Alan L. Pehrson, Ph.D.

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Education

Virginia Commonwealth University – Ph.D. in Psychology (Biological) – 2007
Virginia Commonwealth University – M.S. in Psychology (Biological) – 2003
Virginia Commonwealth University – B.S. in Psychology – 2001

Professional Experience

Research Scientist, May 2014 to 31 December 2015
Postdoctoral Fellow, February 2010 to May 2014
Lundbeck Research USA, Inc – Paramus, NJ
Advisor – Connie Sanchez, D.Sc.

- Responsible for the successful development and differentiation of the multimodal antidepressant vortioxetine from other antidepressants, identifying and managing collaborations with academic researchers and contract research organizations, supporting all non-clinical vortioxetine experiments with target occupancy data, and modelling the effects of vortioxetine on neuronal behavior.
- Played an integral role in identifying vortioxetine's mechanism of action in improving cognitive function in patients with Major Depressive Disorder.
- Developed a theoretical model predicting that the serotonergic antidepressant vortioxetine indirectly enhances glutamate neurotransmission in a regionally-specific manner, which has been empirically confirmed.
- Designed and implemented a non-clinical program that demonstrated cognition enhancing effects of vortioxetine in animal models of depression and other diseases
- Developed target occupancy assays for the 5-HT transporter, as well as the 5-HT_{1A}, 5-HT_{1B}, 5-HT_3, and 5-HT_7 receptors.
- Developed receptor maps of the rodent brain for each receptor targeted by vortioxetine.
- Responsible for mentorship of undergraduate, post-baccalaureate, and master's level student interns. Served as primary thesis supervisor for 5 master's students.

Postdoctoral Fellow, August 2007 to January 2010
University of Pittsburgh Center for Neuroscience – Pittsburgh, PA
Advisor – Bita Moghaddam, Ph.D.

- Responsible for Investigating the relationship between cognitive function, monoamine signaling, and GABA and glutamate neurotransmission using behavioral pharmacology and *in vivo* microdialysis
- Responsible for mentorship of student interns

Laboratory Manager, August 2005 to August 2007
Graduate Student, August 2001 to August 2007
Virginia Commonwealth University Psychology Department – Richmond, VA
Advisor – Joseph H. Porter, Ph.D.

- Recipient of a Predoctoral Ruth L. Kirschstein National Research Service Award from the National Institute of Mental Health (see Grants and Awards, below)
- Responsible for managing all scientific projects, logistics, scheduling and mentorship of undergraduate student interns
- Investigated the relationship between cognitive function and glutamate neurotransmission
- Taught courses on 1) Application of Statistics to Psychology, 2) Biological Psychology

Research Technician, September 1999 to August 2001
Virginia Commonwealth University – Richmond, VA

Publications

Peer-Reviewed Articles

1. Nackenoff AG, Simmler LD, Baganz NL, **Pehrson AL**, Sanchez C, Blakely RD. (submitted). Serotonin transporter-independent actions of the antidepressant vortioxetine as revealed using the SERT Met172 mouse. ACS Chemical Neuroscience.

2. Waller JA, Tamm JA, Abdourhaman A, **Pehrson AL**, Li Y, Cajina M, Sanchez C (2017). Chronic vortioxetine treatment in rodents modulates gene expression of neurodevelopmental and plasticity markers. *European Neuropsychopharmacology*. Epub ahead of print. DOI: 10.1016/j.euroneuro.2016.11.014

3. Kugathasan P, Waller J, Westrich L, Abdourahman A, Tamm JA, **Pehrson AL**, Dale E, Gulinello M, Sanchez C, Li Y. (2016). In vivo and in vitro effects of vortioxetine on molecules associated with neuroplasticity. *J Psychopharmacology*. Epub ahead of print. DOI: 10.1177/0269881116667710.

4. Prus AJ, Wise LE, **Pehrson AL**, Philibin SD, Bang-Andersen B, Arnt J, Porter JH (2016). Discriminative stimulus properties of 1.25 mg/kg clozapine in rats: mediation by 5-HT_2 and dopamine D_4 receptors. *Brain Research*. 1648: 298-305.

5. **Pehrson AL**, Hillhouse TM, Haddjeri N, Rovera R, Porter JH, Mørk A, Smagin G, Song D, Budac D, Cajina M, Sanchez C. (2016). Task- and treatment-dependent effects of vortioxetine on scopolamine-induced cognitive dysfunction and hippocampal extracellular acetylcholine in rats. *Journal of Pharmacology and Experimental Therapeutics*. 358:472-482.

6. Smagin GN, Song D, Waller JA, Li Y, **Pehrson A**, Sanchez C. (2016). Histamine may contribute to vortioxetine's precognitive effects: possibly through an orexigenic mechanism. *Prog Neuropsychopharmacol Biol Psychi.* 68:25-30.

7. **Pehrson AL**, Jeyarajah T, Sanchez C. (2016). Regional distribution of serotonin receptors: A systems neuroscience perspective on the downstream effects of the multimodal-acting antidepressant vortioxetine on excitatory and inhibitory neurotransmission. *CNS Spectrums.* 21(2):162-83.

8. Dale E, **Pehrson AL**, Jeyarajah T, Li Y, Leiser SC, Smagin G, Olsen CK, Sanchez C. (2016). Effects of serotonin in the hippocampus: How SSRIs and multimodal antidepressants might regulate pyramidal cell function. *CNS Spectrums.* 21(2):143-161.

9. Li Y*, **Pehrson AL***, Waller JA, Dale E, Sanchez C, Gulinello M. (2015). The role of the activity-regulated cytoskeleton-associated protein (Arc/Arg3.1) in regulating dendritic plasticity, cognitive processes, and mood in depression. *Frontiers in Neuroscience.* 9:279. DOI: 10.3389/fnins.2015.00279.
   * These authors have contributed equally to this work.

10. Leiser S, Inglesias-Bregna D, **Pehrson A**, Sanchez C. (2015). Differentiated effects of the multimodal antidepressant vortioxetine on sleep architecture: Part 2, pharmacological interactions in rodents suggest a role of 5-HT3 receptor antagonism. *Journal of Psychopharmacology*. 29(10):1092-1105

11. Prus AJ, Mooney-Leiber SM, Berquist MD II, **Pehrson AL**, Porter NJ, Porter JH. (2015). The antidepressant drugs fluoxetine and duloxetine produce anxiolytic-like effects in a schedule-induced polydipsia paradigm in rats: acceleration of fluoxetine's effects by the α2 adrenoceptor antagonist yohimbine. *Behavioral Pharmacology*. 26(5): 489-94.

12. Li Y, Abdourahman A, Tamm J, **Pehrson AL**, Sanchez C, Gulinello G. (2015). Reversal of age-associated cognitive deficits is accompanied with increased plasticity-related gene expression after chronic antidepressant administration in middle-aged mice. *Pharmacology, Biochemistry & Behavior.* 135: 70-82.

13. Leiser SC, Li Y, **Pehrson AL**, Dale E, Smagin G, Sanchez C. (2015). Serotonergic regulation of prefrontal cortical circuitries involved in cognitive processing: A review of 5-HT receptor mechanisms and the net effect of vortioxetine, an antidepressant acting through multiple serotonergic targets. *ACS Chemical Neuroscience.* Epub ahead of print. DOI: 10.1021/cn500340j.

14. Betry C, Overstreet D, Haddjeri N, **Pehrson AL**, Bundgaard C, Sanchez C, Mørk A. (2015). A 5-HT3 receptor antagonist potentiates the behavioural, neurochemical and electrophysiological actions of an SSRI antidepressant. *Pharmacology, Biochemistry & Behavior*. 131:136-42.

15. Betry C, Etievant A, **Pehrson A**, Sanchez C, Haddjeri N. (2015). Effect of the multimodal antidepressant vortioxetine on rat hippocampal plasticity and recognition memory. *Progress in Neuropsychopharmacology & Biological Psychiatry*. 58: 38-46.

16. **Pehrson AL**, Sanchez C. (2015). Altered γ-amino butyric acid neurotransmission in major depressive disorder: A critical review of the evidence and the influence of serotonergic antidepressants. *Drug Design, Development and Therapy*. 9: 603-624

17. **Pehrson AL**, Leiser SC, Gulinello M, Dale E, Li Y, Waller J, Sanchez C. (2015). Treatment of cognitive dysfunction in major depressive disorder – a review of the preclinical evidence for efficacy of selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors and the multimodal-acting antidepressant vortioxetine. *European Journal of Pharmacology*. 753: 19-31.

18. Leiser S, **Pehrson A**, Robichaud A, Sanchez C. (2014). The multimodal antidepressant vortioxetine increases frontal cortical oscillations unlike escitalopram and duloxetine - a quantitative electroencephalographic study in the rat. *British Journal of Pharmacology*. 171(18): 4255-72.

19. Jacobsen JPR, Plenge P, Sachs B, **Pehrson A**, Cajina M, Du U, Roberts W, Rudder M, Dalvi P, Robinson T, O'Niell S, Khoo K, Sanchez C, Zhang X, Caron M. (2014). The interaction of escitalopram and R-citalopram at the human serotonin transporter investigated in the mouse. *Psychopharmacology*. Epub ahead of print. doi: 10.1007/s00213-014-3595-1.

20. Wallace A, **Pehrson AL**, Sanchez C, Morilak DA. (2014). Vortioxetine reverses reversal learning impaired by 5-HT depletion or chronic intermittent cold stress in rats. *International Journal of Neuropsychopharmacology.* 17(10): 1695-706.

21. Maeda K, Sugino H, Akazawa H, Amada N, Shimada J, Futamura T, Yamashita H, Ito N, McQuade RD, Mørk A, **Pehrson AL**, Hentzer M, Nielsen V, Bundgaard C, Arnt J, Stensbøl TB, Kikuchi T. (2014). Brexpiprazole I: *In vitro* and *in vivo* characterization of a novel serotonin-dopamine activity modulator. *Journal of Pharmacology and Experimental Therapeutics*. 350(3): 589-604.

22. Jensen JB, du Jardin KG, Sanchez C, **Pehrson AL.** (2014). Vortioxetine, but not escitalopram or duloxetine, reverses memory impairment induced by 5-HT depletion in rats: evidence for direct 5-HT receptor modulation. *European Neuropsychopharmacology*. 24(1): 148-159.

23. du Jardin KG, Jensen JB, Sanchez C, **Pehrson AL**. (2014). Vortioxetine dose-dependently reverses 5-HT depletion-induced deficits in spatial working and object recognition memory: A potential role for 5-HT_{1A} receptor agonism and 5-HT_3 receptor antagonism. *European Neuropsychopharmacology.* 24(1): 160-171.

24. **Pehrson AL**, Sanchez C. (2014). Serotonergic modulation of glutamate neurotransmission as a strategy for treating depression and cognitive dysfunction. *CNS Spectrums*. 19(2): 121-33.

25. Guilloux JP, Mendez-David I, **Pehrson A**, Guiard BP, Reperant C, Orvoen S, Gardier AM, Hen R, Ebert B, Miller S, Sanchez C, David DJ. (2013). Antidepressant and anxiolytic potential of the multimodal antidepressant vortioxetine (Lu AA21004) assessed by behavioural and neurogenesis outcomes in mice. *Neuropharmacology*. 73: 147-59.

26. Betry C, **Pehrson AL**, Etievant A, Ebert B, Sanchez C, Haddjeri N. (2013). The rapid recovery of 5-HT cell firing induced by the antidepressant vortioxetine involves 5-HT3 receptor antagonism. *International Journal of Neuropsychopharmacology*. 16(5): 1115-27.

27. **Pehrson AL**, Cremers THC, Betry C, van der Hart MG, Haddjeri N, Jorgensen LB, Madsen MM, Ebert B, Sanchez C. (2013). Lu AA21004, a novel multimodal antidepressant, produces regionally selective increases of multiple neurotransmitters – a rat microdialysis and electrophysiology study. *European Neuropsychopharmacology*. 23(2): 133-45.

28. **Pehrson AL**, Bondi CO, Totah NKB, Moghaddam B. (2013). The influence of NMDA and GABA(A) receptors and glutamic acid decarboxylase (GAD) on attention. *Psychopharmacology (Berl)*. 225(1): 31-9.

29. Li Y, **Pehrson AL**, Budac DP, Sanchez C, Gulinello M. (2012). Rodent models of premenstrual dysphoria: progesterone withdrawal induces depression-like behavior in multiple behavioral domains that is differentially sensitive to classes of antidepressants. *Behavioural Brain Research*. 234(2): 238-47.

30. Mørk A, **Pehrson A**, Brennum LT, Nielsen S, Zhong H, Lassen AB, Miller S, Westrich L, Boyle NJ, Sanchez C, Fischer CW, Leibenberg N, Wegener G, Bundgaard C, Hogg S, Bang-Andersen B, Stensbol TB. (2012). Pharmacological effects of LuAA21004: a novel multimodal compound for the treatment of major depressive disorder. *Journal of Pharmacology and Experimental Therapeutics*. 340(3): 666-75.

31. **Pehrson AL**, Moghaddam B. (2010). Impact of metabotropic glutamate 2/3 receptor stimulation on activated dopamine release and locomotion. *Psychopharmacology*. 211(4): 443-455.

32. Prus AJ, **Pehrson AL**, Philibin SD, Wood JT, Vunck SA, Porter JH. (2009). The role of M1 muscarinic receptors and N-desmethylclozapine in the discriminative stimulus properties of the atypical antipsychotic drug clozapine. *Psychopharmacology.* 203(2): 295-301.

33. Prus AJ, Vann RE, Rosecrans JA, James JR, **Pehrson AL**, O'Connell MM, Philibin SD, Robinson SE. (2008). Acute nicotine reduces and repeated nicotine increases spontaneous activity in male and female Lewis rats. *Pharmacology, Biochemistry & Behavior*. 91(1): 150-154.

34. **Pehrson AL**, Philibin SD, Gross D, Robinson SE, Vann RE, Rosecrans JA. (2008). The effects of acute and repeated nicotine doses on spontaneous activity in male and female Sprague-Dawley rats: analysis of brain area epibatadine binding and cotinine levels. *Pharmacology, Biochemistry & Behavior*. 89(3): 424-31.

35. Prus AJ, Philibin SD, **Pehrson AL**, and Porter JH (2006). The discriminative stimulus properties of the atypical antipsychotic drug clozapine in rats trained to discriminate 1.25 mg/kg clozapine vs. 5.0 mg/kg clozapine vs. vehicle. *Behavioural Pharmacology*. 17(2): 185-194.

36. Prus AJ, Philibin SD, **Pehrson AL,** Stephens CL, Cooper RN, Wise LE, and Porter JH. (2005). Generalization testing with atypical and typical antipsychotic drugs in rats trained to discriminate 5.0 mg/kg clozapine from vehicle in a two-choice drug discrimination task. *Drug Development Research*. 64(1): 55-65.

37. Philibin SD, Prus AJ, **Pehrson AL**, and Porter JH. (2005). Serotonin Receptor Mechanisms Mediate the Discriminative Stimulus Properties of the Atypical Antipsychotic Clozapine in C57BL/6 Mice. *Psychopharmacology*. 180(1): 49-56.

38. Prus AJ, Philibin SD, **Pehrson AL,** and Porter JH. (2005). Generalization to atypical antipsychotic drugs depends on training dose in rats trained to discriminate 1.25 mg/kg clozapine versus 5.0 mg/kg clozapine versus vehicle in a three-choice drug discrimination task. *Behavioural Pharmacology*. 16(7): 511-20.

Book Chapters

Moghaddam B, **Pehrson AL.** (2010). Disinhibition of prefrontal cortex neurons in schiozphrenia. In: Advances in Schizophrenia Research 2009 (pg. 99 – 111). Gattaz W and Busatto G, Eds. Springer Publishing, New York.

Bundgaard C, **Pehrson AL**, Sanchez C, Bang-Andersen B. (2015). The discovery and development of the multimodal acting antidepressant vortioxetine. In: Blood Brain Barrier in Drug Discovery: Optimizing Brain Exposure of CNS Drugs and Minimizing Brain Side Effects (pg. 505 – 520). Di L, and Kerns E, Eds. Wiley Publishing, New Jersey.

Selected Peer-Reviewed Published Abstracts

Mørk A, **Pehrson AL**, Betry C, David D, Li Y, Gulinello M, Leiser SC, Haddjeri N, et al. (2013). Vortioxetine (Lu AA21004), a multimodal antidepressant: differentiation from current antidepressants in animal models of depression. *Eur Neuropsychopharmacol*. 23(Suppl 2):S392-S393.

Pehrson A, Li Y, Haddjeri N, Gulinello M, Sanchez C. (2013). Vortioxetine, a novel multimodal antidepressant, modulates GABA and glutamate neurotransmission via serotonergic mechanisms. *Eur Neuropsychopharmacol*. 23(Suppl 2):S196-S197.

Sanchez C, Robichaud PJ, **Pehrson A**, Leiser SC. (2012). The effects of the multimodal antidepressant Lu AA21004 on attention and vigilance as measured EEG activity in the rat. *Eur Neuropsychopharmacol*. 22(Suppl 2):S243-S244.

Mørk A, **Pehrson A**, Montezinho LC, Karlsson JJ, Trippodi Murphy C, Miller S, Fischer CW, Liebenberg N et al. (2012). Preclinical effects of Lu AA21004, a novel multimodal antidepressant. *Eur Neuropsychopharmacol*. 22(Suppl 2):S268-S269.

Haddjeri N, Etievant A, **Pehrson A**, Sanchez C, Betry C. (2012). Effects of the multimodal antidepressant Lu AA21004 on rat synaptic and cellular hippocampal plasticity and memory recognition. *Eur Neuropsychopharmacol*. 22(Suppl 2):S303.

Pehrson A, du Jardin KG, Jensen JB, Sanchez C. (2012). The novel multimodal antidepressant Lu AA21004 improves memory performance in 5-HT depleted rats via 5-HT3 and 5-HT1A receptor mechanisms. *Eur Neuropsychopharmacol.* 22(Suppl 2):S269.

Gulinello M, Li Y, **Pehrson A**, Sanchez C. (2011). Progesterone withdrawal models of depression in rats: behavioral characterization and efficacy of Lu AA21004 and fluoxetine. *Eur Neuropsychopharmacol*. 21(Suppl 3):S377-S378.

Pehrson A, Cremers T, Westerink B, Jorgensen L, Madsen M, Ebert B, Sanchez C. (2011). Acute and subchronic Lu AA21004 induces monoamine release through a

mechanism involving multiple serotonergic receptors. *Eur Neuropsychopharmacol*. 21(Suppl 3):S403.

Sanchez C, Nielsen SM, **Pehrson A**, Zhong H, Lassen AB, Bisulco S, Mørk A, Wegener G, et al. (2011). The novel antidepressant Lu AA21004 exerts its multimodal activity through serotonergic targets. *Eur Neuropsychopharmacol*. 21(Suppl 3):S404-S405

Selected Poster Presentations

Pehrson AL, Plath N, Sanchez C. (2013). Vortioxetine, an investigational antidepressant, reverses executive function deficits in rats treated subchronically with PCP. Poster no. NR 11-58. Presented at the 166th annual meeting of the American Psychiatric Association in San Francisco, CA, USA.

Wallace A, **Pehrson AL**, Sanchez C, Morilak DA. (2013). Vortioxetine improves a reversal learning deficit in rats induced by serotonin depletion with PCPA. Poster no. NR 11-60. Presented at the 166th annual meeting of the American Psychiatric Association in San Francisco, CA, USA.

Pehrson AL, Westrich L, Sanchez C. (2012). Ex vivo autoradiography for the 5-HT7 receptor using [^{3}H]SB269970: Assay validation and estimation of fractional occupancy for SB269970 and the novel multimodal antidepressant vortioxetine. Poster no. 664.23. Presented at the annual Society for Neuroscience meeting in New Orleans, LA, USA.

Pehrson AL, du Jardin KG, Jensen JB, Sanchez C. (2012) The multimodal antidepressant Lu AA21004, but not escitalopram or duloxetine, reverses cognitive dysfunction produced by serotonin depletion in female rats. Poster no. O87. Presented at the 22nd Neuropharmacology conference in New Orleans, LA, USA.

Cremers T, **Pehrson AL**, Jorgensen LB, Madsen MM, Ebert B, Sanchez C (2011). Effects of subchronic treatment with the multimodal antidepressant LuAA21004 on rat brain neurochemistry. Poster number NR4-59. 164th annual meeting of the American Psychological Association in Honolulu, Hawaii

Pehrson AL, Totah NKB, Moghaddam B (2009). Inhibition of NMDA or GABA-A receptors, but not reduction of GAD activity in the prefrontal cortex impairs preparatory attention. Program no. 580.24. 2009 Abstract viewer/itinerary planner. Chicago, IL. Society for Neuroscience. Online.

Pehrson AL, DeFrancesco A, Moghaddam B (2008). Activation of metabotropic glutamate 2/3 receptors reduces amphetamine-induced dopamine release and hyperlocomotion. Program no. 156.9. 2008 Abstract viewer/itinerary planner. Washington, DC. Society for Neuroscience. Online.

Porter JH, Wood JT, **Pehrson AL**, Tollefson GD, Bymaster FP, Cowley MA (2008). Assessing the combination of fluoxetine plus naltrexone in an animal model of obsessive compulsive disorder (schedule-induced polydipsia). Program no. 762.25. 2008 Abstract viewer/itinerary planner. Washington, DC. Society for Neuroscience. Online.

Pehrson AL, Walentiny DM, Wood JT, Vunck SA, and Porter JH (2007). Differential effects of early postnatal NMDA antagonism on memory performance in male and female C57BL/6 mice. Program no. 498.20. 2007 Abstract viewer/itinerary planner, San Diego, CA. Society for Neurosicence, Online.

Tollefson GD, Bymaster FP, Cowley MA, Wood JT, **Pehrson AL**, Porter JH (2007) The Combination of Fluoxetine/Naltrexone Exhibits a Synergistic Reduction in Schedule-

induced Polydipsia – a Model of Obsessive-Compulsive Disorder. 46th ACNP Annual Meeting in Boca Raton, Florida, December 9-13, 2007

Pehrson AL, Porter JH (2006). Subchronic phencyclidine (PCP) administration reduces escape latencies in a working memory task in the Morris water maze in C57BL/6 mice: an in depth analysis. Program no. 753.20. 2006 Abstract viewer/itinerary planner. Atlanta, GA. Society for Neuroscience. 2006, Online.

Wood E, **Pehrson AL**, Wood JT, Prus AJ, Meltzer HY, and Porter JH (2006). Two-lever drug discrimination with the atypical antipsychotic ziprasidone differentiates atypical from typical antipsychotic drugs in rats. Program no. 768.23. 2006 Abstract viewer/itinerary planner. Atlanta, GA. Society for Neuroscience. 2006, Online.

Pehrson AL, Wood E, Prus AJ, Philibin SD, Porter JH (2005) Drug discrimination with the atypical antipsychotic ziprasidone in rats. Program no. 913.16. 2005 Abstract viewer/itinerary planner. Washington, DC. Society for Neuroscience, 2005. Online.

Pehrson AL, Wise LE, Philibin SD, Prus AJ, Rhodes MM, Porter JH (2004). The effects of subchronic administration of phencyclidine (PCP) on performance of C57BL/6 mice in the morris water maze. Neuroscience Abstracts. Program no. 85.4

Philibin SD, Prus AJ, **Pehrson AL**, Porter JH. (2004) Serotonin receptor mechanisms mediate the discriminative stimulus properties of the atypical antipsychotic clozapine in C57BL/6 mice. Neuroscience Abstracts. Program no. 1030.10

Prus AJ, Philibin SD, **Pehrson AL**, Cooper RN, Porter JH (2004). Discriminative stimulus properties of 1.25 mg/kg and 5.0 mg/kg clozapine in a three choice drug discrimination task. Neuroscience Abstracts. Program no. 1030.17.

Pehrson AL, Wise LE, Philibin SD, Prus AJ, Rhodes MM, Porter JH. (2003). The effects of acute and subchronic administration of phencyclidine (PCP) on performance of C57BL/6 mice in the morris water maze. Neuroscience Abstracts. Program no. 754.13.

Porter J. H., Philibin S.D., Barlow A. I., Wade K. L. S., Wilson M. S., **Pehrson AL**., Wise L.E., Hamm R.J. (2003). A comparison of olanzapine to risperidone and haloperidol on spatial learning in the morris water maze in rats with a subchronic dosing regimen. Neuroscience Abstracts. Program no. 625.14. Available online at http://sfn.scholarone.com/itin2003/

Philibin S.D.; Carter S.M.; Vann R.E.; **Pehrson A.L**.; Wise L.E.; Varvel S.A.; Silver K.L.; Porter J.H. (2001). Assessment of the Paw Test Procedure in Mice: A Comparison of the Antipsychotic Drugs Clozapine, Olanzapine, Haloperidol, and Chlorpromazine. Neuroscience Abstracts, 27

Wise L.E.; Vann R.E ;. Philibin S.D; Carter S.M.; Varvel S.A.;. **Pehrson AL**; Silver K.L.; Porter J.H. (2001) Discriminative Stimulus Properties of the Atypical Anti-psychotic Clozapine in Rats With a Low Training Dose. Neuroscience Abstracts, 27

Research Lectures

December 2014 – Serotonergic modulation of glutamate neurotransmission as a strategy for treating cognitive dysfunction associated with Major Depressive Disorder. The Neuroscience Colloquium Series, Northern Michigan University, Marquette, Michigan.

February 2009 – Glutamate neurotransmission in Schizophrenia: New approaches to understanding and treating this disease. The Discourses from the Academy Colloquium Series, Northern Michigan University, Marquette, Michigan.

April 2007 – Early postnatal PCP administration impairs reference and working memory performance, but has no effect on locomotor activity in male C57BL/6 mice. UNC/MCV Lab exchange, Richmond, Virginia

September 2005 – Evaluation of ziprasidone drug discrimination as a screen for atypical antipsychotic drugs: Preliminary results. Society for the Stimulus Properties of Drugs meeting at the 11th Biennial European Behavioral Pharmacology Society Meeting in Barcelona, Spain

April 2005 – The effects of ketamine administration on an operant delayed alternation task: Task design and preliminary data. UNC/MCV Lab exchange, Chapel Hill, North Carolina

March 2003 – In Search of a Deficit: the Effects of Subchronic Dosing of PCP in Mice and Ketamine in Rats in the 8-Arm Radial Maze. UNC/MCV lab exchange, Chapel Hill, North Carolina

Grants and Awards

May 2005 – July 2007: Ruth L. Kirschstein National Research Service Award, National Institute of Mental Health: F-31 MH070154-01A2. Phencyclidine-induced cognitive deficits.

April 2007: VCU Outstanding Biopsychology Student of the Year Award

February 2007: VCU Psychology Department Student Research Award: Awarded an honorarium for purchasing research supplies to complete my dissertation project.

September 2005: Travel Award: Awarded travel grant from the Society for the Stimulus Properties of Drugs to present "Evaluation of ziprasidone drug discrimination as a screen for atypical antipsychotic drugs: Preliminary results" at the SSPD satellite meeting at the 11th biennial meeting of the European Behavioral Pharmacology Society in Barcelona, Spain.

September 2002 - August 2003: VCU Psychology Department Graduate Research Fellowship. This was a fellowship awarded to graduate students that have distinguished themselves in terms of academics and research.

December 2000 – VCU Undergraduate Research Grant Program: Awarded a grant for an independent research proposal *The Eight-Arm Radial Maze: Subchronic Dosing of Mice with PCP*. Research performed under the supervision of Dr. J. H. Porter.

Teaching Experience

Formal University Teaching Experience:

May 2006 – July 2006 – Course Instructor – Application of Statistics in Psychological Research at Virginia Commonwealth University

January 2006 – May 2006 – Co-Instructor with Dr. JH Porter – Research Methods in Biopsychology- Taught a section of this course on programming languages used in preclinical research.

July 2005 – August 2005 – Course Instructor – Application of Statistics in Psychological Research at Virginia Commonwealth University

August 2004 – June 2005 – Course Instructor – Biological Psychology at the Maggie L. Walker Governor's School for Government and International Studies (2 sections)

- This was a dual enrollment course in partnership with the Psychology Department at Virginia Commonwealth University. High school seniors were awarded college credit for their work in this course.

July 2003 – May 2004 – Teaching Assistant – Application of Statistics in Psychological Research at Virginia Commonwealth University.

January 2002 – May 2002 – Teaching Assistant – Abnormal Psychology at Virginia Commonwealth University

August 2001 – May 2002 – Teaching Assistant – Psychology 101 at Virginia Commonwealth University

Teaching Experience at Lundbeck Research USA, Inc.

February 2010 – December 2015 - While working at Lundbeck, I have had a number of opportunities to serve in a teaching capacity.

- Thesis Supervisor – I served as the primary thesis advisor for five master's level students conducting their thesis projects at our facility while matriculated at Aalbørg University in Denmark (see below, under former advisees). Each of these students have successfully defended their thesis projects, graduated, and have either published or are currently working on publishing their research. I have maintained regular contact with several of these students and continue to act as a mentor in a more informal capacity.
- Student Intern Mentor/Supervisor – I served as mentor and supervisor for five additional students that did student internships at Lundbeck after completing a bachelor's or master's degree in neuroscience-related fields.
- Technical Mentor –I served as a technical mentor for several research investigators, postdocs, and student interns at Lundbeck seeking to learn techniques such as *ex vivo* autoradiography, transcardial perfusion, stereotaxic surgery, or the use of a cryostat to prepare slides from fresh frozen brain tissue. I also regularly consulted with other Lundbeck researchers on the most appropriate way to run behavioral experiments and to statistically analyze data.
- Subject Matter Expert – Vortioxetine (Lu AA21004) – While at Lundbeck I played a critical role in developing an understanding of the mechanism of action underlying the cognitive effects of the novel multimodal-acting antidepressant vortioxetine. One of my responsibilities was to educate Lundbeck's medical science liaisons on the biology underlying this drug's effects, so that they could disseminate that information

to interested psychiatrists during the product's launch. I served in this capacity several times per year while at Lundbeck.

Former Advisees

- Kirstine Tølbøl – M.S. from Aalborg University, Denmark. Class of 2015.
- Kristian Gaarn du Jardin – M.S. from Aalborg University. Class of 2012.
- Jesper Jensen – M.S. from Aalborg University. Class of 2012.
- Lærke Brygger Jørgensen – M.S. from Aalborg University. Class of 2010.
- Mathias Madsen – M.S. from Aalborg University. Class of 2010.

Service

Guest Associate Editor at *Frontiers in Neuropharmacology* (November 2016-present)

- Special topic: Glutamate neurotransmission in Major Depressive Disorder (MDD) – The role of glutamate and its modulatory systems in MDD pathology and novel treatment strategies.

Ad hoc reviewer:

- *Progress in Neuropsychopharmacology and Biological Psychiatry*
- *International Journal of Neuropsychopharmacology*
- *Expert Review of Clinical Pharmacology*
- *Neuropharmacology*
- *Drug Design, Development and Therapy*
- *Medical Research Archives*

Member, Biorails Superuser Committee; Lundbeck Research USA, Inc

- This committee helped to test, implement, and provide user support for Biorails, an online laboratory notebook system developed for Lundbeck.

Graduate Faculty at Northern Michigan University (2015-present)

- Thesis Committee member, Katelin Matazel at Northern Michigan University Department of Psychology. Thesis Supervisor: Adam J. Prus, Ph.D.

Organizational Affiliations

- Society for Neuroscience (member, 2002-present)

Programming and Computing Skills

Expertise:

- Matlab
- Python
- MedState Notation
- Statistical Package for Social Sciences
- Graphpad Prism

- Microsoft Excel (including writing functions and macros)

Proficiency

- R
- Machine Learning

Research Description

The overarching focus of my research is to discover novel biological strategies to treat the cognitive impairments associated with psychiatric illness. More specifically, I use a systems neuroscience perspective to model the ways in which neuromodulatory systems alter GABA and glutamate neurotransmission, based on the hypothesis that these systems are critical for optimal cognitive function. Using the resulting models, I develop and test theories on the effects of specific neuromodulatory mechanisms on cognitive impairments in memory (working or long-term), attention, and executive function, using a variety of techniques from behavioral, neurochemical, molecular pharmacological, and histological sub-disciplines. Currently, I am focused on the cognitive impairments associated with Major Depressive Disorder (MDD); however, the resulting concepts may be applicable to other diseases. Below, I present my previous research achievements along with two novel research goals and evidence supporting their feasibility.

Previous research achievements: Treating MDD-related cognitive dysfunction via indirect glutamate modulation. MDD is associated with high functional disability and socioeconomic costs, and is now the leading cause of disability worldwide. Although MDD is primarily conceptualized as a mood disorder, MDD patients experience significant cognitive impairment, and cognitive dysfunction is thought to be the strongest driver of MDD-related functional disability. Traditional antidepressants can attenuate MDD-related cognitive dysfunction to some degree; however, much of the cognitive impairment associated with MDD persists even after "successful" treatment with these drugs. Thus, cognitive dysfunction is an important unmet need in clinical MDD populations.

Glutamatergic neurotransmission has emerged as a common target for treating cognitive dysfunction, with the broad theme that moderately increasing glutamate neurotransmission improves cognition in adults (e.g. AMPAkines, or mGluR5 agonists), while reducing glutamate tone impairs cognition (e.g. AMPA or NMDA receptor antagonists). But directly increasing glutamate signaling by pharmacological action may be an impractical strategy for treating cognitive dysfunction. Glutamate receptors are nearly ubiquitous in the forebrain, making side effects difficult to avoid, and failure to tightly regulate glutamate activation can induce cognitive impairment, psychosis, motor impairment, or cellular excitotoxicity. Another strategy is to use mechanisms that indirectly modulate glutamate neurotransmission in a more regionally specific and gentle manner.

My research suggests that serotonergic neurotransmission can be used to indirectly increase glutamate neurotransmission, and improve cognitive function. Vortioxetine is a recently approved antidepressant that is an antagonist at 5-HT_{1D}, 5-HT_3 and 5-HT_7 receptors, a partial agonist at 5-HT_{1B} receptors, an agonist at 5-HT_{1A} receptors and an inhibitor at the 5-HT transporter. I developed a theoretical model that suggested vortioxetine, despite its purely serotonergic pharmacological actions, would suppress GABAergic neurotransmission, leading to an indirect increase in glutamate neurotransmission (Pehrson and Sanchez 2014, Pehrson et al. 2016). Importantly, vortioxetine targets such as the 5-HT_3 receptor are largely circumscribed to brain regions that play important roles in cognitive function (see simplified model, Figure 1), suggesting that this drug's indirect enhancement of glutamate neurotransmission is regionally specific. Research from my group and our collaborators empirically confirmed this model, showing that vortioxetine inhibits GABA neurotransmission (Dale et al. 2014), and increases in glutamatergic principle cell firing (Riga et al 2016) in regions such as the hippocampus and frontal cortex. My research demonstrates that vortioxetine improves cognitive function in non-clinical MDD models (e.g. du Jardin et al. 2014; Jensen et al. 2014), while several reports from other researchers have found that it improves aspects of cognition in depressed patients. Although more work is required to tie vortioxetine's glutamatergic effects to its cognitive benefits, this compound may provide proof-of-principle that indirect modulation of glutamate neurotransmission can be an effective strategy for treating MDD-related cognitive dysfunction.

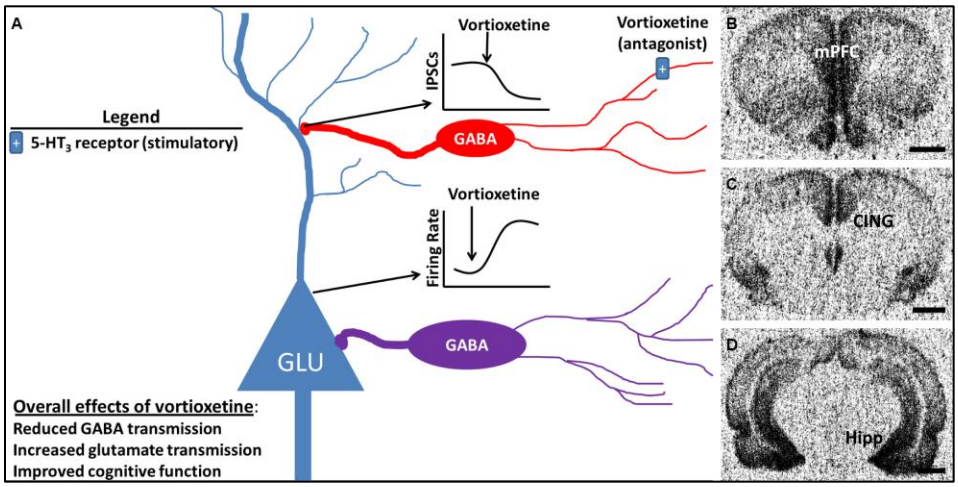

Figure 1. A likely mechanism for vortioxetine's cognition-enhancing effects. (A) Vortioxetine indirectly enhances glutamate neurotransmission through its actions on 5-HT_3 receptors expressed on GABAergic interneurons. (B-D) 5-HT_3 receptors are largely circumscribed to cognition-relevant brain regions. Abbreviations: antagonist (antag), cingulate cortex (CING), glutamate (GLU), hippocampus (Hipp), inhibitory postsynaptic currents (IPSCs), medial prefrontal cortex (mPFC). Scale bars represent 1mm.

Research Goal I: Controlled reorganization of neural circuits: low-dose ketamine-induced plasticity as a novel pathway to modulating cognitive function. Traditional antidepressants are limited from the perspective that mood symptom relief is slow to set in (4-12 weeks) for most patients, and never occurs in a substantial subpopulation. Perhaps the most significant recent advance in treating MDD-related mood dysfunction has been the observation that low-doses of the glutamatergic NMDA receptor antagonist ketamine engender a fast reduction in treatment-resistant patient mood symptoms (6 hours) that lasted in one study for 7-10 days before relapse. Some aspects of this effect have been replicated in nonclinical models, including fast onset and extension of antidepressant-like effects past ketamine's elimination from the body (du Jardin et al. 2016). Interestingly, key mechanistic data suggest that ketamine's fast-acting mood effects are the result of plasticity events featuring increased synaptogenesis (Duman 2014), and glutamatergic AMPA receptor-mediated neurotransmission (Maeng et al. 2008). But the cognitive effects of this treatment regimen have largely not been established, either in the clinic or in animal models. Moreover, given the outsized role cognitive function plays in the functional rehabilitation of MDD patients, the cognitive effects of this treatment may ultimately control the degree of its clinical usefulness.

Ketamine can reasonably be expected either to impair or enhance cognitive function, and indeed it may act in both directions in different phases of its neurobiological actions. The glutamatergic NMDA receptor is considered critically important in a variety of cognitive functions, thus acute antagonism of this target by ketamine can be expected to impair function. However, given that higher-order cognitive functions critically depend on neural plasticity, and that modest increases in postsynaptic glutamate neurotransmission can be beneficial for cognition, low-dose ketamine treatment may also lead to improvements in cognitive function after inactivation of its NMDA receptor antagonist effects. Moreover, there is at least one report suggesting that low-dose ketamine improves function in a frontal cortex-mediated cognitive task in this late phase of its biological actions (Jett et al. 2015).

If ketamine does induce improvements in cognition via fast induction of plasticity events, then it is critical to understand the underlying mechanisms. Until this point, drug discovery programs seeking to improve disordered cognition have focused in a reductionist manner on high selectivity compounds to control activation of a single target, usually a neurotransmitter receptor, enzyme or transporter protein. But low-dose ketamine may provide a novel paradigm for cognition-focused drug discovery programs, focused on controlled reorganization of neural circuitry. But before a program based on this novel strategy can be realized, we must first determine whether or not the beneficial cognitive effects of low-dose ketamine are related to its plasticity-driving effects, and further parse which portions of ketamine's mechanism of action are important for these effects on plasticity.

Importantly, it may be possible to use serotonergic receptor targets to modulate ketamine's effects on cognitive function, or mood. At least two separate labs have found that depletion of central serotonin in rodents blocked ketamine's sustained antidepressant-like effects (Gigliucci et al. 2013; du Jardin et al 2016). These data suggest that serotonergic neurotransmission is partly responsible for ketamine's plasticity effects, and opens for the possibility that action at serotonergic receptors can extend ketamine's long-term effects on cognition or mood. Additionally, given that ketamine and other noncompetitive NMDA receptor antagonists are activity dependent (Foster & Wong 1987), and further that glutamate activation can be selectively enhanced in cognition-relevant

brain regions via 5-HT_3 receptor antagonism (see Figure 1), it may be possible to focus ketamine's effects into cognition-relevant brain regions by combining lower ketamine doses with 5-HT_3 receptor antagonism, thereby reducing or eliminating ketamine's transient side effects. Thus, the goals of my first research stream are to 1) conduct an in-depth examination of ketamine's effects on cognitive function, 2) elucidate the mechanisms underlying ketamine-induced improvements in cognitive function, and 3) to investigate whether serotonergic mechanisms can be used to modulate ketamine's effects on plasticity and cognitive function.

Research Goal II: Investigating the role of glia in MDD-related cognitive dysfunction. Glial cells make up about half of the volume of the adult human brain and outnumber neurons in the cerebral cortex by a ratio of about 4:1. Glia play a critical role in supporting neuronal function, but at this time there is relatively little scientific inquiry into the role glial cells play in psychiatric disease. However, a bourgeoning line of postmortem evidence has recently shown that MDD patients have significant reductions in the size and density of glia in the prefrontal cortex, as well as reductions in glial cell-specific markers such as the calcium binding protein S100B, excitatory amino acid transporters (EAATs) 1 and 2, and glutamine synthetase. Animal models of depression such as chronic unpredictable stress are also associated with reductions in glial density, and importantly, glia-specific lesions in the prefrontal cortex are sufficient to induce a depression-like phenotype in rodents (Banasr and Duman 2008). Additionally, drugs that can increase the expression of EAATs, such as riluzole, have shown antidepressant-like effects in non-clinical animal models and have at least preliminary support for antidepressant activity in the clinic (Bansr et al. 2010). These data suggest that MDD is associated with glial pathology. Interestingly, there is also evidence suggesting that MDD patients have reduced glutamate and GABA concentrations in brain regions that are relevant for cognitive function, including the prefrontal cortex (Yuksel and Ongur 2010). These two lines of data may be connected to one another because the synthesis of GABA and glutamate is regulated by glial mechanisms including EAAT1/2 and glutamine synthetase (Pehrson and Sanchez, 2015).

Moreover, if glial pathology drives reductions in glutamate and GABA concentrations in regions like the prefrontal cortex, then it is plausible that glial pathology is partly responsible for MDD-associated cognitive impairments, which is a novel perspective on the pathology of these dysfunctions. Moreover, glial dysfunction could contribute to impaired cognition via a variety of mechanisms including dysregulated GABA or glutamate neurotransmission, aberrations in cellular respiration, or the sequelae of increased oxidative stress and ammonia concentrations, etc. In support of a role for glia in regulating cognitive function, there has been at least one study demonstrating that a glia-specific lesion can induce impairments in the active avoidance model of memory in rodents (Banasr and Duman 2008). However, the effects of glial pathology on cognitive function and whether those effects are directly related to altered glutamate and GABA neurotransmission have largely not been investigated. The goals of my second research stream are to elucidate the mechanisms by which glial pathology contributes to cognitive dysfunction and to discover pharmacological mechanisms that can reverse the effects of glial pathology on cognitive function.

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Statement on Contributing to Diversity in Research, Teaching and Mentorship

During my scientific career, I have had a number of experiences that have strongly reinforced in my mind the value of diversity as a driving force in science, and of the skills required to navigate in multicultural social environments. For example, while I was a Research Scientist at Lundbeck, I had the opportunity to be part of a research team that was highly diverse, in that it brought together scientists from a variety of ethnic, national, disciplinary, and specific research backgrounds in order to focus on a single development goal – to elucidate the mechanism of action underlying the cognition-enhancing effects of an experimental drug. This goal was a difficult one, to say the least – neuroscience to date has historically produced few examples of drugs capable of enhancing cognitive function to use as precedent and even fewer in which circuit-level mechanisms are understood. However, our research group was successful in meeting this goal, and I believe it was in large part due to the diversity of the team. The ability to access varying perspectives and diverging scientific techniques allowed us to identify important scientific concepts that would have otherwise been missed, and to approach the problem using a variety of tactics. This experience cemented in my mind the high value of diversity in research as a critical factor for driving innovation and novel understandings in science.

Moreover, I believe I can add meaningfully to the diversity of the research at your institution if added as an assistant professor. First, over the course of my 15 years in neuroscience research, I have trained under scientists representing a variety of neuroscience sub-disciplines, including behavioral science, neurochemistry, molecular pharmacology, and histology, and further have collaborated extensively with electrophysiologists. The resulting experiences have helped me to develop not only a diverse technical skill set, but also a multifaceted understanding of the brain's function. This multifaceted viewpoint and technical repertoire allow me to approach scientific problems from a variety of perspectives, and aids in collaborative efforts with other neuroscientists. Importantly, given that my scientific background extends across academia and industry, I can provide a viewpoint that is uncommon among academic scientists. Thus, adding me to your team of can add diversity to your university's research endeavors in meaningful ways.

In order to be successful, a diverse team requires members with the skills to navigate in a diverse environment – principally empathy, the ability to understand and accept other perspectives, and the ability to have constructive disagreements and discourse. These skills can only be developed via repeated and long-term exposure to other perspectives within an intellectually challenging environment. Thus, in order to reap the benefits of diverse viewpoints for scientific innovation, team members and their leaders must first have the interpersonal skills that can only come from an education marked by consistent exposure to cultural diversity. Additionally, diverse educational experiences can be critical for preparing students to become thoughtful citizens capable of understanding the complex issues that tend to confront multicultural democratic societies. From this perspective, a multicultural education is valuable whether or not a student chooses a career in science. Therefore, it is my intention to create an atmosphere in my laboratory and classrooms that models the interpersonal skills required to navigate diverse social environments, with the intention of developing and reinforcing those skills in my students.

I have a strong track record for diversity in my mentorship and teaching activities. During my time at Lundbeck, I had the opportunity to provide scientific mentorship to ten students that were either interns in my lab, or Master's level students conducting thesis projects under my supervision. Of these students, half were women, and half were international students, and the students came from a variety of educational levels (Post baccalaureate, Master's level, Post Master's), and ethnic backgrounds. Additionally, as a postdoctoral fellow at University of Pittsburgh and as a graduate student at Virginia Commonwealth University (VCU), I had the opportunity to mentor dozens of undergraduate students in the lab. Each of these laboratories was ethnically diverse, and had a friendly, collegial atmosphere that was conducive to free scientific discourse. I learned a great deal about how to create and support similar environments from my experiences in these laboratories. Furthermore, both VCU and the Maggie L. Walker Governor's School for Government and International Studies are institutions characterized by highly diverse student bodies, therefore the experience I gained teaching at these institutions has prepared me well for teaching in a multicultural environment. Thus, I believe that I am well equipped to develop the skills required to succeed in diverse social environments within my students.

Pehrson, Alan Lars

Statement of Teaching Philosophy

Central to my teaching philosophy is the idea that students at the university level are highly capable learners, given an appropriate environment. I see it as a teacher's responsibility to build a space that will enable students to achieve their best learning by helping them become maximally engaged in appropriately challenging material. Additionally, I believe that the value of a degree in the sciences is not derived solely from gaining a large set of discipline-specific knowledge, which may only be situationally relevant. Rather, the strongest value of scientific training for many students are transferable skills in critical thinking, planning, problem solving, and written/oral communication to name a few, all of which are valuable whether or not one pursues a career in the sciences. Therefore, in my view, the primary goal of a university-level science education is to develop these transferable skills, whether at the undergraduate or advanced level. In order to develop these transferable scientific skills, I use several strategies, which are enumerated below:

Strategy 1: Building rapport with students. In my own experience as a student, I had several opportunities to develop positive mentorship relationships with teachers and active scientists. These were transformative experiences that first awakened and later strengthened my desire to be a professional scientist. Thus, I believe that a teacher or mentor can have a profound constructive effect on a student's level of confidence and engagement. Whether acting as a mentor in the lab or a teacher in the classroom, I have found that a little encouragement and patience on the part of a teacher can make seemingly difficult course material or scientific techniques less daunting and thus easier to grasp. In addition, I think that building trust between teacher and student makes the teacher more approachable, leading to an easier experience identifying and clarifying student misunderstandings.

Strategy 2: Appropriately high expectations and scaffolding. I believe that students will achieve the maximum amount of learning if the instructor sets high expectations in the course goals. This is related to my notion that a teacher who believes strongly in his students' abilities will positively influence student confidence and self-efficacy. On the other hand, I understand that material that is outside the students' range of proximal development may have an adverse effect on confidence and student engagement. Thus, although I do not shy away from including some material that may be initially perceived as difficult in my courses, I always strive to ensure the material is achievable. Additionally, I work to include appropriate levels of scaffolding for difficult concepts (i.e. course materials or activities designed to support a student's understanding of a concept; e.g. 'explainers', non-lecture materials wherein complex problems are broken down step by step by the instructor in order to make appropriate thought processes explicit; having students work collaboratively on a subset of course materials, etc). Thus, I strive to set appropriately high expectations, and to provide enough help, examples, and repetition to ensure all concepts can be firmly grasped.

Strategy 3: Learning by doing. My experience as a student and as a researcher suggests that understanding of content material as well as scientific techniques are enhanced when students have the chance to learn by doing, particularly in an environment where an expert in that material or technique is available for questions. For example, despite doing well in statistics as an undergraduate, I did not acquire a lasting understanding of inferential statistics until I used it to answer my own research questions. Moreover, in order for students to truly become savvy consumers of information, they need to have many opportunities to actively engage with various types of information. While I believe the best way to achieve this is for students to engage in independent laboratory-based research projects, this can also be achieved in the classroom. For example, I use the lab section of my statistics courses to give students the opportunity to engage with data using statistical techniques, and to learn about what kinds of inference can be drawn from a given type of data. In courses that don't include labs, I try to include opportunities for discussion and project-based activities in order to demonstrate how course content is applicable outside the classroom. Moreover, I believe that teacher-centered lectures on content material are of limited learning value and should be used as sparingly as possible; thus, even when running the lecture portion of the course, I prefer to break students into working groups regularly to actively engage with content material.

Strategy 4: Subject matter relevance. It is a generally accepted tenet of education that making connections between a course's content and prior knowledge or other areas of a student's life aids in the learning process (ie; see Stanovitch KE & Cunningham AE (1993) J educational psychology. 85:211-229). With this tenet in mind, I

have found that it is useful while teaching content-heavy courses such as Physiological Psychology or Statistics Applied to Psychology to draw connections wherever possible to current events. In addition, I have found it useful to develop hands on demonstrations or assignments where ever possible. Moreover, these practices have several beneficial effects including improved student engagement in the course, and better retention of the course material.

As a way of unifying my beliefs about relationship building, learning by doing, and subject matter relevance, I believe that one-on-one mentorship in the context of independent laboratory-based projects provides a large number of opportunities to train students in transferable skills mentioned above, particularly in the context of an independent laboratory-based project, which is why I plan to involve undergraduate and graduate students in my research projects as much as possible.

Strategy 5: A focus on writing. In order to be successful in the modern world, whether in the pursuit of a scientific career or not, one must be able to effectively express oneself. Towards this end, I believe it is important for educators in all disciplines to provide students with opportunities to practice writing. Thus, each of the courses that I have taught in the past has emphasized writing in some way. For example, in my Statistics classes I focus heavily on proper interpretation of inferential statistics. Thus, every assignment involving inferential statistics requires students to interpret results from a theoretical experiment in paragraph form. Additionally, in a graduate level version of my Physiological Psychology course I would include several writing assignments that ultimately culminate in the production of a mock grant, in which students highlight a neuroscience–related problem and propose a research program to investigate that problem. Moreover, these assignments provide opportunities for instructors to develop and assess each of the transferable skills mentioned above in students within the context of an authentic neuroscience- or statistics-related activity.

Strategy 6: Technology in the classroom – Technological advances in the last two decades have provided pedagogical opportunities that can be advantageous for students if used appropriately, and I intend to make use of technology in my classrooms to whatever extent is possible. On the most general level, the availability of course websites on platforms such as Blackboard allows teachers to provide scaffolding materials, such as 'explainers' in video or pdf form, course notes, etc. on an essentially constant basis. Additions such as these can be especially helpful for working students who may not have time to make it to office hours and ask for one-on-one help. Moreover, with the addition of video chat functions, distance learning becomes feasible, and indeed courses using online or hybrid formats have become increasingly common. In online or hybrid courses I will use a combination of synchronous (e.g. video-supported teacher-centered lectures, student work group meetings that either include or don't include the teacher) and asynchronous materials (e.g. 'explainer' videos) to foster student learning. Additionally, some courses may require practical experience with specific programs in order to allow course content to become relevant outside of the classroom. For example, no course on inferential statistics can be truly complete without experience using a statistical program such as R or SPSS, given the high level of penetration these computing platforms have achieved among professional researchers or statisticians. And indeed, my statistics courses have traditionally included a lab portion of the course that allowed for this kind of practical experience. Moreover, I have found that experience with such programs allows students to engage with course material on a deeper level than might otherwise be achievable.

In conclusion, my teaching philosophy consists of a set of strategies that will ably prepare students for scientific careers if they choose them, but will also meet the pragmatic goal of developing students with strong critical thinking, problem solving, and communication skills.

Teaching Experience

Although the scholarly experience I have attained during my postdoctoral fellowships has focused primarily on research, I have a substantial base of varied teaching experience to draw upon should I be appointed as an Assistant Professor. I gained my formal university-level teaching experience at Virginia Commonwealth University from August 2001 through July 2006. During this five-year period of time, I served in a variety of teaching capacities ranging from Teaching Assistant in courses such as Psychology 101, Abnormal Psychology, and Application of Statistics in Psychological Research to full Course Instructor for multiple sections of Application of Statistics, and Biological Psychology. Through each of these teaching experiences, I consistently

received high marks in terms of teaching effectiveness and student rapport (please see Teaching Effectiveness section of application). During this five-year period of time I was also actively involved in research mentorship activities at my graduate advisor's laboratory, where I was consistently expected to oversee between 3 and 5 undergraduate research interns at any given time.

Additionally, during my postdoctoral fellowships I have continued to accrete experience as a research mentor and teacher. For example, during my time at Lundbeck Research USA, Inc., I worked with Aalborg University in Denmark to supervise five Master's level students through their laboratory-based thesis projects at my research facility in Paramus, New Jersey. I was the primary thesis supervisor for these students and in each case they were able to successfully complete and defend their research projects, and graduate from their programs. Importantly, each of these students has either successfully published their research in peer-reviewed scientific journals or is currently working on doing so. In addition, during this period I served as a mentor for another five American students who were research interns in my lab and have had opportunities to publish with me in peer-reviewed scientific journals. Finally, I am currently serving as a member of the Graduate Faculty at Northern Michigan University, where I am acting as a thesis committee member for one student. Given the fact that these activities were performed during a period of time when I was working in an industrial neuroscience firm, these anecdotes demonstrate my strong desire to mentor young scientists as well as my ability to successfully incorporate student researchers into meaningful research programs.

In addition to these student mentorship activities, I have had a number of opportunities to serve in a teaching capacity while I worked at Lundbeck Research USA, Inc. While working at this firm, I played a critical role in elucidating the mechanism of action underlying the beneficial cognitive effects exerted by the novel multimodal antidepressant vortioxetine. This drug was approved by the FDA for treatment of major depressive disorder while I was at Lundbeck, and one of my responsibilities during the product's launch was to educate Lundbeck's Medical Science Liaisons on this mechanism, so that they could disseminate that information to interested psychiatrists. I served in this capacity multiple times per year while at Lundbeck.

In conclusion, I have had a variety of relevant teaching and research mentorship experiences from traditional and nontraditional environments upon which I can draw as an Assistant Professor.

Teaching Interests

My fifteen years of training and experience in the fields of neuroscience, pharmacology, and psychology prepares me to teach a variety of courses offered at the undergraduate and graduate levels at your university. My specialization in the biological basis of cognitive function leaves me especially well prepared for teaching related courses such as **Learning and Memory**, and a **special topics course on cognitive dysfunction in psychiatric illness**. I am also well qualified to teach courses on **Biological Psychology or Behavioral Neuroscience**, **Psychopharmacology** or **Behavioral Pharmacology**, and indeed I have taught courses on Physiological Psychology in the past. I am also strongly interested in teaching courses on the **Application of Statistics**, and **Research Methods**, both of which are uniquely well suited to emphasizing the important transferrable skill sets mentioned above.

A course on Learning and Memory would focus on the central nervous system biology that drives these forms of cognitive function, while special topics courses on cognitive dysfunction in psychiatric illness would focus on the ways in which cognition is disrupted in various psychiatric illnesses such as schizophrenia and major depressive disorder, and what is known about the biology driving those deficits. A course on Biological Psychology or Behavioral Neuroscience would be conceived as a survey course seeking to emphasize understanding of the biological basis of functions ranging from sensation and perception, to the regulation of basic drives like hunger, thirst, or sex, to more complex cognitive functions such as learning, memory, and attention. Students taking a course in Behavioral Pharmacology would develop a strong understanding of pharmacodynamics and pharmacokinetics, as well as psychological concepts such as Pavlovian and operant conditioning, before going on to learn about how the major classes of psychoactive drugs alter behavior. My statistics course is focused primarily on developing students' ability to recognize the proper situation in which to use standard parametric and non-parametric statistical tests, and the ability to interpret the results of those tests in the context of experiments.

In each case, these courses could be taught at the undergraduate or graduate level, with differing levels of detail and increasing levels of emphasis on reading the primary literature.

Evidence of Teaching Effectiveness

Teaching Evaluations:

Table 1. Teacher evaluations for Alan L. Pehrson

	Mean Rating			
	Biopsych	Stats	Stats Lab 1	Stats Lab 2
1. How would you rate the instructor?	4.25	4.57	4.8	4.13
2. How would you rate this course?	4.09	4.14	4.1	4.1
3. How would you rate the learning you achieved?	4.27	4.43	4.5	4.4

Items 1-3 rated on Likert scale with possible scores ranging from 1 (Poor) to 5 (Outstanding)

Excerpts from Written Evaluations:

PSY401 Biological Psychology

Note on course context: I taught 2 Sections of Biological Psychology (approximately 25 students each) as a dual enrollment course between Virginia Commonwealth University and the Maggie L. Walker Governor's School for Government and International Studies (a magnet high school in Richmond, VA).

Student Comments

"Despite the challenging nature of this course, he managed to make it fun and pretty easy to learn."

"This was one of my most enjoyable classes this year – I always looked forward to it. If I choose to pursue the sciences in college – and that very well may happen – this class will be the reason I do so."

"Best teaching job I've ever experienced. Took a difficult subject matter and made it readily understandable"

"I've had such an amazing time in this class. It was the only course that I go home to eagerly tell my family what I learned. I hope to continue it in college"

"I really enjoyed this course: The material was very interesting and the instructor made it as captivating as science can be. In the beginning it was tough just because there's so much material for a group of students who are not the best in science, but I was thoroughly impressed by the class"

PSY214 – Statistics Applied to Psychology (Virginia Commonwealth University)

Student comments

"Professor was very good for such a short summer course and for such a hard course. He was fair and understanding"

"Very good teacher, knows his subject well and was able to teach it very effectively. Hard class as it was only 5 weeks but teacher made it possible"

"The instructor did such a good job at teaching. I really felt like I learned and understood everything that was taught to me. I really enjoyed his teaching style"

"Very helpful professor, one of the best I've had"

"Alan is a great teacher who made all the concepts I had learned in STAT210 much clearer in one week than my statistics professor could in one full semester. Great class – enjoyable and useful"

"Alan was very helpful and explained everything very well. He wanted us to learn and stayed after numerous times to help. I would recommend him to my friends and I hope to take another course taught by Alan in the future."

PSY214 – Statistics Applied to Psychology Laboratory Section 1 &2 (Virginia Commonwealth University)
Student comments
"If ever I didn't get something in lecture, I always came out of Alan's lab understanding it."

"Alan is a very good teacher. I really loved his class. I only went to lecture to turn my assignments in and even though I stayed the whole time, I didn't really get a good understanding of the material. Alan made the work seem so much easier to learn"

"Coming to lab is what helped me understand the material. [Alan] would help me understand things in 20 minutes that I didn't get in a class that was almost 2 hours long"

"I thought Alan was a great instructor. He always would help with questions and he made us all feel equal"

August 11th 2016
Aarhus, Denmark

To whom it may concern,

It is with great pleasure that I am writing this letter to give Alan Pehrson my highest recommendation as a supervisor. During my years as a medical research undergraduate and graduate student, my scientific education and work has been supervised by a number of post-doctoral fellows, associate and assistant professors, as well as professors and I can say without doubt that the Alan's supervision and mentorship has been the amongst the most inspirational and educational I have experienced.

I started working with Alan when I was presented with the opportunity to conduct my master thesis at Lundbeck Research USA, Inc (late 2011). As an undergraduate student from a Danish University (University of Aalborg) preparing for an internship in the USA, there are considerable practical issues to work out, including obtaining visa, student grants, social security number, and accommodations, as well as writing a scientifically relevant and interesting project protocol to be approved by immigrations authorities and the School of Medicine at the University of Aalborg. Throughout these preparatory processes Alan was very supportive and helpful, and I believe the successful resolution of these challenges undoubtedly depended on Alan's knowledge and guidance.

Alan is an internationally well-recognized neuroscientist, and the significance of being to be able to draw on his scientific expertise for my development as a young researcher cannot be underestimated. The project that I conducted under Alan's supervision and mentorship involved examining the effects of the novel multimodal antidepressant vortioxetine on a rodent model of depression-related deficits in cognition. Using a combination of behavioral techniques and *ex vivo* autoradiography, both of which Alan is an expert on and successfully taught me, we were able to demonstrate memory enhancing effects of vortioxetine. Moreover, Alan's expertise and innovative ideas enabled us to identify two separate biologies that may drive vortioxetine's nootropic effects. This project resulted in the publication of two scientific papers as well as a number of presentations at scientific meetings.

As a supervisor, Alan was always accessible for questions, aid and guidance; even if he was out of office I was always able to reach him by mail and he replied immediately. He was always willing to help no matter how busy his own schedule was, and he did so with patience and a smile.

During my 8 month stay at Lundbeck Research USA, inc, Alan always gave constructive criticism and suggestions of improvements without impairing my creativity; always respecting and strengthening my independence as a young researcher. He showed trust in my abilities which gave me the confidence and motivation to continue improving them. With his support and help, I went on to obtain a position as a PhD-student at Aarhus University in Denmark (2012), and during my graduate program, I have continuously used Alan as an external mentor. With Alan's invaluable help, I have successfully graduated with my PhD (2016), and today, I am working as a post doc.

In conclusion, I believe Alan Pehrson is an outstanding supervisor with a dedication, expertise and source of inspiration that only few can offer. I am very privileged to have him as my mentor and supervisor.

Sincerely,

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AARHUS UNIVERSITY
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To Whom it May Concern:

I'm writing to support the application of Dr. Alan Pehrson for the position of assistant professor. Upon graduating from college, I began my first industry pharmaceutical job under the supervision and instruction of Dr. Pehrson. From the get-go, it was clear to see that he was a dedicated and accomplished scientist, which proved to be slightly intimidating for a newcomer such as myself. Despite this, I never felt that I couldn't ask questions, regardless as to how unimportant I may have thought they were.

I had the pleasure of working with Dr. Pehrson for about two years post-graduation. Initially, I had been brought on to help the team with cryosectioning rodent brain tissue. Due to my curiosity and enthusiasm, I was quick to ask for multiple projects. Although I had asked only to do more cryosectioning, Dr. Pehrson saw far more potential in my abilities. Soon after I became fairly comfortable with my initial tasks, he suggested to try my hand at autoradiography, a skill he was quite proficient in. Although I doubted my abilities, he continued to be an encouraging mentor; he always provided constructive feedback and made it a point to spend time with me while I learned to perform this assay. With this steady support, I was able to master a skill I once thought was quite daunting. I am sure that if it weren't for his words of encouragement and patience, I wouldn't have accomplished as much as I did under his supervision. In addition to Dr. Pehrson being a strong teacher and mentor, he is kind and caring demeanor make him easy to work with. Not only did he show compassion for his team members, he took the time to make sure that I was okay when it came to balancing my projects, as well as providing guidance when I applied to medical school.

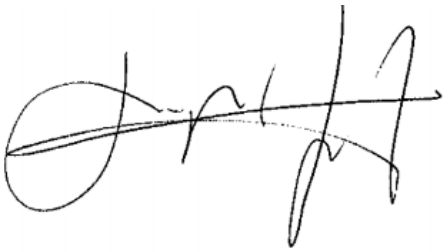
It is pertinent to note that Dr. Pehrson has always shown a supportive nature when it came to learning both in and out of the laboratory. I balanced my in-between time by reading articles and asking questions. Dr. Pehrson was eager to answer them as well as take the time to go the extra mile to explain the theory behind his answers, breaking down ideas and concepts into bite-sized bits in order for me to truly understand his rationale. He made himself readily available if I needed assistance in the lab, as well as if I had any last minute questions. Moreover, he always welcomed my own feedback and consistently made sure that he took my ideas into account when having team discussions as well as one-on-one. Although I had started the position feeling unsure of my own abilities, by the time I left Lundbeck, I was able to showcase a variety of important skills, which I can only thank him for. He welcomed my curiosity and encouraged me to talk to and shadow other scientists in our facility, insisting that my position was not just to work for him, but to learn and grow as a scientist myself.

Working under a scientist and mentor such as Dr. Pehrson was an important step on my road to being a better scientist, and a future physician. He never ceased to assure me of my capabilities and praise me for all I had done, making it a point to thank me for the work I had accomplished on a daily basis. It was easy for me to go the extra mile for a supervisor like him; although I volunteered for an ambulance squad and pulled overnight shifts, I never once thought to come

to work later or take days off. With his help, I was able to accumulate an impressive amount of work to which he credited me authorship in two scientific articles alongside my team members.

I believe that my drive, my love for the scientific field, and my way of thinking have all been molded by his teachings. If granted a position to teach, I have no doubts that he would be an impressive addition to any department. The importance of having qualified and caring teachers is paramount, especially within the sciences. Dr. Pehrson's attributes fit this position in many ways, but most importantly, I believe that he will help prepare future scientists to be successful in their respective careers through university and beyond.

Sincerely,



Theepica Jeyarajah