BIOGRAPHICAL SKETCH

NAME: Alexander J. Shackman

eRA COMMONS USER NAME: SHACKMAN

POSITION TITLE: Assistant Professor, Department of Psychology, University of Maryland, College Park

EDUCATION/TRAINING

INSTITUTION	DEGREE	Completion Date	FIELD OF STUDY
University of Wisconsin—Madison	B.A.	05/97	Psychology
University of Wisconsin—Madison	M.S.	05/04	Psychology
University of Wisconsin—Madison	Ph.D.	08/08	Psychology (Distributed Minor in Neuroscience)

A. Personal Statement

I am an Assistant Professor in the Department of Psychology (clinical and CNS area groups), a member of the executive board for the interdepartmental Neuroscience Training Program, and a core faculty member of the Maryland Neuroimaging Center at the University of Maryland. I have published 30 papers—many involving large samples, multi-disciplinary research teams spread across multiple institutions, or both—focused on the neurobiology of anxiety-related traits, states, and disorders. My work underscores the value of combining neuroimaging measures (fMRI/PET), behavioral assays, and clinical interviews to understand the neural systems underlying individual differences in dispositional anxiety and neuroticism, two of the most robust prospective risk factors for the development of emotional disorders, co-morbid substance abuse, and other adverse outcomes. My research highlights the importance of circuits encompassing the amygdala, bed nucleus of the stria terminalis (BNST), anterior insula (AI), and mid-cingulate cortex (MCC) and lays a strong conceptual and methodological foundation for the proposed study.

1. **Shackman, A. J.**, McMenamin, B. W., Maxwell, J. S., Greischar, L. L. & Davidson, R. J. (2009). Right dorsolateral prefrontal cortical activity and behavioral inhibition. *Psychological Science, 20*, 1500-1506. [PMC2858783]
2. **Shackman, A. J.**, Salomons, T. V., Slagter, H. A., Fox, A. S., Winter, J. J. & Davidson, R. J. (2011). The integration of negative affect, pain and cognitive control in the cingulate cortex. *Nature Reviews Neuroscience, 12,* 154-167. [PMC3044650] **cited 590x**
3. **Shackman, A. J.**, Fox, A. S., Oler, J. A., Shelton, S. E., Davidson, R. J., & Kalin, N. H. (2013). Neural mechanisms underlying heterogeneity in the presentation of anxious temperament. *Proceedings of the National Academy of Sciences USA*, *110*, 6145-50. [PMC3713090] **N=238**
4. Birn, R. M.*, **Shackman, A. J.***, Oler, J. A., Williams, L. E., McFarlin, D. R., Rogers, G. M., Shelton, S. M., Alexander, A. L., Pine, D. S., Slattery, M. J., Davidson, R. J., Fox, A. S. & Kalin, N. H. (2014). Evolutionarily-conserved prefrontal-amygdalar dysfunction in early-life anxiety. *Molecular Psychiatry,* 19, 915-922. *** equal authorship**

B. Positions and Honors

Positions

2008-2009 Postdoctoral Scientist, UW—Madison, Supervisor: RJ Davidson, Ph.D.
2010-2011 Postdoctoral Scientist, UW—Madison, Supervisor: BR Postle, Ph.D.
2011-2013 Postdoctoral Scientist, UW—Madison, Supervisor: NH Kalin, M.D.
2013- Assistant Professor, Clinical Area Group, Department of Psychology, University of MD
2013- Assistant Professor, Neuroscience Training Program, University of MD
2013- Faculty Member, Maryland Neuroimaging Center, University of MD
2015- Member of the Executive Board, Neuroscience Training Program, University of MD

Professional Memberships

1998- Member, Society for Psychophysiological Research (SPR)
2004- Member, Society for Neuroscience (SFN)
2005- Member, Cognitive Neuroscience Society (CNS)
2011- Member, Social & Affective Neuroscience Society (SANS)
2012- Member, Anxiety and Depression Association of America (ADAA)
2013- Member, Society of Biological Psychiatry (SOBP); American Psychological Association (APA); Association for Psychological Science (APS); Society for Affective Science (SAS); Society for Research in Psychopathology (SRP); Society for a Science of Clinical Psychol (SSCP)

Other Professional Experience

2012-2015 Guest Co-Editor (with T. Hendler, **L. Pessoa**, and H. Okon-Singer), Special issue of *Frontiers in Human Neuroscience*, "The neurobiology of emotion-cognition interactions," incorporating 34 reports and reviews from leading international investigators
2013- Associate Editor, *Cognition & Emotion*
2013- Associate Editor, *Frontiers in Human Neuroscience*
2013- Invited speaker: McLean/Harvard Medical School; NIMH; University of Virginia; German National Science Foundation Symposium on Fear, Anxiety & Anxiety Disorders, Hamburg, Germany; Cornell; 2015 annual meetings of the Society for Affective Science (SAS), Social and Affective Neuroscience Society (SANS), and Society for Psychophysiological Research (SPR)
2014- Editorial Board, *Cognitive Affective & Behavioral Neuroscience (CABN)*
2014- Editorial Board, *Emotion*
2014- Associate Editor, *Frontiers in Psychology* (Section on *Emotion Science,* edited by **L. Pessoa**)
2014-2016 Program Planning Committee, Society of Biological Psychiatry (SOBP)

Honors

1996 Phi Beta Kappa
1996-1997 Hilldale Research Fellowship (Senior Thesis), UW—Madison
1997-1998 Distinguished Graduate Fellowship, UW—Madison
1998-2001 Graduate Research Fellowship, NSF
2001-2003 Predoctoral Fellowship, NIMH, Training Program in Emotion Research (T32-MH018931)
2006 Graduate Student Mentoring Award, UW—Madison
2011 Fellowship, NIMH Summer Institute in Cognitive Neuroscience, UC, Santa Barbara
2012 Travel and Poster Awards, NIMH Conference, *Determinants of executive function/dysfunction*, University of CO, Boulder
2013 Fellowship, NIMH Summer Institute in Cognitive Neuroscience, Univ. of CA—Santa Barbara
2014 Fellowship, Career Development Leadership Program, Anxiety and Depression Association of America (ADAA)

C. Contributions to Science

1. **Understanding the neurobiology of phenotypic risk for the development of emotional disorders:** Individuals with an inhibited or anxious disposition are at increased risk for developing emotional disorders. Using a combination of behavioral and psychometric assays, neuroendocrine measures, and brain imaging techniques in monkeys, patients, and young adults, we have provided compelling evidence that individual differences in the anxious phenotype reflect altered activity in several brain regions, including the amygdala, anterior insula (AI), and dorsolateral prefrontal cortex (dlPFC). Our work demonstrates that individuals who are at greatest phenotypic risk show elevated threat-related activity in the amygdala and AI, aberrant resting EEG activity on the scalp overlying the dlPFC, and reduced functional connectivity between dlPFC regulatory regions and the amygdala. Capitalizing on large samples (N=238-592), our observations suggest that elevated threat-related activity in the dorsal amygdala is a common neurobiological signature across different outward presentations of the anxious phenotype. More recently, we have begun to identify the molecular and genetic mechanisms governing trait-like differences in the activity of these key brain regions. This work has enabled us to identify, for the first time, regions of the brain (e.g. bed nucleus of the stria terminalis/BNST and AI) that mediate the inter-generational transmission of the at-risk phenotype. This work, which links brain imaging measures of the extended amygdala and other regions to individual differences in phenotypic risk, lays the groundwork for the proposed project and several other on-going fMRI studies led by my students at

Maryland (in collaboration with Luiz Pessoa, John Curtin (Wisconsin), Talma Hendler (Tel Aviv), Siri Leknes (Oslo), Leah Somerville (Harvard), and others).

a. **Shackman, A. J.**, McMenamin, B. W., Maxwell, J. S., Greischar, L. L. & Davidson, R. J. (2009). Right dorsolateral prefrontal cortical activity and behavioral inhibition. *Psychological Science, 20*, 1500-1506. [PMC2858783]
b. **Shackman, A. J.**, Fox, A. S., Oler, J. A., Shelton, S. E., Davidson, R. J., & Kalin, N. H. (2013). Neural mechanisms underlying heterogeneity in the presentation of anxious temperament. *Proceedings of the National Academy of Sciences USA*, *110*, 6145-50. [PMC3713090] **N=238**
c. Birn, R. M.*, **Shackman, A. J.***, Oler, J. A., Williams, L. E., McFarlin, D. R., Rogers, G. M., Shelton, S. M., Alexander, A. L., Pine, D. S., Slattery, M. J., Davidson, R. J., Fox, A. S. & Kalin, N. H. (2014). Evolutionarily-conserved prefrontal-amygdalar dysfunction in early-life anxiety. *Molecular Psychiatry,* 19, 915-922. *** equal authorship**
d. Fox, A. S., Oler, J. A., **Shackman, A. J.**, Shelton, S. E., Alexander, A. L., Davidson, R. J., Blangero, J., Rogers, J. & Kalin, N. H. (2015). Intergenerational neural mediators of early-life anxious temperament. *Proceedings of the National Academy of Sciences USA, 112*, 9118-22. **N=592**

2. **Understanding the neurobiology of depression:** Individuals with a neurotic, anxious disposition are at risk for developing major depression, a leading burden on global public health. As a graduate student working with Richard Davidson, Lyn Abramson, and Lauren Alloy, I provided evidence highlighting the importance of prefrontal regulatory circuits to the development and maintenance of depression. Using EEG and longitudinal clinical assessments, we demonstrated for the first time that aberrant EEG activity over the left dorsolateral PFC (dlPFC) prospectively predicts the first onset of depression in young adults. A parallel line of work using fMRI suggests that young adults with depression have difficulty using the left dlPFC to maintain activity in the ventral striatum/nucleus accumbens, a key node in the brain circuitry supporting appetitive motivation and approach-related positive affect. Relevant to the present proposal, this line of work provided an important opportunity to cultivate the expertise needed to design and successfully carry out longitudinal studies of the brain and psychopathology.

a. Nusslock, R., **Shackman, A. J.**, Coan, J. A., Harmon-Jones, E., Alloy, L. B. & Abramson, L. Y. (2011). Cognitive vulnerability and frontal brain asymmetry: Common predictors of first prospective depressive episode. *Journal of Abnormal Psychology*, *120,* 497-503. [PMC3130533]
b. Heller, A. S., Johnstone, T., **Shackman, A. J.**, Light, S., Peterson, M. J., Kolden, G. G., Kalin, N. H. & Davidson, R. J. (2009). Reduced capacity to sustain positive emotion in major depression reflects diminished maintenance of fronto-striatal brain activation. *Proceedings of the National Academy of Sciences USA, 106*, 22445-22450. [PMC2796908] **cited 174x**

3. **Emotion and cognition are integrated in the mid-cingulate cortex (MCC):** Human experience suggests that emotion and cognition are fundamentally different: emotion is saturated with feelings and manifests in readily discerned changes in the body, whereas cognition often seems devoid of significant hedonic, motivational, or somatic features. The first wave of imaging research seemed to confirm this basic dichotomy, but recent work by my group encourages a fundamentally different view, one in which emotion and cognition are functionally integrated in a variety of brain regions, including the mid-cingulate cortex (MCC) and AI. In a highly cited meta-analysis incorporating data from nearly 3,000 participants, I demonstrated that imaging studies of negative affect and cognitive control consistently activate an overlapping territory in the anterior MCC. In more recent, unpublished work supported by a University of MD seed grant (Shackman, PI; Pessoa, co-I), we have replicated this pattern using different meta-analytic databases and more recently developed statistical tools. Importantly, the same pattern emerged in a new sample of individuals performing emotional and cognitive tasks within the same fMRI session. In other work, Jim Cavanagh and I demonstrated that control-sensitive signals generated in the MCC are exaggerated in individuals prone to anxiety and predict heightened passive and active avoidance on subsequent trials. Based on these and other observations, we proposed the Adaptive Control Hypothesis, which suggests that MCC is a hub, where ascending punishment-relevant signals are integrated and used to regulate regions involved in expressing negative affect, executing aversively-motivated behavior, and tuning attention in response to action-outcome uncertainty. At the invitation of the respective program planning committees, I have presented this line of work at the 2015

annual meetings of the Society for Affective Science (SAS), Social and Affective Neuroscience Society (SANS), and Society for Psychophysiological Research (SPR). From a translational perspective, this work provides a novel framework for understanding the mechanisms underlying exaggerated avoidance in anxious individuals. This line of work was independently developed by me when I was a graduate student at Wisconsin and has continued to flourish in my new laboratory at Maryland (in collaboration with Luiz Pessoa, David Seminowicz (Baltimore) and Jarrod Lewis-Peacock (UT—Austin)).

a. **Shackman, A. J.**, Salomons, T. V., Slagter, H. A., Fox, A. S., Winter, J. J. & Davidson, R. J. (2011). The integration of negative affect, pain and cognitive control in the cingulate cortex. *Nature Reviews Neuroscience, 12,* 154-167. [PMC3044650] **cited 590x**
b. Cavanagh, J. F. & **Shackman, A. J.** (2015). Frontal midline theta reflects anxiety and cognitive control: Meta-analytic evidence. *Journal of Physiology Paris, 109*, 3-15. [PMC4213310]

4. **The interplay of anxiety and cognition:** There is growing evidence that the allocation of excessive attention to threat contributes to the development and maintenance of pathological anxiety. Using a combination of emotional faces and threat-of-shock, as in the proposed project, my work demonstrates that dispositionally-anxious individuals are biased to attend to threat-related cues. Anxious individuals also appear to have difficulties filtering threat-related cues from working memory, enabling threat to bias thoughts, feelings, and behaviour when it is no longer present in the immediate environment. These maladaptive cognitive biases appear to be potentiated by stress and adversity and may promote the development of emotional disorders. This line of work reflects research that I began as a graduate student in the lab of Richard Davidson as well as on-going collaborations with Seth Pollak (Wisconsin) and Christine Larson (UW—Milwaukee).

a. **Shackman, A. J.**, Sarinopoulos, I., Maxwell, J. S., Pizzagalli, D. A., Lavric, A., & Davidson, R. J. (2006). Anxiety selectively disrupts visuospatial working memory. *Emotion, 6*, 40-61. **cited 179x**
b. Shackman, J. E., **Shackman, A. J.** & Pollak, S. D. (2007). Physical abuse amplifies attention to threat and increases anxiety in children. *Emotion, 7*, 838-852. **cited 104x**
c. **Shackman, A. J.**, Maxwell, J. S., McMenamin, B. W., Greischar, L. L. & Davidson, R. J. (2011). Stress potentiates early and attenuates late stages of visual processing. *Journal of Neuroscience, 31,* 1156-1161. [PMC3037336]
d. Stout, D. M., **Shackman, A. J.**, Johnson, J. S. & Larson, C. L. (2015). Worry is associated with impaired gating of threat from working memory. *Emotion*, 15, 6-11. [PMC4324005]

5. **Theoretical contributions to affective science:** In addition to my empirical contributions, I have regularly contributed to the theoretical development of affective science. This conceptual line of work is important for strategically identifying what we know, what we don't know, and the most fruitful avenues and strategies for future research.

a. Davidson, R. J., Maxwell, J. S. & **Shackman, A. J.** (2004). The privileged status of emotion in the brain. *Proceedings of the National Academy of Sciences USA, 101*, 11915-11916.
b. Okon-Singer*, H., Hendler, T., **Pessoa, L.** & **Shackman, A. J.*** (2015). The neurobiology of emotion-cognition interactions: Fundamental questions and strategies for future research. *Frontiers in Human Neuroscience*, *9*, 58. [PMC4344113] **** equal authorship***
c. **Shackman, A. J.**, Fox, A. S. & Seminowicz, D. A. (*in press*). The cognitive-emotional brain: Opportunities and challenges for understanding neuropsychiatric disorders. *Behavioral and Brain Sciences*.
d. Fox, A. S., Lapate, R. C., **Shackman, A. J.** & Davidson, R. J. (*in press*). *The nature of emotion. Fundamental questions* (2nd edition). NY: Oxford University Press.

Complete List of Published Work in MyBibliography (30 Publications | *h*-index: 23):
http://www.ncbi.nlm.nih.gov/pubmed/?term=Shackman%20AJ%5BAuthor%5D&cauthor=true&cauthor_uid=26150480

D. Research Support

Ongoing Support

Dean's Research Initiative Seed Grant, University of Maryland July 2015—June 2016

The role of anxiety-related brain circuits in tobacco dependence and withdrawal

The goal of this project is to use a combination of fMRI and ecological momentary assessment (EMA) to identify the brain circuits underlying the heightened anxiety and negative affect characteristic of acute drug withdrawal and elucidate their relevance to clinically-relevant features of withdrawal in daily life. A central focus of this small pilot project is to elucidate the role of circuits encompassing the bed nucleus of the stria terminalis (BNST), which play a key role in models of addiction derived from mechanistic work in rodents.

Role: Co-PI ***(MacPherson, Co-PI; Pessoa, Curtin, and Piper, co-Is)***

New faculty start-up package, University of Maryland June 2013—July 2019

The package supports the acquisition of EMA and fMRI feasibility data. To date, my group has collected and processed ~200 EMA datasets and ~100 fMRI datasets from subjects recruited from the College Park community. These funds also provide time-limited salary support for Dr. Jason Smith, a staff scientist in my laboratory, and two graduate students.

Role: PI

Prior Support

Dean's Research Initiative Seed Grant, University of Maryland June 2014—July 2015

Dissecting the functional organization and significance of the neural circuitry of pain

This fMRI project harnesses a combination of single-subject co-activation analyses, functional connectivity "finger-printing," and multi-voxel pattern analyses (MVPA) to understand the contribution of circuits centered on the mid-cingulate cortex (MCC) and anterior insula (AI) to anxiety, pain, and cognitive control.

Role: PI ***(Pessoa, co-I)***