

BIOGRAPHICAL SKETCH

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NAME Mark S. Brodie		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME MBRODIE			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION		DEGREE <i>(if applicable)</i>	YEAR(s)
Northwestern University, Evanston, IL		B.A.	1979
University of Illinois At Chicago, Chicago, IL		Ph.D.	1984
			FIELD OF STUDY
			Biological Sciences
			Pharmacology

A. Personal Statement

The goal of the present application is to determine the action of purinergic neurotransmission, especially that mediated by P2X4 receptors, in brain areas related to the rewarding and reinforcing properties of alcohol. My portion of the project involves the investigation of the interaction of ATP and ethanol in mice, either wild-type mice, or KO mice, with and without dysfunction of the P2X4 receptor by knockout or after shRNA treatment. I have been studying the physiology of neurons of the VTA in brain slices from rats and mice since 1985, and I have used a number of electrophysiological techniques (extracellular, sharp electrode intracellular, patch clamping in brain slices, patch clamping in acutely dissociated neurons, loose-patch recording in acutely dissociated neurons) in those studies. Initial pharmacological studies generally are most efficient using extracellular single unit recording, which is the method proposed in this application. I have studied the effects of ethanol on putative dopaminergic VTA neurons since 1986, (our first article on this appearing in 1990), and I continue to examine ethanol effects in the VTA to this day. In addition to studying the primary mechanism of ethanol excitation of pDA VTA neurons, I have studied the interaction between ethanol and a number of agents for the past two decades. Working in my laboratory, I obtained preliminary data for the current application on interaction between ATP inhibition of pDA VTA neurons and ethanol antagonism of that inhibition, and I'm excited and enthusiastic about the prospect of further exploration of this interaction. In summary, I have a long-standing record of successful and productive exploration of ethanol actions in the VTA using the brain slice preparation, and my expertise makes me well prepared to participate in the proposed project.

B. Positions and Honors.

Positions and Employment

- 1984 – 1986 Postdoctoral training, Department of Pharmacology, University of Colorado Health Sciences Center, Denver, CO. Post-doctoral research with Dr. Thomas V. Dunwiddie.
- 1986 – 1988 Research Scientist, Neuroscience Research, Abbott Laboratories, Abbott Park, IL.
- 1988 - 1990 Senior Research Scientist, Neuroscience Research, Abbott Laboratories, Abbott Park, IL.
- 1990 - 1998 Research Assistant Professor, Department of Physiology and Biophysics, College of Medicine, University of Illinois at Chicago, Chicago, IL.
- 1998-2005 Research Associate Professor, Department of Physiology and Biophysics, College of Medicine, University of Illinois at Chicago, Chicago, IL.
- 2005- present Associate Professor, Department of Physiology and Biophysics, College of Medicine, University of Illinois at Chicago, Chicago, IL.

C. Selected publications (selected from 40, in chronological order).

1. **Brodie, M.S.**, Shefner, S.A., and Dunwiddie, T.V., Ethanol increases the firing rate of dopamine neurons of the rat ventral tegmental area in vitro, *Brain Research* 508: 65-69, 1990. PMID: 2337793
2. **Brodie, M.S.**, Lee, K., Fredholm, B.B., Stähle, L., and Dunwiddie, T.V., Central versus peripheral mediation of responses to adenosine receptor agonists: Evidence against a central mode of action, *Brain Research* 415: 323-330, 1987. PMID: 3038272
3. **Brodie, M.S.** and Dunwiddie, T.V., Cocaine effects in the ventral tegmental area: Evidence for an indirect dopaminergic mechanism of action, *Naunyn-Schmiedeberg's Archives of Pharmacology* 342: 660-665, 1990. PMID: 6284315
4. **Brodie, M.S.**, Low concentrations of nicotine increase the firing rate of neurons of the rat ventral tegmental area in vitro, *ADVANCES IN PHARMACOLOGICAL SCIENCES Effects of Nicotine on Biological Systems*, F. Adlkofer and K. Thurau (ed.), Birkhäuser Verlag, 1991, pp. 373-377.
5. **Brodie, M.S.** and Appel, S.B., The effects of ethanol on dopaminergic neurons of the ventral tegmental area studied with intracellular recording in brain slices, *Alcoholism: Clinical and Experimental Research*, 22(1): 236-244, 1998. PMID: 9514313
25. 6. **Brodie, M.S.**, Pesold, C., and Appel, S.B., Ethanol directly excites dopaminergic ventral tegmental area reward neurons, *Alcoholism: Clinical and Experimental Research*, 23: 1848-1852, 1999. PMID: 10591603
7. **Brodie, M.S.**; McElvain, M.A.; Bunney, E.B.; Appel, S.B., Pharmacological reduction of small conductance calcium-activated potassium current (SK) potentiates the excitatory effect of ethanol on ventral tegmental area dopamine neurons, *Journal of Pharmacology and Experimental Therapeutics* 290(1): 325-333, 1999. PMID: 10381795
8. **Brodie, M.S.** and Appel, S.B., Dopaminergic neurons in the ventral tegmental area of C57BL/6J and DBA/2J mice differ in sensitivity to ethanol excitation. *Alcoholism: Clin. Exp. Res.*, 24(7): 1120-1124, 2000. PMID: 10924018
9. Bunney, E.B., Appel, S.B., and **Brodie, M.S.**, Electrophysiological effects of cocaethylene, cocaine and ethanol on dopaminergic neurons of the ventral tegmental area, *Journal of Pharmacology and Experimental Therapeutics*, 297(2): 696-703, 2001. PMID: 11303060
10. **Brodie, M.S.**, Increased ethanol excitation of dopaminergic neurons of the ventral tegmental area following chronic ethanol treatment, *Alcoholism: Clinical and Experimental Research* 26: 1024-1030, 2002.
11. Appel, S.B., Liu, Z.P., McElvain, M.A. and **Brodie, M.S.**, Ethanol excitation of dopaminergic ventral tegmental area neurons is blocked by quinidine, *Journal of Pharmacology and Experimental Therapeutics*, 306 (2): 437-446, 2003. PMID: 12721326
12. Appel, S.B., Wise, L., McDaid, J., Koyama, S., McElvain, M.A., **Brodie, M.S.**, The effects of long chain length n-alcohols on the firing frequency of dopaminergic neurons of the ventral tegmental area. *The Journal of Pharmacology and Experimental Therapeutics*, 318: 1137-1145, 2006. PMID: 16740620
13. Koyama S., **Brodie M.S.** and Appel S.B., Ethanol inhibition of M-current and ethanol-induced direct excitation of ventral tegmental area dopamine neurons. *The Journal of Neurophysiology*, 97: 1977-1985 (2007). PMID: 16956995
114. McDaid, J., McElvain, M.A. and **Brodie, M.S.**, Ethanol effects on dopaminergic ventral tegmental area neurons during block of I_h : involvement of barium-sensitive potassium currents. *The Journal of Neurophysiology* 100: 1202-1210, 2008. PMCID: PMC2544469
15. Nimitvilai, S. and **Brodie, M.S.**, Reversal of prolonged dopamine inhibition of dopaminergic neurons of the ventral tegmental area: Involvement of glutamatergic neurotransmission, *The Journal of Pharmacology and Experimental Therapeutics*, online, 2-17-2010; 333(2):555-563, 2010, PMID: 20164301

D. Research Support

Ongoing Research Support

1 R01 AA05846 (PI: Mark S. Brodie)	4/1/2007 - 3/31/2012	
National Institute of Alcohol Abuse and Alcoholism		
Intracellular Study of Ethanol Effects on Brain Neurons		
The long-term objective of this project is to understand the mechanism of action of acute ethanol on brain neurons. This project studies dopaminergic neurons of the ventral tegmental area in rat brain slice preparations, and is directed toward understanding the ionic mechanism underlying the direct effect of ethanol on these neurons. Specifically, this project will identify and characterize the quinidine sensitive potassium channel through which ethanol excitation of dopaminergic VTA neurons is mediated		
2 R01 DA013951-06 (PI: J.J. Woodward, PI) Subcontract: M.S. Brodie	3/1/2009 to 12/31/ 2014	
National Institute of Drug Abuse		
"Neural actions of Toluene"		
The long-term objective of this project is to understand how the action of toluene on dopaminergic neurons of the ventral tegmental area (DA-VTA neurons), the neurotransmitter systems involved in mediating toluene action, and the affect of toluene on neural circuits. My component on the project involves examining the excitatory action of toluene on DA-VTA neurons, and whether toluene interacts with the same systems that ethanol acts on in the VTA, including the quinidine-sensitive potassium channel. Dr. John Woodward of the Medical University of South Carolina is the PI on this project.		

Completed Research Support

1 R01 AA 09125 (PI: Mark S. Brodie, Ph.D)	8/1/2004 to 6/30/ 2010	
National Institute of Alcohol Abuse and Alcoholism		
"Ethanol-Neurotransmitter Interactions in Brain Neurons"		
The long-term objective of this project is to understand how the action of ethanol on dopaminergic neurons of the ventral tegmental area (DA-VTA neurons) is modified by neurotransmitters, specifically serotonin. During project years 7 to 10, this project studies the mechanism by which serotonin, via activation of 5-HT2 receptors, potentiates the excitatory action of ethanol on DA-VTA neurons.		

(PI: Brodie)	2/1/2008 - 1/31/2009	
Abbott Laboratories		
α 4 β 2 NNR Modulation of Dopamine Neuron Firing in VTA		
The objective of this project is to understand the action of nicotine and selective compounds on dopaminergic VTA neurons. This project studies dopaminergic neurons of the ventral tegmental area in rat brain slice preparations, and is directed toward understanding the excitation produced by nicotine and proprietary compounds in these neurons. The PI on this grant is Dr. Mark S. Brodie.		

K01 (DA 00285-01) (PI: E.B. Bunney) Co-Mentor: Brodie	4/20/1997 - 3/31/2002	
National Institute on Drug Abuse		
"Electrophysiology of cocaine, ethanol and cocaethylene"		
The research objective of this training grant was to study the interaction of ethanol and either cocaine or cocaethylene. The interaction between these agents was studied using intracellular and extracellular recording of dopaminergic neurons in rat brain slices containing the ventral tegmental area. Low concentrations of cocaine and cocaethylene enhance the excitatory action of ethanol on DA-VTA neurons through a serotonergic mechanism. Dr. E. Bradshaw Bunney was the PI on this project.		