BIOGRAPHICAL SKETCH

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NAME: ENGIN, ELIF

eRA COMMONS USER NAME (credential, e.g., agency login): eegin1

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.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Middle East Technical University, Ankara	BSci	06/2001	Business Administration
Middle East Technical University, Ankara		06/2001	International Economics
Middle East Technical University, Ankara	MA	06/2004	Psychology
University of Alberta, Edmonton, Alberta	PHD	10/2009	Psychology / Behavioral Neuroscience
McLean Hospital / Harvard Medical School, Belmont, MA	Postdoctoral Fellow	12/2012	Laboratory of Genetic Neuropharmacology; PI: Dr. Uwe Rudolph

A. Personal Statement

My research aims to take a reductionist approach to studying mood and anxiety disorders using rodents by breaking these disorders into specific symptoms and behavioral components rather than treating them as overall syndromes. The components I am most interested are related to cognitive symptoms of depression, such as deficits in attentional processes, reward processing, working memory and cognitive flexibility; and to anxiety-related behaviors, which are often disrupted in depressed patients. I am interested in how each of those components are regulated in a healthy organism, as well as what mechanisms go awry in depression, with a particular focus on brain inhibitory neurotransmission. Citations for relevant recent work is provided below:

1. Engin E, Smith KS, Gao Y, Nagy D, Foster RA, Tsvetkov E, Keist R, Crestani F, Fritschy JM, Bolshakov VY, Hajos M, Heldt SA, Rudolph U. Modulation of anxiety and fear via distinct intrahippocampal circuits. eLife 2016 Mar 14;5:e14120. PubMed PMID: 26971710; PubMed Central PMCID: PMC4816644.
2. Engin E, Zarnowska ED, Benke D, Tsvetkov E, Sigal M, Keist R, Bolshakov VY, Pearce RA, Rudolph U. Tonic Inhibitory Control of Dentate Gyrus Granule Cells by α5-Containing GABAA Receptors Reduces Memory Interference. The Journal of Neuroscience 2015 Oct 7;35(40):13698-712. PubMed PMID: 26446222; PubMed Central PMCID: PMC4595621. **
3. Engin E, Bakhurin KI, Smith KS, Hines RM, Reynolds LM, Tang W, Sprengel R, Moss SJ, Rudolph U. Neural basis of benzodiazepine reward: requirement for α2 containing GABAA receptors in the nucleus accumbens. Neuropsychopharmacology 2014 Jul;39(8):1805-15. PubMed PMID: 24553732; PubMed Central PMCID: PMC4059902.

B. Positions and Honors

Positions and Employment

2009 - 2012	Postdoctoral Fellow, McLean Hospital / Harvard Medical School, Belmont, MA
2012 - 2016	Assistant Neuroscientist, McLean Hospital
2016-	Neuroscientist, McLean Hospital
2012 - 2016	Instructor in Psychiatry, Harvard Medical School
2016 -	Assistant Professor, Harvard Medical School

Other Experience and Professional Memberships

2005 -	Member, Society for Neuroscience
2016 -	Member, Joint Committee for the Status of Women, Harvard Medical School
2016-	Member, Community Outreach Subcommittee, Joint Committee for the Status of Women
2017-	Member, Institutional Animal Care and Use Committee, McLean Hospital

Honors

2004	Master's Thesis Award, Institute of Sciences, Turkey
2010	Certificate of Academic Excellence (PhD Thesis Award), Canadian Psychological Association
2010	Eleanor and Miles Shore Harvard Medical School Fellow, Harvard Medical School
2012	Andrew P. Merrill Memorial Fellow, McLean Hospital
2017	Alfred Pope Award for Young Investigators, McLean Hospital

C. Contribution to Science

a. Anxiety disorders are the most common psychiatric disorders with a lifetime prevalence of approximately 15%. At a fundamental level, our understanding of the brain mechanisms of normal anxiety and brain circuitry malfunctions that lead to anxiety disorders is very limited. At a translational level, there is urgent need for pharmacotherapies that are effective with limited unfavorable side effects, and are appropriate for long-term use. So, exploration of potential new targets for anxiolytics needs to take place in parallel with the fundamental circuitry research.

1A. A large part of my research focused on understanding the brain circuitry of how anxiety-like behavior is managed, and what brain mechanisms underlie anxiolysis. As a part of this more basic science focused work, I have also recently aimed to distinguish between anxiety and fear processes and the distinct brain mechanisms of each behavior. My work showed that anxiety and fear behaviors can be dissociated at the level of intrahippocampal circuits, and that $GABA_A$ receptors, intrinsic $GABA_A$ receptor modulator allopregnanolone, and neuropeptides expressed in inhibitory interneurons, such as somatostatin and vasopressin, affect anxiety-related behavior in a brain site specific manner.

a. Engin E, Treit D. The anxiolytic-like effects of allopregnanolone vary as a function of intracerebral microinfusion site: the amygdala, medial prefrontal cortex, or hippocampus. Behav Pharmacol. 2007 Sep;18(5-6):461-70. PubMed PMID: 17762514.

b. Engin E, Treit D. Dissociation of the anxiolytic-like effects of Avpr1a and Avpr1b receptor antagonists in the dorsal and ventral hippocampus. Neuropeptides. 2008 Aug;42(4):411-21. PubMed PMID: 18508119.

c. Yeung M, Engin E, Treit D. Anxiolytic-like effects of somatostatin isoforms SST 14 and SST 28 in two animal models (Rattus norvegicus) after intra-amygdalar and intra-septal microinfusions. Psychopharmacology (Berl). 2011 Aug;216(4):557-67. PubMed PMID: 21424237.

d. Engin E*, Smith KS*, Gao Y, Nagy D, Foster RA, Tsvetkov E, Keist R, Crestani F, Fritschy JM, Bolshakov VY, Hajos M, Heldt SA, Rudolph U. Modulation of anxiety and fear via distinct intrahippocampal circuits. Elife. 2016 Mar 14;5:e14120. PubMed PMID: 26971710; PubMed Central PMCID: PMC4816644. *Authors contributed equally to this work.

1B. Another part of my research focused on discovering possible new targets for anxiolytic drugs, as well as delineating the effects of current anxiolytics. My studies were one of the first to indicate possible anxiolytic-like effects of somatostatin and ketamine, and I also contributed to a better understanding of $GABA_A$ receptor subtypes that mediate anxiolytic-like and fear-reducing effects of benzodiazepines.

a. Engin E, Stellbrink J, Treit D, Dickson CT. Anxiolytic and antidepressant effects of intracerebroventricularly administered somatostatin: behavioral and neurophysiological evidence. Neuroscience. 2008 Dec 2;157(3):666-76. PubMed PMID: 18940236.

b. Engin E, Treit D, Dickson CT. Anxiolytic- and antidepressant-like properties of ketamine in behavioral and neurophysiological animal models. Neuroscience. 2009 Jun 30;161(2):359-69. PubMed PMID: 19321151.

c. Engin E, Treit D. Anxiolytic and antidepressant actions of somatostatin: the role of sst2 and sst3 receptors. Psychopharmacology (Berl). 2009 Oct;206(2):281-9. PubMed PMID: 19609508.

d. Smith KS*, Engin E*, Meloni EG, Rudolph U. Benzodiazepine-induced anxiolysis and reduction of conditioned fear are mediated by distinct GABAA receptor subtypes in mice. Neuropharmacology. 2012 Aug;63(2):250-8. PubMed PMID: 22465203; PubMed Central PMCID: PMC3372637. *Authors contributed equally to this work.

2. In studies investigating the brain mechanisms of benzodiazepine reward, we identified α2-containing $GABA_A$ receptors as an important component of the brain reward circuitry and an essential mediator of reward-related effects of the benzodiazepine diazepam.

a. Reynolds LM*, Engin E*, Tantillo G, Lau HM, Muschamp JW, Carlezon WA Jr, Rudolph U. Differential roles of GABA(A) receptor subtypes in benzodiazepine-induced enhancement of brain-stimulation reward. Neuropsychopharmacology. 2012 Oct;37(11):2531-40. PubMed PMID: 22763624; PubMed Central PMCID: PMC3442348. *Authors constibuted equally to this work.

b. Engin E, Bakhurin KI, Smith KS, Hines RM, Reynolds LM, Tang W, Sprengel R, Moss SJ, Rudolph U. Neural basis of benzodiazepine reward: requirement for α2 containing GABAA receptors in the nucleus accumbens. Neuropsychopharmacology. 2014 Jul;39(8):1805-15. PubMed PMID: 24553732; PubMed Central PMCID: PMC4059902.

3. In work that formed the basis for my current K01 Award, we showed the essential role of tonic inhibition mediated by α5-containing $GABA_A$ receptors in the dentate gyrus in behavioral flexibility. This finding is extremely important, as behavioral rigidity is a central cognitive symptom of a number of neuro-psychiatric disorders, including autism spectrum disorders, schizophrenia and mood disorders.

a. Engin E, Zarnowska ED, Benke D, Tsvetkov E, Sigal M, Keist R, Bolshakov VY, Pearce RA, Rudolph U. Tonic Inhibitory Control of Dentate Gyrus Granule Cells by α5-Containing GABAA Receptors Reduces Memory Interference. J Neurosci. 2015 Oct 7;35(40):13698-712. PubMed PMID: 26446222; PubMed Central PMCID: PMC4595621.

4. Finally, I have contributed to a number of well-cited empirical reviews, aimed at summarizing the current state of research and guiding future research directions regarding the brain mechanisms of anxiety, as well as our knowledge of $GABA_A$ receptors and their role in anxiety and mood disorders.

a. Engin E, Treit D. The role of hippocampus in anxiety: intracerebral infusion studies. Behav Pharmacol. 2007 Sep;18(5-6):365-74. PubMed PMID: 17762507.

b. Engin E, Treit D. The effects of intra-cerebral drug infusions on animals' unconditioned fear reactions: a systematic review. Prog Neuropsychopharmacol Biol Psychiatry. 2008 Aug 1;32(6):1399-419. PubMed PMID: 18495312.

c. Engin E, Liu J, Rudolph U. α2-containing GABA(A) receptors: a target for the development of novel treatment strategies for CNS disorders. Pharmacol Ther. 2012 Nov;136(2):142-52. PubMed PMID: 22921455; PubMed Central PMCID: PMC3478960.

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

Ongoing Research Support

K01 MH107787-01A1
ENGIN, ELIF (PI)
04/01/16-03/31/20
Intrahippocampal dynamics underlying cognitive rigidity
The goal of this project is to determine the real-time changes in hippocampal population and single unit activity during behavioral tasks that require flexible responding.
Role: PI

Completed Research Support

19266, Brain and Behavior Research Foundation, NARSAD Young Investigator Grant
ENGIN, ELIF (PI)
01/15/13-01/14/15
Alpha2-containing GABAA receptors as putative targets for antidepressant therapy
The project focused on the role of α2-GABAA receptors in the antidepressant effects of SSRIs.
Role: PI

Andrew P. Merrill Memorial Research Fellowship
Elif Engin (PI)
07/01/12-06/30/14
Optogenetic interrogation of the role of hippocampal CA3 region in fear learning and consolidation
The goal of this project was to determine the role of the CA3 pyramidal cells in acquisition, retrieval and extinction of fear memories.
Role: PI

Eleanor and Miles Shore Harvard Medical School Fellowship
ENGIN, ELIF (PI)
07/01/10-06/30/12
The Effects of Hippocampal Region-Specific Deletion of the Gabra5 Gene on Extinction and Reversal Learning
The major goal of this project was to investigate the role of α5-containing GABAA receptors in CA1, CA3 and dentate gyrus subregions of the hippocampus in fear-conditioning and reversal learning processes.
Role: PI