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Paul D. Shepard, PhD

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Education and Training

- Ph.D. Medical Physiology, University of Texas Health Southwestern Graduate School of Biomedical Sciences, 1986
- NRSA Postdoctoral Fellowship, Neuropsychopharmacology, Yale University School of Medicine, 1986-1989

Biosketch

For nearly three decades, my work has centered on defining the role of dopamine neurons in neuropsychiatric disease and its treatment. As a doctoral student with Dwight German, I developed a strong interest in the cellular mechanisms regulating neuronal firing pattern and whether drugs capable of altering the temporal organization of spike

trains could be used to modulate neurotransmitter release and thus dopamine's effects on behavior. During a post-doctoral fellowship with Steve Bunney, my work became increasingly focused on the cell autonomous biophysical mechanisms that regulate dopamine cell excitability. As an independent investigator at the Maryland Psychiatric Research Center, I have maintained an active interest in exploring the potential of individual voltage and ligand-gated ion channels to serve as therapeutic targets. For the past decade, our lab has also been interested in the habenula and its connections with the rostromedial tegmental area in the context of salience/reward processing and major depressive disorder.

We use a multidisciplinary approach to record and manipulate activity in the rodent brain including in vivo single unit and in vitro whole cell patch recording techniques, conventional and optogenetic stimulation techniques, and immunohistochemical methods. We also collaborate with investigators using a variety of behavioral methods, conductance-based computational modeling techniques, magnetic resonance imaging and transcranial magnetic stimulation.

Research/Clinical Keywords

Schizophrenia, Depression, Dopamine, Habenula, Animal Models, Antidepressants

Highlighted Publications

- Brown, PL Palacorolla H Brady D Riegger K Elmer GI, Shepard PD. Habenular-induced inhibition of midbrain dopamine neurons is diminished by lesions of the rostromedial tegmental nucleus. *Journal of Neuroscience* 2017 37:217–225.
- Brown PL, Shepard PD Functional evidence for a direct excitatory projection from the lateral habenula to the ventral tegmental area in the rat. *J. Neurophysiology* 2016 116:1161–1174.
- Wang L Lu H Rea W Brown PL Vaupel B Yang Y Stein E, Shepard PD. Activity-independent and activity-dependent labeling of the habenulomesencephalic pathway in the rat using manganese-enhanced magnetic resonance imaging. *PLoS ONE*. 2015 10: e0127773.
- Ji H Tucker K Putzier I Levitan ES Canavier CC HornJP, Shepard PD. Functional Characterization of ERG Channels in Midbrain Dopamine Neurons: Implications for a Role in Depolarization Block. *European Journal of Neuroscience*. 2012 36:2906–2916.
- Herrik KF, Redrobe JP, Holst D, Hougaard C, Sandager-Nielsen K, Nielsen AN, Ji H, Holst NM, Rasmussen HB, Nielsen EØ, Strøbæk D, Shepard PD, Christophersen P. CyPPA, a positive SK3/SK2 modulator, reduces activity of dopaminergic neurons, inhibits dopamine release, and counteracts hyperdopaminergic behaviors induced by methylphenidate. *Front Neuropharmacol*. 2012 3:11.
- Ji HF, Hougaard C, Herrik KF, Strøbæk D, Christophersen P, Shepard P. Tuning the excitability of midbrain dopamine neurons by modulating the Ca²⁺ sensitivity of SK channels. *European Journal of Neuroscience*. 2009 29:1883–1895.
- Ji HF, Shepard PD. Lateral habenula stimulation inhibits rat midbrain dopamine neurons through a GABA_A receptor-mediated mechanism. *Journal of Neuroscience*. 2007 27:6923–6930.
- Shepard PD, Holcomb HH, Gold JM. The presence of absence: habenular regulation of dopamine neurons and the encoding of negative outcomes. *Schizophrenia Bulletin*.

2006 32:417-421.

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