BACKGROUND AND SIGNIFICANCE

Withdrawal from drugs of abuse directly impacts the brain's stress and memory systems, which may underlie individual susceptibility to persistent drug seeking behavior and stress-induced relapse. Preclinical studies demonstrate impaired fear memory processes in rodents withdrawn from alcohol, including abnormally heightened fear responses that are resilient to subsequent attenuation through various training protocols such as exposure therapy—a process in which the original relapse-inducing stimulus is repeatedly shown to the subject (Koob, 2008; Quinones-Laracuente et al. 2015). Fear suppression and addiction share several features including sensitivity to contextual cues and stress-induced relapse of maladaptive behaviors though the underlying neural circuits mediating, and sufficient to intervene with, heightened fear responses following alcohol withdrawal have remained elusive. A mechanistic and circuit-level understanding of withdrawal-induced fear enhancement may lead to the development of effective treatments that facilitate abstinence and prevent relapse in alcohol and other drug disorders.

Alcohol is the most commonly abused drug world-wide. Alcohol Use Disorders (AUDs) is a diagnostic term referring to maladaptive behaviors associated with alcohol abuse and addiction – the continuation of alcohol consumption in the face of negative social, behavioral, and health outcomes (DSM-5; Grant et al. 2015). AUDs affect an estimated 29.1% of the US population at some time in their lives and pose significant personal and economic costs; costs include lost productivity, healthcare, criminal justice, and quality of life, accounting for $249.0 billion to the US economy in 2010 (Sacks et al. 2015). Behavioral and pharmacotherapies improve outcomes, yet even after formal treatment abstinence rates (one measure of treatment effectiveness) range from 25% to 43% suggesting that more than half of individuals that obtain current treatments relapse within a year. These findings underlie the view that alcohol addiction is a chronically relapsing disorder. Understanding the neurobehavioral mediators of relapse – specifically, context- and stress-induced relapse of drug seeking behavior following withdrawal - will facilitate the development of effective treatments to prevent relapse in individuals with AUD.

Activity-dependent and optogenetic approaches to memory manipulation. Ensembles of neurons distributed throughout the brain are thought to encode and maintain specific memory. These neurons can be tagged during learning for subsequent identification and manipulation (Ramirez et al. 2013a). The hippocampus in particular is pivotal for the encoding and retrieval of personally experienced memories. Recently, our work has demonstrated that hippocampus cells in the dentate gyrus (DG) subregion that were active during learning are sufficient to activate the neuronal and behavioral expression of negative, neutral, and positive memory recall, thus raising the possibility of modulating their activity to alter a variety of addiction-related states (Ramirez et al. 2015).

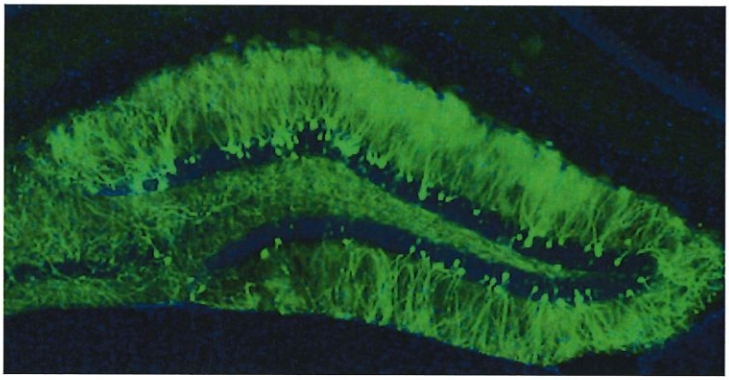
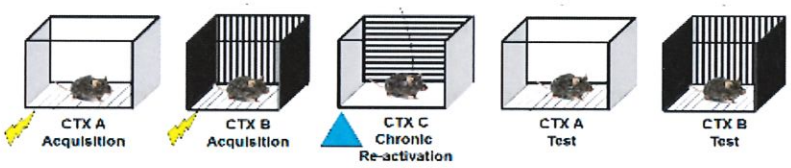


Figure 1*. Genetically engineering hippocampus cells active during learning to express light-sensitive proteins. A mouse is injected with a virus cocktail that tags only active hippocampus cells with any light-sensitive protein of interest, thus permitting optical control of discrete memories. We will focus on the dentate gyrus (DG) subregion of the hippocampus, which here has active cells labeled in green (Ramirez et al. 2013).*

To activate memories in ethanol-withdrawn mice, we will utilize an activity-dependent system to tag hippocampus neurons active during memory formation. This system permits only active cells to be labeled by any light-sensitive protein of interest (**Figure 1**), such as channelrhodopsin-2 (ChR2), which when optically stimulated are sufficient to drive the expression of specific memories (Ramirez et al. 2013b). By utilizing these tools, my recent unpublished data, which forms the foundation of this proposal and thus remains unfunded, demonstrate that repeated optical activation of hippocampus cells processing discrete fear memories is sufficient to induce context-specific suppression of the associated memory. As shown in **Figure 2,** freezing, which is a behavioral proxy of fear memory recall, was significantly reduced in Context A relative to context B in experimental mice. The goal of this proposal is to directly modulate fear memories artificially to facilitate fear memory suppression and permanently mitigate the return of fear in mice withdrawn from alcohol.



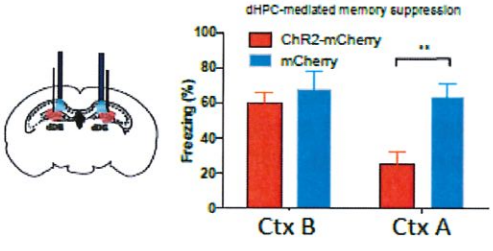


Figure 2. *Subjects acquired a fear memory in Context A (Ctx A) and in Context B (Ctx B), but only Ctx A fear cells were tagged and chronically reactivated in Context C (Ctx C). During Ctx A and B fear recall tests, the experimental group showed a reduction in Ctx A fear responses only. Experimental group: ChR2-mCherry; Control group: mCherry.*

APPROACH: Artificially preventing addiction-induced fear memories

The goal of these experiments is to determine if fear memories resistant to fear suppression in ethanol-withdrawn mice can be mitigated through artificial reactivation of a fear memory and whether such optical manipulations permanently reduce the return of fear over time. These experiments provide a highly novel strategy and a departure from my lab's general research (i.e. interrogating the basic mechanisms of learning and memory) by directly bridging the fields of addiction research, optogenetics, and memory modulation.

Experiment 1. Briefly, mice will receive infusions of our activity dependent viruses and optic fiber implants in the hippocampus to permit delivery of light during defined periods of time. After recovery, mice will undergo a fear conditioning protocol in which they are given mild foot shocks while simultaneously having active hippocampus cells tagged with light-sensitive proteins (**Figure 1**). The following day, they will receive another fear conditioning session in Context B but cells that are active here will not be tagged with light-sensitive proteins. With this strategy, Context A fear cells will be optically modulated, whereas cells active during fear conditioning in Context B will remain untagged. Next, mice will undergo a four-day ethanol exposure paradigm (e.g., Drinking in the Dark paradigm) followed by a two-day ethanol-free period (i.e. withdrawal) which heightens subsequent fear responses that are resistant to natural behavioral attenuation. This strategy also will allow us to specifically tag hippocampus cells processing a fear memory prior to subsequent changes induced by ethanol withdrawal and offers a more ethologically valid paradigm to induce addiction- and withdrawal-related phenotypes. Following the withdrawal period, Control and ethanol-withdrawn mice will be placed into a novel environment and receive repeated light-stimulation of hippocampus cells processing a discrete fear memory of Context A, as outlined in **Figure 2**. Mice will then be tested for fear in both Context A and Context B. Importantly, we predict that ethanol-withdrawn mice will show reduced freezing in Context A relative to Context B, thus demonstrating context-specific suppression of fear's behavioral outputs. Together, these experiments provide an original intervention for suppressing fear responses that are normally resistant to reduction as a result of drug withdrawal and offer a novel bridge between addiction and memory research.

Experiment 2. These lines of experiments will examine the effects of manipulating hippocampus cells processing fear memories in the service of permanently attenuating the return of fear that normally occurs with the passage of time. Indeed, while various exposure therapy protocols are successful in humans to mitigate fear responses, these interventions are acute and are known to be "undone" both outside the training environment and over the course of months. First, all mice will receive a viral infusion, optical implants, fear conditioning, and withdrawn from ethanol as described above. Next, active hippocampus cells processing the fear memory of Context A will be chronically modulated as described in Experiment 1 to suppress the memory. However, two new groups will be utilized: one group will then be given a session in which a mild foot shock is delivered to induce the return of the original fear memory—a process known as reinstatement of fear. The second group will undergo a one month resting period after optically-induced suppression of fear, as the passage of time itself is known to unmask previously suppressed fear—a process termed

spontaneous recovery. If our artificial protocol is sufficient to lastingly suppress a fear memory, then we predict that the levels of fear memory recall after reinstatement and after spontaneous recovery will be *permanently diminished*, and thus demonstrate that artificial manipulation of discrete fear memories is sufficient to bypass the maladaptive effects of ethanol withdrawal on memory. Fittingly, our overall research strategy directly resonates with the Beckman's foundations goal to spearhead truly innovative and high-risk research in the service of advance our understanding of the life sciences. Thus with experiments outlined in this proposal, I firmly believe that our proposed work has the capacity to open a new way of intervening with the cognitive and behavioral pathophysiology underlying addiction-related behaviors.

References:

1. G. F. Koob, A role for brain stress systems in addiction. *Neuron* 2008
2. Grant et al., Epidemiology of DSM-5 Alcohol Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA Psychiatry* 2015.
3. K. Quinones-Laracuente, et al., The effect of repeated exposure to ethanol on pre-existing fear memories in rats. *Psychopharmacology* 2015
4. Ramirez et al. (a), Creating a false memory in the hippocampus *Science* 2013
5. Ramirez et al. (b), Identification and optogenetic manipatulion memory engrams in the hippocampus *Frontiers in behavioral neuroscience* 2013
6. Ramirez et al., Optogenetic stimulation of a hippocampus engram activates fear memory recall *Nature* 2015
7. Sacks et al., National and State Costs of Excessive Alcohol Consumption *Am J Prev Med*, 2015

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: Ramirez, Steve

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

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
Boston University	BA	05/2010	Neuroscience
MIT	PhD	07/2015	Neuroscience
Harvard		01/2016	Neuroscience
Boston University		07/2017	Neuroscience

A. Personal Statement

I am an Assistant Professor at Boston University and Junior Fellow at Harvard University. The mission of my lab's research is to artificially modulate memories to reverse and prevent psychiatric disease-like states, such as depression- and anxiety-related phenotypes. My previous work identified a defined set of cells active during various memory formation, genetically engineered these cells to respond to light, and optically activated or inhibited these cells while measuring the associated behavioral outputs. These projects focused on mapping out which brain regions were necessary and/or sufficient for memory recall, artificially creating false memories in the rodent brain, modulating the emotional strength associated with specific memories, and leveraging these aforementioned manipulations to reverse depression-like phenotypes. My future projects aim to study the brain-wide cellular mechanisms that confer therapeutic or deleterious value to artificially activated positive and negative memories in mice. To compliment these in vivo perturbations, inherent to my aims is a multidisciplinary approach in which I will perform brain-wide analyses utilizing intersectional strategies to identify key cellular loci and physiological signatures mediating memory's putative antidepressant and anxiolytic effects. My working hypothesis is that stimulated memories can lastingly reverse or prevent a trifecta of stress-induced pathologies, including abnormal cellular phenotypes such as dendritic atrophy, circuit-wide malfunctioning such as irregular gene expression patterns, and psychiatric-disease like states such as anehdonia.

My substantial training in neuroscience and teaching has provided me with the comfort and leadership necessary to successfully organize and execute my proposed projects. To that end, my areas of expertise include rodent molecular and behavioral neuroscience, opto- and pharmacogenetics, immunohistochemistry and pharmacology. For instance, in Howard Eichenbaum's lab at Boston University, I performed in vivo single-unit recordings in awake behaving animals to study how hippocampus cells represent the temporal dimension during various behaviors, which contributed to the discovery of "time cells" published in Neuron. In Susumu Tonegawa's lab at MIT, I created the aforementioned genetic tagging system that has enabled numerous projects centered on testing a variety of exciting hypotheses regarding memory formation and retrieval—each of the four ensuing discoveries by my team was published in Nature or Science. Moreover, in terms of mentorship, throughout my career in neurobiology I have mentored numerous undergraduates, graduate students, and postdoctoral fellows. I am grateful that each undergraduate has gone on to a top graduate or medical school; and, each graduate student and postdoctoral fellow has successfully published a high impact

paper on memory. Fittingly, I firmly believe that, as a current Junior Fellow at Harvard and Assistant Professor at Boston University, my lab is in a leading position to resolve the neurobiological mechanisms mediating memory's therapeutic significance and its role in generating maladaptive behavior.

1. Ramirez S, Liu X, MacDonald CJ, Moffa A, Zhou J, Redondo RL, Tonegawa S. Activating positivememory engrams suppresses depression-like behaviour. Nature. 2015 Jun 18;522 (7556):335-9. PubMed PMID: 26085274.
2. Redondo RL, Kim J, Arons AL, Ramirez S, Liu X, Tonegawa S. Bidirectional switch of the valence associated with a hippocampal contextual memory engram. Nature. 2014 Sep 18;513(7518):426-30. PubMed PMID: 25162525; PubMed Central PMCID: PMC4169316.
3. Ramirez S, Liu X, Lin PA, Suh J, Pignatelli M, Redondo RL, Ryan TJ, Tonegawa S. Creating a false memory in the hippocampus. Science. 2013 Jul 26;341(6144):387-91. PubMed PMID: 23888038.
4. Liu X, Ramirez S, Pang PT, Puryear CB, Govindarajan A, Deisseroth K, Tonegawa S. Optogenetic stimulation of a hippocampal engram activates fear memory recall. Nature. 2012 Mar 22;484(7394):381-5. PubMed PMID: 22441246; PubMed Central PMCID: PMC3331914.

B. Positions and Honors

PositionsandEmployment

2007 - 2010 Teaching Assistant, Boston University
2010 - 2014 Teaching Assistant, MIT
2014 - 2014 Visiting Lecturer of Neuroscience, Tufts University
2015 - Junior Fellow, Harvard University
2017 - Assistant Professor, Boston University

OtherExperienceandProfessionalMemberships

2010 - Member, Molecular and Cellular Cognition Society
2010 - Member, Society for Neuroscience
2010 - Member, American College of Neuropsychopharmacology

Honors

2012 Best Abstract, MIT
2012 Angus MacDonald Award for Excellence in Undergraduate Teaching, MIT
2013 Walle Nauta Award for Continued Dedication to Teaching, MIT
2013 World's Top 35 Innovators Under the Age of 35, Technology Review
2013 Top 10 discoveries of 2013, La Recherche
2013 Speaker, TED
2014 World's Top 30 Thinkers Under the Age of 30, Pacific Standard Magazine
2014 Speaker, TEDx
2014 American Ingenuity Award, in the area of the Natural Sciences, Smithsonian Magazine
2014 Top 10 Breakthroughs of the year, Science Magazine
2015 Office of the Dean Graduate Education Diversity Fellowship, MIT
2015 Breakthrough Explorer, National Geographic
2015 30 Innovators Under the Age of 30 , Forbes
2015 Top 10 Bright Young Minds, Science News
2016 Travel Award, American College of Neuropsychopharmacology
2016 Travel Award, Gordon Research Conference
2017 NARSAD Young Investigator Award, Brain and Behavioral Research Foundation
2017 Early Independence Award, NIH

C. Contribution to Science

1. My early publications identified a key node in the brain sufficient for activating discrete memories. Recent studies had indicated that defined populations of neurons were cellular correlates of a specific

memory trace, or "engram". Previously, other groups had found that selective ablation or inhibition ofsuch neuronal populations erased memory responses, indicating that these cells are necessary for memory expression. However, to demonstrate that a cell population is the cellular basis of a specific engram, it was crucial to conduct a sufficiency experiment to show that direct activation of such a population is capable of inducing the associated behavioral output. I was co-first author on these studies identifying a subset of cells in the hippocampus that processed a specific engram and that were sufficient to activate memory recall.

   a. Ramirez S, Tonegawa S, Liu X. Identification and optogenetic manipulation of memory engrams in the hippocampus. Front Behav Neurosci. 2013;7:226. PubMed PMID: 24478647; PubMed Central PMCID: PMC3894458.
   b. Liu X, Ramirez S, Pang PT, Puryear CB, Govindarajan A, Deisseroth K, Tonegawa S. Optogenetic stimulation of a hippocampal engram activates fear memory recall. Nature. 2012 Mar 22; 484(7394):381-5. PubMed PMID: 22441246; PubMed Central PMCID: PMC3331914.

2. We next sought to experimentally demonstrate the malleability of memory by creating a false memory in mice. We accomplished this by optogenetically manipulating engram–bearing cells in the hippocampus to artificially update a neutral memory with aversive information. Importantly, the recall of this false memory was context-specific and activated similar downstream regions engaged during natural memory recall. Thus, our data demonstrated that it is possible to artificially alter the contents of an internally represented and behaviorally expressed memory. I was co-first author on these studies, which provided the conceptual and experimental basis for my more recent experiments seeking to modulate memories in the context of psychiatric disease-like states.
   a. Liu X, Ramirez S, Tonegawa S. Inception of a false memory by optogenetic manipulation of a hippocampal memory engram. Philos Trans R Soc Lond B Biol Sci. 2014 Jan 5; 369(1633):20130142. PubMed PMID: 24298144; PubMed Central PMCID: PMC3843874.
   b. Liu X, Ramirez S, Redondo RL, Tonegawa S. Identification and Manipulation of Memory Engram Cells. Cold Spring Harb Symp Quant Biol. 2014;79:59-65. PubMed PMID: 25637263.
   c. Ramirez S, Liu X, Lin PA, Suh J, Pignatelli M, Redondo RL, Ryan TJ, Tonegawa S. Creating a false memory in the hippocampus. Science. 2013 Jul 26;341(6144):387-91. PubMed PMID: 23888038.

3. I recently led research seeking to bridge artificially activated memories and animal models of psychiatric disorders. Chronic stress is a potent diathesis for abnormal gene, cellular, and systems-level processing in the brain and is capable of precipitating depression- and anxiety-like states. Traditionally, reversing these conditions has relied on drug-based interventions, which by their nature produce brain-wide non-specific effects and rely on drugs that are iterations of, and without improved efficacy over, their 1960s counterparts. As first author or co-author on these studies, our work first showed that we could switch the valence driven by a defined set of memory-bearing hippocampus cells from negative to positive, and vice versa. This work provides the basis for my lab's future experiments seeking to attenuate the emotionally salient components of PTSD-like states, for instance. We then went on to show that optogenetically reactivating positive memories was sufficient to acutely suppress depression-like behaviors and, when chronically activated, was also sufficient to lastingly alleviate stress-induced behaviors as well as to promote neurogenesis.
   a. Tonegawa S, Liu X, Ramirez S, Redondo R. Memory Engram Cells Have Come of Age. Neuron. 2015 Sep 2;87(5):918-31. PubMed PMID: 26335640.
   b. Ramirez S, Liu X, MacDonald CJ, Moffa A, Zhou J, Redondo RL, Tonegawa S. Activating positive memory engrams suppresses depression-like behaviour. Nature. 2015 Jun 18; 522(7556):335-9. PubMed PMID: 26085274.
   c. Redondo RL, Kim J, Arons AL, Ramirez S, Liu X, Tonegawa S. Bidirectional switch of the valence associated with a hippocampal contextual memory engram. Nature. 2014 Sep 18;513(7518):426-30. PubMed PMID: 25162525; PubMed Central PMCID: PMC
   d. Ramirez S, Denny CA and Lebois E. From engrams to pathologies of the brain. Front. Neural Circuits 2017 11:23

D. Research Support

Ongoing Research Support

DP5 OD023106 Ramirez (PI) 09/19/16-08/31/21
NIH
Artificially Modulating Memories to Alleviate Psychiatric Disease-Like States
The major goal of this project is to identify key nodes necessary and/or sufficient for the behavioral expression of positive and negative memories.
Role: PI

NARSAD 07155992-01 Ramirez (PI) 01/01/17-12/31/18
Brain and Behavior Research Foundation
Chronically Activating Positive Memories to Prevent Stress-Related Maladaptive States
The major goal of this project is to chronically stimulate positive memories to induce stress resilience at the neuronal, circuit-level, and behavioral levels.
Role: PI

7168241-01 Ramirez (PI) 09/01/16-08/31/18
Ludwig Family Foundation
Preventing Maladaptive States by Deconstructing Hippocampal Outputs
The major goal of this project is to deconstruct the functional role of hippocampus outputs to the amygdala, prefrontal cortex, and nuceus accumbens in an activity-dependent manner.
Role: PI

Completed Research Support

None.

Beckman Young Investigator Research Support Form

PI Information

APPLICANT NAME:	Steve Ramirez
INSTITUTION:	Boston University
START DATE AT INSTITUTION:	7/1/17
START UP FUND AMOUNT:	$1,250,000
DEPARTMENT WIDE INSTRUMENTATION GRANT NAME AND AMOUNT:	N/A
"TRANSITION GRANTS" (NIH K99/R00) NAME AND AMOUNT:	NIH Early Independence Award (DP5) $1,250,000.00. To transition from graduate student to principal investigator
NUMBER OF UNDERGRADS GRADS POSTDOCS	3 Undergrads, 1 Grad, 4 Postdocs, 3 Research Technicians
PRIMARY RESEARCH OF LAB:	Our lab focuses on artificially manipulating positive and negative memories in both healthy and psychiatric disease-related states.

APPLICATION STAGE (select from drop down):	**SELECT ONE**

CURRENT FUNDING

STOP: Do not enter text in the below charts. Charts will autofill upon completion of pages 3-5.

AWARD NAME	August 2017-July 2018 Amount	August 2018-July 2019 Amount	August 2019-July 2020 Amount	August 2020-July 2021 Amount
0	$ -	$ -	$ -	$ -
0	$ -	$ -	$ -	$ -
0	$ -	$ -	$ -	$ -
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ANNUAL TOTAL:	$ -	$ -	$ -	$ -

PENDING FUNDING

AWARD NAME	August 2017-July 2018 Amount	August 2018-July 2019 Amount	August 2019-July 2020 Amount	August 2020-July 2021 Amount
0	$ -	$ -	$ -	$ -
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0	$ -	$ -	$ -	$ -
ANNUAL TOTAL:	$ -	$ -	$ -	$ -

Beckman Young Investigator Application: Research Support Form

List all Current and Pending Funding as requested in below boxes. If current funding exceeds $225,000 in direct, external annualized funding, you will not be considered for award.

AWARD TYPE (select from drop-down)		SELECT ONE					
Award Name				Grant Source		Grant Title	
Start Date		End Date		Total Amount/ Direct Amount:			
Please provide an annual breakdown of DIRECT funding anticipated during each distribution year (required):							
August 2017- July 2018 Amount		August 2018- July 2019 Amount		August 2019- July 2020 Amount		August 2020- July 2021 Amount	
Overlap (estimated as a percentage) with proposed BYI research (required):							
Please provide a brief synopsis for the above Grant Title in the space below:							
					Is the above grant renewable?		

AWARD TYPE (select from drop-down)		SELECT ONE					
Award Name				Grant Source		Grant Title	
Start Date		End Date		Total Amount/ Direct Amount:			
Please provide an annual breakdown of DIRECT funding anticipated during each distribution year (required):							
August 2017- July 2018 Amount		August 2018- July 2019 Amount		August 2019- July 2020 Amount		August 2020- July 2021 Amount	
Overlap (estimated as a percentage) with proposed BYI research (required):							
Please provide a brief synopsis for the above Grant Title in the space below:							
					Is the above grant renewable?		

AWARD TYPE (select from drop-down)		SELECT ONE					
Award Name				Grant Source		Grant Title	
Start Date		End Date		Total Amount/ Direct Amount:			
Please provide an annual breakdown of DIRECT funding anticipated during each distribution year (required):							
August 2017- July 2018 Amount		August 2018- July 2019 Amount		August 2019- July 2020 Amount		August 2020- July 2021 Amount	
Overlap (estimated as a percentage) with proposed BYI research (required):							
Please provide a brief synopsis for the above Grant Title in the space below:							
					Is the above grant renewable?		

Beckman Young Investigator Application: Research Support Form

List all Current and Pending Funding as requested in below boxes. If current funding exceeds $225,000 in direct, external annualized funding, you will not be considered for award.

AWARD TYPE (select from drop-down)	SELECT ONE				
Award Name		**Grant Source**		**Grant Title**	
Research Grant		Ludwig Family Foundation		Deconstructing memory-bearing hippocampus outputs	
Start Date	8/1/16	**End Date**	8/1/18	**Total Amount/ Direct Amount:**	$150,000.00 / $120,000.00

Please provide an annual breakdown of DIRECT funding anticipated during each distribution year (required):

August 2017- July 2018 Amount	$60,000.00	August 2018- July 2019 Amount		August 2019- July 2020 Amount		August 2020- July 2021 Amount	

Overlap (estimated as a percentage) with proposed BYI research (required):	0

Please provide a brief synopsis for the above Grant Title in the space below:

The goal of this award is to modulate projections from the hippocampus to the amygdala, prefrontal cortex, and nucleus accumbens, in an activity-dependent manner. We hypothesize that independent features of depression, anxiety, and memory-related phenotypes are differentially processed by each projection.

Is the above grant renewable?	No

AWARD TYPE (select from drop-down)	SELECT ONE				
Award Name		**Grant Source**		**Grant Title**	
NARSAD		Brain and Behavior Research Foundation		Manipulative positive memories to prevent stress-induced maladaptive states	
Start Date	1/1/16	**End Date**	12/31/18	**Total Amount/ Direct Amount:**	$70,000

Please provide an annual breakdown of DIRECT funding anticipated during each distribution year (required):

August 2017- July 2018 Amount	$ 35,000.00	August 2018- July 2019 Amount		August 2019- July 2020 Amount		August 2020- July 2021 Amount	

Overlap (estimated as a percentage) with proposed BYI research (required):	0

Please provide a brief synopsis for the above Grant Title in the space below:

Is the above grant renewable?	No

AWARD TYPE (select from drop-down)	SELECT ONE				
Award Name		**Grant Source**		**Grant Title**	
Start Date		**End Date**		**Total Amount/ Direct Amount:**	

Please provide an annual breakdown of DIRECT funding anticipated during each distribution year (required):

August 2017- July 2018 Amount		August 2018- July 2019 Amount		August 2019- July 2020 Amount		August 2020- July 2021 Amount	

Overlap (estimated as a percentage) with proposed BYI research (required):	

Please provide a brief synopsis for the above Grant Title in the space below:

Is the above grant renewable?	

Beckman Young Investigator Application: Research Support Form

List all Current and Pending Funding as requested in below boxes. If current funding exceeds $225,000 in direct, external annualized funding, you will not be considered for award.

AWARD TYPE (select from drop-down)		SELECT ONE					
Award Name			Grant Source		Grant Title		
Start Date		End Date		Total Amount/ Direct Amount:			
Please provide an annual breakdown of DIRECT funding anticipated during each distribution year (required):							
August 2017- July 2018 Amount		August 2018- July 2019 Amount		August 2019- July 2020 Amount		August 2020- July 2021 Amount	
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Please provide a brief synopsis for the above Grant Title in the space below:							
					Is the above grant renewable?		

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Award Name			Grant Source		Grant Title		
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August 2017- July 2018 Amount		August 2018- July 2019 Amount		August 2019- July 2020 Amount		August 2020- July 2021 Amount	
Overlap (estimated as a percentage) with proposed BYI research (required):							
Please provide a brief synopsis for the above Grant Title in the space below:							
					Is the above grant renewable?		

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Award Name			Grant Source		Grant Title		
Start Date		End Date		Total Amount/ Direct Amount:			
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Overlap (estimated as a percentage) with proposed BYI research (required):							
Please provide a brief synopsis for the above Grant Title in the space below:							
					Is the above grant renewable?		