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: Fischer, Adina

eRA COMMONS USERNAME (credential, e.g., agency login): ASFISCHER

POSITION TITLE: Clinical Scholar and Postdoctoral Research Fellow

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
Massachusetts Institute of Technology	B.S.	06/2008	Brain and Cognitive Sciences
Dartmouth College	Ph.D.	06/2013	Neuroscience
Dartmouth Geisel School of Medicine	M.D.	06/2015	Medicine
Stanford University School of Medicine	Residency	10/2019*	Psychiatry
Stanford University School of Medicine	Postdoctoral	Ongoing	Psychiatry & Neuroscience

A. Personal Statement

I am currently a Clinical Scholar and T32 Postdoctoral Research Fellow within the Department of Psychiatry at Stanford University. I have spent the past 12 years completing medical, neuroscience and psychiatry training to develop the necessary skills to conduct translational neuroscientific research related to the clinical care of transition age youth with depressive disorders and problematic cannabis use. In graduate school, my dissertation research characterized the acute effects of cannabis on resting state functional connectivity and psychiatric symptoms in patients with schizophrenia and co-occurring cannabis use disorder. My post-graduate research has focused on examining functional neuroimaging biomarkers of risk and resilience in adolescent depression and intrinsic connectivity biomarkers of antidepressant treatment response. For my Klingenstein Third Generation Foundation cross-sectional pilot research, I am examining the effects of cannabis exposure in adolescent depression (ages 14-18), which has helped lay the groundwork for the proposed program of research. The current application builds upon my prior research and clinical experiences and will provide me with the opportunity to obtain training in new areas that are essential for my career goals including (1) learning to characterize multidimensional reward system processes via task-based fMRI (MID) and the multidimensional assessment of reward function and impairment; (2) learning to collect and interpret cannabinoid biospecimens to quantify cannabis exposure via LC/MS and cortisol biospecimens to characterize stress-axis function; and (3) the longitudinal investigation and statistical analysis of translational cannabis and depression research in youth. I have worked with my mentorship team to develop and refine the proposed program of research and training in order to rigorously characterize the impact of cannabis exposure on reward and stress neurobiological systems, and how it may contribute to depressive symptomatology in transition age youth. My primary mentor, Dr. Knutson, is an expert in the characterization of reward system function and impairment in relation to substance abuse and clinical psychopathology. In combination with mentorship from leading experts in their respective fields -- Dr. Piomelli: phyto/endo-cannabinoid pharmacology; Dr. Schatzberg: HPA stress axis physiology and pathophysiology in depression; Dr. Jo: statistical methods for analyzing longitudinal data; and Dr. Tapert: adolescent substance abuse research and Associate Director of the ABCD Study -- the facilities, collaborative community, and institutional support at Stanford will provide an exceptional environment for this K23 Career

Development Award. With the support of the mentored research training I will receive, I will be well prepared to launch my independent research career and conduct mechanism-oriented translational research to improve our understanding of the neurobiological and psychiatric effects of cannabis and assist in developing neurobiologically-informed interventions for cannabis use and depressive disorders.

*Please note that my residency training was extended due to maternity leave in 2017 and 2019.

Recent publications most relevant to this application:

- Fischer AS, Camacho MC, Ho TC, Whitfield-Gabrieli S, Gotlib IH. Neural Markers of Resilience in Adolescent Females at Familial Risk for Major Depressive Disorder. JAMA Psychiatry. 2018 May 1;75(5):493-502. PMID: 29562053.
- 2. <u>Fischer AS</u>, Tapert SF, Lee Louie D, Schatzberg AF, Singh MK. *Cannabis and the Developing* Adolescent Brain. Curr Treat Options Psychiatry. 2020 Jun; 7(2):144-161. PMID: 32714742.
- **3.** Fischer AS, Hagan KE, Gotlib IH. Functional neuroimaging biomarkers of resilience in major depressive disorder. Curr Opin Psychiatry. 2021 Jan; 34(1):22-28. PMID: 33027183.
- 4. Fischer AS, Holt-Gosselin B, Fleming SL, Hack LM, Ball TM, Schatzberg AF, Williams LM. Intrinsic reward circuit connectivity profiles underlying symptom and quality of life outcomes following antidepressant medication: a report from the iSPOT-D trial. Neuropsychopharmacology. 2021 Mar; 46(4): 809-819. PMID: 33230268.

B. Positions and Honors

Positions and Employment

- 2015-2019 Resident in Psychiatry, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA
- 2018- T32 post-doctoral research fellow and Clinical Scholar, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA

Other Experience and Profession al Memberships

- 2013- Member, American Physician Scientist Association
- 2015- Member American Medical Association
- 2015- Member, American Psychiatric Association
- 2018- Member, Northern California Psychiatric Society
- 2020- Member, American Academy of Child and Adolescent Psychiatry

<u>Honors</u>

2007	MIT Tau Beta Pi Honor Society, Mass Beta Chapter
2007	National Society of Collegiate Scholars
2008	Walle Nauta Award for Outstanding Research in Brain & Cognitive Sciences at MIT
2008	Han-Lukas Teuber Award for Outstanding Academic Achievement at MIT
2008	Phi Beta Kappa Honor Society (MIT Chapter)
2008	Society of Sigma Xi (Scientific Research Honor Society)
2013	C. Everett Koop Scholar in Addiction Studies
2013	C. Everett Koop Community Outreach and Advocacy in Mental Health Award
2014	Dartmouth Medical School Award for Excellence in Clinical Psychiatry
2014	American College of Neuropsychopharmacology Travel Award
2015	Society of Biological Psychiatry Medical Student Scholars Fellowship Award
2016	Stanford Society of Physician Scholars
2017	Stanford Counseling and Psychological Services Outstanding Psychiatry Resident Award
2019	American Psychiatric Association Research Colloquium Fellow (Alcohol, Pain and Drug Abuse)
2020	Society of Biological Psychiatry Travel Award
2018-2021	NIMH T32 Ruth L. Kirschstein National Research Service Award Postdoctoral Fellowship
2019-2021	Career Development Institute (CDI) for Psychiatry Fellowship
2019-2022	Klingenstein Third Generation Foundation Fellowship in Adolescent Depression
<u>2021</u>	American Academy of Child and Adolescent Psychiatry Research Colloquium

C. Contribution to Science

1. Early Childhood Cognition

My undergraduate research within the Early Childhood Cognition Laboratory at MIT (PI: Laura Schultz) examined developmental changes in the cognitive structure of children's early beliefs and longitudinal changes in associative learning and theory of mind. Specifically, we examined the role of statistical inference and prior beliefs on children's reasoning about theory-violating evidence. Preschool aged children who failed to endorse a statistically more probable (but a priori unlikely) cause after they were presented with ambiguous evidence were assigned to a statistical reasoning training or a control condition. Relative to the children in the control condition, children in the training condition were more likely to endorse the a priori unlikely variable on a free-explanation task. Findings from this work demonstrated that statistical reasoning training improves preschoolers' ability to learn from data that was inconsistent with their prior beliefs. By delineating developmental differences in children's cognitive framework when learning cause and effect relationships, this research helped inform the development of improved screening tools for earlier diagnosis of neurodevelopmental disorders.

- Bonawitz E, Fischer AS, Schulz L. Teaching 3.5-Year-olds to revise their beliefs given ambiguous evidence. Journal of Cognition and Development 13.2 (2012): 266-280. DOI: 10.1080/15248372.2011.577701
- b. **Fischer AS**, Bonawitz E, Schulz L. *Teaching preschoolers to reason about ambiguous evidence*. Psychology Press (2011): 255-261.
- Bonawitz E, Fischer AS, Schulz L. Training a Bayesian: three-and-a-half-year-olds' reasoning about ambiguous evidence. Proceedings of the Annual Meeting of the Cognitive Science Society, 30 (2008): 837-842.
- 2. Examining the Acute Effects of Cannabis in Patients with Schizophrenia and Cannabis Use Disorder

During my graduate studies, I investigated the effects of acute cannabis administration (3.5% THC inhaled cannabis and 10mg THC ingestion) on brain circuitry (via fMRI), psychiatric symptoms, and neuropsychological functioning in patients with schizophrenia and co-occurring cannabis use disorder relative to healthy controls. Specifically, my dissertation research characterized (1) the effects of acute cannabis administration on changes in resting state functional connectivity of reward, default mode, and cognitive control brain networks, (2) psychopharmacological profiles of cannabinoid agonist administration, and (3) the effects of cannabis on psychiatric symptoms, craving, and withdrawal. My graduate work also demonstrated that intrinsic functional connectivity using nucleus accumbens seed regions of interest could be used to delineate brain reward circuitry and characterize dysfunction in patients with schizophrenia and co-occurring cannabis use disorder.

- a. Fischer AS, Whitfield-Gabrieli S, Roth RM, Brunette MF, Green AI. Impaired functional connectivity of brain reward circuitry in patients with schizophrenia and cannabis use disorder: Effects of cannabis and THC. Schizophrenia Research. 158 (2014): 176-182. PMID: 25037524; PMCID: PMC4778557. DOI: 10.1016/j.schres.2014.04.033.
- b. **Fischer AS**, Whitfield-Gabrieli, S, Roth, R, Brunette M, Green, A. *Cannabinoid agonists, functional connectivity of the default mode network, and working memory performance in patients with schizophrenia and cannabis use disorder.* Neuropsychopharmacology (2014); 39: S203-204.
- c. **Fischer AS**, Whitfield-Gabrieli S, Roth RM, Brunette MF, Green AI. *Response to: Corticoaccumbens circuitry in schizophrenia merely a reward system?* Schizophrenia Research. 161 (2015): 519-520. PMID: 25465412; PMCID: PMC4785886. DOI: 10.1016/j.schres.2014.10.008.
- d. Whitfield-Gabrieli S*, Fischer AS*, Henricks AM, Khokhar JY, Roth RM, Green, AI. Understanding marijuana's effects on functional connectivity of the default mode network in patients with schizophrenia and co-occurring cannabis use disorder. Schizophrenia Research. 194 (2018): 70-77. PMID: 28823723; PMCID: PMC6886576. DOI: 10.1016/j.schres.2017.07.029. *Authors contributed equally.
- 3. Risk and Resilience in Depression

My post-graduate research has focused on investigating functional neuroimaging biomarkers of risk and resilience in adolescent depression and functional connectivity profiles underlying symptom and quality of

life treatment response with antidepressant medication. This program of research has been guided by the collaborative mentorship of Drs. Ian Gotlib, Leanne Williams and Alan Schatzberg. This work centered on characterizing functional connectivity within emotion regulation, executive control, and reward circuitry in youth at high versus low familial risk for major depressive disorder. In addition to delineating functional connectivity profiles that distinguish familial risk, I characterized the influence of stressful life events and family environment on subsequent resilience versus conversion to psychopathology. In a separate project, I characterized intrinsic functional connectivity biomarkers of antidepressant treatment response with respect to symptoms and quality of life in patients with depression. We found that nucleus accumbens functional connectivity may be a mechanistic response biomarker of treatment outcomes.

- a. Fischer AS, Keller CJ, Etkin A. The clinical applicability of functional connectivity in depression: Pathways toward more targeted intervention. Biological Psychiatry CNNI. 1 (2016): 262-270. PMID: 29560882. DOI: 10.1016/j.bpsc.2016.02.004.
- b. Fischer AS, Elwood-Lowe M, Colich N, Cichoki A, Ho T, Gotlib I. Reward circuit biomarkers of risk and resilience in adolescent depression. Journal of Affective Disorders. 246 (2019): 902-909. PMID: 30795497; PMCID: PMC6391738. DOI: 10.1016/j.jad.2018.12.104.
- c. <u>Nimarko AF, Fischer AS, Hagan KE, Gorelik AJ, Lu Y, Singh MK. Neural correlates of positive</u> <u>emotion processing that distinguish healthy youth at familial risk for bipolar versus major depressive</u> <u>disorder. Am Acad Child Adolesc Psychiatry. 2020 Jul 29:S0890-8567(20)31332-0. Epub ahead of</u> <u>print. PMID: 32738282.</u>
- d. Fischer AS, Holt-Gosselin B, Fleming SL, Hack LM, Ball TM, Schatzberg AF, Williams LM. Intrinsic reward circuit connectivity profiles underlying symptom and guality of life outcomes following antidepressant medication: a report from the iSPOT-D trial. Neuropsychopharmacology. 2021 Mar; 46(4): 809-819. PMID: 33230268.

4. Applied Statistical Modeling to Neuropsychiatric Outcomes Research

In addition to the contributions described above, I have collaborated with other investigators to learn and apply statistical models to neuropsychiatric outcomes research during my graduate and post-graduate studies: I worked with a team of neurosurgeons and biostatisticians to apply predictive models that could help identify risk factors contributing to elevated morbidity and mortality following brain aneurysm surgery. As part of a separate project, I helped examine measures of executive function in young adults with attention deficit hyperactivity disorder using confirmatory factor analysis. At Stanford, I am part of a multidisciplinary study to identify unique patient signatures that optimize treatment selection in major depressive disorder and help predict whether a patient is likely to respond or remit with antidepressant medication (manuscript in preparation). I anticipate building on this work through the training I will receive in this K23, which will allow me to integrate advanced statistical research methods for longitudinal data including linear mixed-effects, regression modeling and mediation analyses.

- a. Roth RM, Lance C, **Fischer AS**, Isquith P, Giancola P. *Confirmatory factor analysis of the BRIEF-A in young adults and its application to ADHD*. Archives of Clinical Neuropsychology. 28 (2013): 425-434. PMID: 23676185; PMCID: PMC3711374. DOI:10.1093/arclin/act031.
- b. Bekelis K, Missios S, Desai A, MacKenzey T, Labropoulos P, Fischer AS, Roberts, D. Predicting inpatient complications from cerebral aneurysm clipping: The Nationwide Inpatient Sample 2005-2009. Journal of Neurosurgery. 120 (2014): 591-598. PMID:24032701. DOI: 10.3171/2013.8.JNS13228.
- c. Bekelis K, Missios S, **Fischer AS**, Desai A, MacKenzey T, Labropoulos N, Eskey, C. *A predictive model of outcomes during cerebral aneurysm coiling.* Journal of Neurointerventional Surgery. 6(2014): 342-348. PMID: 23828326. DOI: 10.1136/neurintsurg-2013-010815.
- d. Fischer AS,* Fleming SL,* Holt-Gosselin B, Ball TM, Williams LM. Interpretable machine learning models for precision psychiatry: A predictive model of antidepressant treatment response in the International Study to Predict Optimized Treatment for Depression (iSPOT-D). Under Revision. *Authors contributed equally.

A complete list of my published work can be found on MyBibliography: <u>https://www.ncbi.nlm.nih.gov/myncbi/adina.fischer.1/bibliography/public/</u>

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

Ongoing Research Support

02/2020- <u>08/2023</u>	Klingenstein Third Generation Foundation in Adolescent Depression Role: PI		
	Award amount: \$30,000 annually for 2 years <u>(no-cost extension through 2023 due to</u> pandemic)		
	A cross-sectional Investigation of the impact of regular cannabis use in adolescent depression		
<u>07/2020-06/2025</u>	<u>Taube Foundation Endowed Fellowship in the Youth Addiction Initiative at Stanford</u> <u>Role: Fellow</u> <u>Award amount: \$60,000 annually for 5 years</u>		
	Funding to support my salary and youth addiction-focused research at Stanford		

Completed Research Support

06/2018 - 12/2018 Stanford Center for Neurobiological Imaging Seed Grant Role: PI Executive control network functional connectivity and resilience to depression in adolescence

Scholastic Performance

MIT Undergraduate GPA: 4.8/5.0

United States Medical Licensing Examinations: Step 1: 254 Step 2 CK: 261 Step 2 CS: Pass (Pass/Fail) Step 3: 260

Board Certification 2020 Board Certified in Psychiatry, American Board of Psychiatry and Neurology (ABPN)