion-weighted MRI to characterize the structural connections in humans. I also successfully linked the structural connectivity of the circuits to task-based functional MRI activity, then to behaviors such as risky gambling (Leong et al, 2016, Neuron; Seaman et al., 2017) and response inhibition in the face of monetary incentives (Leong et al, 2018, NeuroImage). Thus, my research illustrates the promise of using multimodal neuroimaging to build models that link brain structure to brain function to motivated behaviors (Leong et al., Trends in Cognitive Sciences, in review).

- **Leong, J. K.**, Pestilli, F., Wu, C. C., Samanez-Larkin, G. R., and Knutson, B. (2016). White-matter tract connecting anterior insula to nucleus accumbens correlates with reduced preference for positively skewed gambles. *Neuron*, 89, 63-69.
- Seaman, K. L**., Leong, J. K.**, Wu, C. C., Knutson, B., and Samanez-Larkin, G. R. (2017). Individual differences in skewed financial risk taking across the adult life span. *Cognitive Affective and Behavioral Neuroscience*, 17(6), 1232-1241.
- **Leong, J. K.**, Hennigan, K., Samanez-Larkin, G. R., and Knutson, B. Distinct neural circuits support incentivized inhibition. *NeuroImage*, 178, 435-444.
- **Leong, J. K.**, Pestilli, F., and Knutson, B. Linking structural brain connections to value-based choice. *Trends in Cognitive Sciences,* invited submission in review.

I am extending my previous research to study human development with data from the Adolescent Brain Cognitive Development study. The study is longitudinally collecting multi-modal neuroimaging, genetic, and behavioral data from 11,000 adolescents. I automated the analyses from my previous research to deploy on the large dataset. One question I am currently addressing is how subcortical circuits develop reciprocally during adolescence. Preliminary analyses suggest that the structural coherence of a white-matter tract connecting the anterior insula to the nucleus accumbens is associated with nucleus accumbens activity during reward anticipation. Furthermore, both brain structure and function measures relate to self-reported trait impulsivity two years later (Ho et al., 2017, Social Cognitive Affective Neuroscience; Leong et al., Developmental Cognitive Neuroscience, in press). Thus, another question I will test is whether targeted brain measurements early in life can predict adolescents' future life outcomes, such as drug abuse and neuropsychiatric disorders.

- **Leong, J. K.**, Ho, T. C., Colich, N. L., Sisk, L., Knutson, B., and Gotlib, I. H. White-matter tract connecting anterior insula to nucleus accumbens predicts greater future motivation in adolescents. *Developmental Cognitive Neuroscience*, in press. doi: 10.1016/j.dcn.2020.100881.
- Ho, T. C., King, L. S., **Leong, J. K.**, Colich, N. L., Humphreys, K. L., Ordaz, S. J., and Gotlib, I. H. (2017). Effects of sensitivity to life stress on uncinate fasciculus segments in early adolescence. *Social Cognitive and Affective Neuroscience*, 12(9),1460-1469. doi: 10.1093/scan/nsx065

My research program also integrates across clinical and computational neuroscience. For example, I am currently studying individuals who abused stimulant drugs with data from the Stanford NeuroChoice Initiative. Measurements of targeted brain structures may help to predict which individuals will relapse to drug use after leaving an intervention (MacNiven, Leong, & Knutson, 2020, Science Advances).

- MacNiven, K. H., **Leong, J. K.**, and Knutson, B. (2020). Medial forebrain bundle structure is associated with trait impulsivity. *Science Advances*, 6(38), eaba4788. doi: 10.1126/sciadv.aba4788

A novel research area that I developed in my postdoctoral research is the influence of affect on early visual processes. This research seeks to link the neuromodulatory systems that drive approach versus avoidance behaviors to the early cortical systems that process visual stimuli. Specifically, I am studying whether the anticipation of monetary incentives can influence visual appearance (i.e., the momentary apparent contrast of stimuli). I designed psychophysics experiments to study the phenomenon, which is distinct from tasks that study visual perception (e.g., contrast sensitivity, orientation discrimintion, and object categorization). I submitted this novel work for in-principle-publication in Psychological Science as a preregistered report. The detailed consideration of space and time in designing psychophysics and neuroimaging experiments are additional skills that I teach to my research team.

- **Leong, J. K.**, and Pestilli, F. Monetary incentives alter appearance. Psychological Science, preregistration accepted for in-principle publication.

Finally, my research team strives to make all stages of empirical research more accessible and reproducible, from experimental design to data analysis to scientific communication. All of my research is conducted with open-source code on GitHub, and the raw data and statistical analysis code for my publications are on the Open Science Framework (https://osf.io/yavsn/). Neuroimaging analyses are performed on the cloud-based platform Brainlife (https://brainlife.io), which was funded by grants through the BRAIN Initiative. Brainlife allows researchers to perform neuroimaging analyses in an internet web browser. This is a logistical revolution that democratizes access to neuroimaging research and can dramatically change the landscape of research and education in neuroscience. The size and complexity of neuroscience research is rapidly increasing, and these resources help research teams to more faithfully share methods, data, and results.

B. Positions and Honors

Positions and Employment

2007 – 2008	Research Assistant, University of California at Berkeley, Allison Harvey, Ph.D.
2009 – 2010	Research Assistant, University of California at Berkeley, Richard Ivry, Ph.D.
2010 – 2013	Research Associate, University of California at San Francisco, Howard J. Rosen, M.D.
2013 – 2019	Graduate Student Researcher, Stanford University, Brian Knutson, Ph.D.
2019 – 2020	Postdoctoral Researcher, Indiana University, Franco Pestilli, Ph.D.
2020 –	Assistant Professor, Psychological Science, University of Arkansas, Fayetteville, AR

Honors

2007	American Psychological Association Summer Science Institute Trainee (UC San Diego)
2010	UC Berkeley Departmental Honors in Psychology
2013 – 2014	Stanford Center for Cognitive and Neurobiological Imaging Seed Grant ($8,000)
2014	NIH / Stanford Psychology Department Pilot Grant ($10,000)
2014 – 2016	NIMH Predoctoral Training Consortium in Affective Science Trainee (T32 MH020006)
2016	NSF Society for Neuroscience Travel Award (ID: 1543122; PI: Cacioppo)
2017	Kavli Summer Institute in Cognitive Neuroscience Fellowship
2018	Stanford Center at Peking University Predoctoral Fellowship ($7,500)
2018	Stanford Centennial Teaching Assistant Award
2018	Kavli Summer Institute in Cognitive Neuroscience Fellowship (Lake Tahoe meeting)
2019	Indiana University Pervasive Technology Institute Fellowship ($14,000)

Other Experience and Professional Memberships

2011 – 2013	Member, Cognitive Neuroscience Society
2014 –	Member, Society for Neuroscience
2014 –	Reviewer, Social Cognitive and Affective Neuroscience
2015 –	Reviewer, Neurology: Genetics
2015 –	Reviewer, Neurocase
2015 –	Reviewer, Human Brain Mapping
2016 –	Member, Society for NeuroEconomics
2016 –	Reviewer, NeuroImage
2017 –	Reviewer, Science Advances
2018 –	Reviewer, Journal of Neuroscience
2019 –	Reviewer, Scientific Reports
2019 –	Reviewer, Brain Structure and Function
2019 –	Reviewer, Scientific Data
2019 –	Member, Association for Psychological Science
2020 –	Member, Advanced Computational Neuroscience Network

C. Contributions to Science

1. Post-baccalaureate Research: I was a research associate at the University of California, San Francisco Memory and Aging Center for three years prior to starting my doctoral program. I coordinated the Alzheimer's Disease Neuroimaging Initiative (ADNI), an international multi-site effort to characterize biomarkers for Alzheimer's disease. I served an additional role as neuroimaging data analyst. I helped build a database to house longitudinal MRI data from over ten thousand individuals who had been seen by the research center. The tools I developed helped biomedical researchers to perform analyses that combined multi-modal neuroimaging data with additional measurements such as clinical outcomes, genetic and proteomic analyses, and peripheral physiology.

   - Bonham, L. W., Geier, E. G., Fan, C. C., **Leong, J. K.,** Besser, L., Kukull, W. A., Kornak, J., Andreassen, O. A., Schellenberg, G. D., Rosen, H. J., Dillon, W. P., Hess, C. P., Miller, B. L., Dale, A. M., Desikan, R. S., and Yokoyama, J. S. (2016). Age-dependent effects of APOE e4 in preclinical Alzheimer's Disease. *Annals of Clinical and Translational Neurology*, 3(9), 668-677.

2. Graduate Research: I discovered a novel white-matter tract connecting the anterior insula to the nucleus accumbens (NAcc) in humans. I found that the tract's structural coherence was associated with reduced NAcc functional responses to risky gambles and decreased gambling behavior. I believe that anchoring psychological models of motivated behaviors on prior knowledge from neuroanatomy is a useful endeavor. The models should link brain structure to brain function to motivated behaviors, and span levels from physiological measures in animals to neuroimaging measures in humans to psychological theories. The full stack can reciprocally provide targets to manipulate and control motivated behaviors, such as risk taking.

- Ho, T. C., King, L. S., **Leong, J. K.**, Colich, N. L., Humphreys, K. L., Ordaz, S. J., and Gotlib, I. H. (2017). Effects of sensitivity to life stress on uncinate fasciculus segments in early adolescence. *Social Cognitive and Affective Neuroscience*, 12(9),1460-1469.
- **Leong, J. K.**, Ho, T. C., Colich, N. L., Sisk, L., Knutson, B., and Gotlib, I. H. White-matter tract connecting anterior insula to nucleus accumbens predicts greater future motivation in adolescents. *Developmental Cognitive Neuroscience*, in press.
- MacNiven, K. H., **Leong, J. K.**, and Knutson, B. Medial forebrain bundle structure is associated with trait impulsivity. *Science Advances*, in revision.

3. Postdoctoral Research: My postdoctoral research developed a novel research program to study how rewards can enhance visual appearance. The research adapts an established paradigm where covert attention can increase the subjective contrast of visual stimuli. My goals are to first establish the basic mechanisms of the effect, then study the variability of the effect in the healthy human population, and finally attempt to reduce the effect in populations struggling with repeated risk taking, such as drug addiction and problematic gambling. During my postdoctoral research, I additionally contributed to the Brainlife platform, which hosts neuroimaging analyses in an internet web browser. I analyzed a large diffusion MRI dataset (~2000 subjects) with modern whole-brain and targeted tractography analyses, and I am preparing this work for publication. I also built an application on Brainlife for task-based functional MRI analyses, which allows researchers to reproducibly analyze large datasets that local computers cannot handle.

   - **Leong, J. K.**, and Pestilli, F. Monetary incentives alter appearance. *Psychological Science*, in review.
   - Hayashi, S., Caron, B., McPherson, B., Bullock, D., Kitchell, L., Qian, Y., Arya, A., O'Riley, S., **Leong, J. K.**, Avesani, P., Berto, G., Garyfallidis, E., Henschel, R., Dinov, I., Wang, L., and Pestilli, F. Brainlife.io: Reproducible applications and data management using cloud computing for brain imaging analysis. In preparation.
   - Tisdall, L., MacNiven, K. H., **Leong, J. K.**, and Knutson, B. Can the white-matter tracts converging on the nucleus accumbens predict stimulant drug relapse? Preregistered report on AsPredicted.org.

4. Teaching: I taught introductory neuroscience at Stanford University for 4 years. My class included visiting undergraduate and graduate students from other universities, high school students, and international exchange students. Teaching the course was challenging because my students came from different backgrounds, but the experience was rewarding and useful. I discovered new ways to convey the depth and breadth of questions that neuroscience research can address. My teaching reviews were positive, and some students remarked that I had stirred in them a lasting passion for psychology and neuroscience. My commitment to teaching persisted even in my postdoctoral research position, and I was a guest lecturer at Indiana University for a Cognitive Psychology course. As an Assistant Professor at the University of Arkansas, I adapted my introductory neuroscience course for undergraduate students who may have diverse academic backgrounds and intersts. I additionally teach a graduate course on neuroimaging data analysis, which includes a laboratory component that works with real MRI datasets; and an upper division undergraduate course on affective science, which introduces students to the empirical study of emotions by tracing linguistic theories to early physiological research to emerging synergies between human and animal neuroscience.

D. Additional Information: Research Support

Ongoing Research Support

UA Chancellor's Office of Research and Innovation Leong (PI) 08/17/2020 – 08/17/2023
The University of Arkansas is providing $409,814 across 3 years for the development of my laboratory (https://fullstackneuro.io). The funds are currently budgeted to pay for lab renovations to conduct psychophysics and behavioral experiments, computing resources, graduate student stipends, travel support for trainess to attend conferences, and miscellaneous research fees.