BIOGRAPHICAL SKETCH

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NAME: Victoria Risbrough

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

POSITION TITLE: Associate Director of Neuroscience, Center of Excellence for Stress and Mental Health, San Diego VA Health Services; Professor of Psychiatry, University of California San Diego

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
UCSD, La Jolla, CA	BA	03/1995	Psychology
UCSD, La Jolla, CA	PhD	04/2004	Neuroscience

A. Personal Statement

I have had 20 years of experience in translational pharmacology and genetic studies of neuropsychiatric disorders with particular emphasis on stress. I lead both a preclinical and clinical laboratory, with the preclinical laboratory focusing on mechanisms of stress and fear and the clinical laboratory focusing on biomarker and psychophysiology studies examining the mechanisms of risk and resilience for trauma-related disorders and pharmacological approaches to augmenting learned fear processes. I am Associate Director of Neuroscience for the Center of Excellence for Stress and Mental Health at the Veteran's Affairs Hospital in San Diego in the VA San Diego Healthcare System (VASDHS) as well as Professor of Psychiatry at UCSD. I am also the PI of the CESAMH Biorepository Core. I have directed as PI both preclinical and clinical projects for anxiety-related research funded by NIH, DOD and Veterans Affairs (VA). I have extensive experience in psychophysiological and behavioral pharmacology in both healthy controls and anxiety disorder patients. I have mentored graduate and post-doctoral and medical trainees (NIH NRSA fellows, NARSAD and NIH minority supplement awardees, VA fellowship awardees, Canadian Research Institute fellows, and T32 fellows). My trainees have gone on to academic positions in both the US and Europe as well as to pharmaceutical companies to conduct drug discovery research. As a translational scientist working across species I can support the P50 goals in understanding quantitative traits that relate to increased risk for neuropsychiatric disorders, in particularly anxiety disorders.

Relevant to the current proposal, I have worked with Dr. Baker (Multi-PI), for over 10 years. We have co-authored 20 publications and completed 5 funded projects together including the Marine Resiliency Project, which will be leveraged for the CC renewal application (see contributions to science for details of the Marine Resiliency Study Project). I am thrilled at the opportunity to work with the UCI CC team headed by Dr. Baram, a long-time "virtual mentor" for me as a colleague in preclinical research of developmental factors contributing to mental disorders. Under her leadership, we have worked extensively with the CC team to develop the preliminary data described in our project that strongly supports the CC hypothesis that anhedonia is a prospective risk factor for development of trauma-related symptoms, supporting the potential success of our studies in Aim 2. In collaboration with the CC team have published a review discussing the current evidence for a link between anhedonia and trauma-related disorders, and the potential contribution of FRAG to PTSD risk*. Our preliminary data also indicate that anhedonia is linked to increased FRAG in a veteran/active duty population, supporting our hypothesis in Aim 1. Project 4 will draw on the extensive infrastructure and research experience of the MRS team to test the CC hypotheses in an at-risk population. As corresponding PI I will work with Dr. Baram and her team to communicate with NIMH, and with Dr. Baker to ensure timely completion of study goals and milestones, and dissemination of data.

*Risbrough V, Glynn L, Davis E, Sandman C, Obenaus A, Stern H, Keator D, Yassa M, Baram T, Baker DG. (2018) Does Anhedonia Presage Increased Risk of Posttraumatic Stress Disorder? *Current Topics in Behavioral Neuroscience: PTSD*. 2018: [Epub ahead of print] PMID:29796839. PMC in process

B. Positions and Honors

Professional Experience

2004, 2006: Visiting Scholar, Max Planck Institute for Psychiatry, Munich, Germany.
2005-2007: Chair, Education & Training Committee, International Behavioral Neuroscience Society.
2005-2007: Assistant Project Scientist, Dept. of Psychiatry, University of California, San Diego, CA.
2007-2012: Assistant Professor, Dept. of Psychiatry, University of California, San Diego, CA.
2012-2016: Associate Professor, Dept. of Psychiatry, University of California, San Diego, CA.
2016-Pres: Professor, Dept. of Psychiatry, University of California, San Diego, CA.
2007-2014: Chief, Psychophysiology Unit, Center of Excellence for Stress and Mental Health, SDVA
2014-Pres: Associate Director of Neuroscience, Center of Excellence for Stress and Mental Health, SDVA
2009-Pres: Editorial Board Member, *Neuropharmacology*
2009-Pres: Editorial Board Member, *Frontiers in Psychopharmacology*
2010: Guest editor for a PTSD Special Issue, for the journal *Neuropharmacology.*
2012-pres: Member, Scientific Council, Anxiety and Depression Association of America
2015: Editor for PTSD Special Issue for *Current Topics in Behavioral Neuroscience*
2016-pres: Associate Editor, *Neurobiology of Stress*
2017: NASA Human Research Program's Space Radiation and Human Factors & Behavioral Performance Workshop presenter.

Honors & Awards

09/99:	Merck Neuroscience Graduate Research Fellowship
06/01 & 04/02:	VA Mental Illness Research, Education and Clinical Center (MIRECC) Pilot Grant
06/02, 06/03, 06/04:	International Behavioral Neuroscience Society Student Travel Award
12/03:	Individual NRSA Pre-doctoral Fellowship, NIMH
06/03:	Survival Skills and Ethics Start-Up Grant, University of Pittsburg
03/05:	Anxiety Disorders Association of America/American College of Neuropsychopharmacology Career Development Travel Award
2006:	NARSAD Young Investigator Award

Review Panels

2005	Canadian Institutes of Health Research
2008	Neurobiology Panel, PTSD and TBI, Department of Defense CDMRP
2009	Mental Health and Behavioral Science Panel A, Veterans Affairs
2009	National Institute of Mental Health Special Emphasis Panel, ZMH1 ERB-C
2011	Mental Health and Behavioral Science Panel A, Veterans Affairs
2014	Chair, Department of Defense, Congressionally Directed Medical Research Programs, Discovery-Psychotropic Medications Review Panel
2015-present	Ad hoc, Mental Health and Behavioral Science Panel A, Veterans Affairs
2014-Present	Member, Molecular Neuropharmacology and Signaling Study Section (MNPS)
2017-pres:	Board of Scientific Councilors, Brain and Behavioral Research Foundation (BBRF), formerly NARSAD)

C. Contribution to Science

1. I directed the psychophysiology project for the **Marine Resiliency Study (MRS)** and was Multi-PI of the renewal funding **MRS-II. MRS/MRS-II** is a prospective, longitudinal study of risk factors for PTSD in >3500 active duty Marines, we have identified specific physiological markers of both PTSD risk and symptom state. We found that reduced heart rate variability is a risk factor for development of PTSD, and that reductions in HRV are independent of TBI, trauma burden and depression symptoms. We have also used RDoC-related dimensional approaches to show that increased arousal (i.e. startle reactivity) is not a risk factor for PTSD, but instead is linked to symptom severity in specific domains (e.g. avoidance).

1. Minassian A, Maihofer A, Baker DG, Nievergelt CM, Geyer MA, **Risbrough VB.** Pre-deployment heart rate variability predicts onset of post-deployment Posttraumatic Stress Disorder in Active-Duty Marines. *JAMA Psychiatry*. 2015; 72:979-86. PMID:26353072
2. Breen M, Maihofer A, Glatt S, Tylee D, Chandler S, Tsuang M, **Risbrough V**, Baker D, O'Connor D, Nievergelt C, Woelk C. (2015) Gene Networks Specific for Innate Immunity Define Post-Traumatic Stress Disorder. *Molecular Psychiatry.* 2015; 20:1538-45. PMC4565790

3. Acheson DT, Geyer MA, Baker DG, Nievergelt C, Yurgil K, **Risbrough VB.** Conditioned fear and extinction learning performance and its association with psychiatric symptoms in active duty Marines. *Psychoneuroendocrinology.* 2015; 51:495-505. PMC4345165
4. Glenn DE, Acheson DT, Geyer MA, Nievergelt CM, Baker DG, **Risbrough VB**; MRS Team. High And Low Threshold For Startle Reactivity Associated With PTSD Symptoms But Not PTSD Risk: Evidence From A Prospective Study Of Active Duty Marines *Depress Anxiety*. 2016; 33(3):192-202. PMID:26878585

2. In the last 5 years my lab has contributed to the field's understanding of mechanisms of fear learning as underlying mechanisms of PTSD development and symptom maintenance. We have shown that sleep, especially REM supports safety signaling recall after fear conditioning and that sleep deprivation reduces extinction recall. These data are important as sleep disturbances are a common problem after trauma exposure and in PTSD patients, suggesting sleep therapy may augment exposure therapy efficacy. We were also the first group to show that oxytocin enhances fear extinction learning in humans.

1. Marshall A, Acheson D, **Risbrough V**, Straus L, and Drummond S. Fear Conditioning, Safety Learning, and Sleep in Humans. *Journal of Neuroscience*, 2014; 34(35):11754-60. PMID:25164670
2. Acheson D, Feifel D, de Wilde S, McKinney R, Lohr J, **Risbrough V.** The effect of intranasal oxytocin treatment on conditioned fear extinction and recall in a healthy human sample. *Psychopharmacology.* 2013; 229(1):199-208. PMC5458114
3. Acheson DT and **Risbrough VB**. Oxytocin enhancement of fear extinction: a new target for facilitating exposure-based treatments? *Biological Psychiatry.* 2015; 78:154-155. PMID:26143973
4. Straus L, Acheson A, **Risbrough V***, Drummond S*. Sleep Deprivation Disrupts Recall of Conditioned Fear Extinction. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. *equal contributions as senior author. 2017; 2:123-129. PMC5526630

3. My work in examining mechanisms of acute and chronic Corticotropin Releasing Factor (CRF) signaling on stress physiology contributed to our understanding of a how CRF1 and CRF2 receptors drive anxiety and stress recovery. For example, my study of the comparative effects of CRF1 and CRF2 receptor activation on defensive startle supported the then relatively contentious discovery that the CRF2 receptor had anxiolytic as well as anxiogenic properties, and has accrued over 120 citations. Our reviews of CRF mechanisms and how they might contribute to anxiety disorders have also been cited over 200 times (see biosketch for reviews).

1. **Risbrough V**, Hauger R, Pelleymounter M, Geyer M. Role of corticotropin releasing factor receptor 1 and 2 in CRF-potentiated acoustic startle in mice. *Psychopharmacology.* 2003; 170(2):178-87. PMID:12845406
2. **Risbrough VB**, Hauger RL, Roberts AL, Vale WW, Geyer MA (2004) Corticotropin-releasing factor receptors CRF1 and CRF2 exert both additive and opposing influences on defensive startle behavior. *Journal of Neuroscience.* 2004; 24:6545-6552. PMID:15269266
3. **Risbrough VB**, Geyer MA, Hauger RL, Coste S, Stenzel-Poore M, Wurst W, Holsboer F. CRF(1) and CRF(2) Receptors are required for potentiated startle to contextual but not discrete cues. *Neuropsychopharmacology* 2009; 34(6):1494-503. PMC2900918
4. Flandreau E*, **Risbrough V***, Lu A, Ableitner M, Geyer MA, Holsboer F, Deussing JM. Cell type-specific modifications of corticotropin-releasing factor (CRF) and its type 1 receptor (CRF1) on startle behavior and sensorimotor gating. *Psychoneuroendocrinology*. 2015; 53:16-28. *Co-first authors. PMC4364548

4. Relevant to this application, I have also contributed to the understanding of how early-life environmental signals affect psychiatric risk using sophisticated genetic mouse models. Our studies using conditional, tissue-specific CRF overexpression showed that high CRF signaling in the forebrain limited to early-life is sufficient to induce increased trait anxiety, increased susceptibility to trauma and dramatically alters CRF signaling pathways in adulthood. These phenotypes were not recapitulated simply by inducing CRF overexpression in adulthood, which may explain why CRF antagonists have failed in the clinic for mood and anxiety-disorders. We have also developed a humanized mouse model of the COMTval158met SNP to test the causal effects of this SNP in PTSD-related phenotypes including fear learning and cognition, showing that like in humans, Met carriers exhibit increased fear responding and reduced extinction.

1. Toth M, Flandreau EI, Deslauriers J, Geyer MA, Mansuy IM, Merlo Pich E, **Risbrough VB**. Overexpression of Forebrain CRH During Early Life Increases Trauma Susceptibility in Adulthood. *Neuropsychopharmacology*. 2016; 41:1681-90. PMC4832031
2. Toth M, Gresack JE, Bangasser DA, Plona Z, Valentino RJ, Flandreau EI, Mansuy IM, Merlo-Pich E, Geyer MA, **Risbrough VB**. Forebrain-specific CRF overproduction during development is sufficient to induce enduring anxiety and startle abnormalities in adult mice. *Neuropsychopharmacology*. 2014; 39:1409-19. PMC3988544
3. Adamec R, Fougere D, **Risbrough V.** CRF receptor blockade prevents initiation and consolidation of stress effects on affect in the predator stress model of PTSD*. International Journal of Neuropsychopharmacology*. 2010; 13: 747-57. PMC3092595
4. **Risbrough V**, Ji B, Hauger R, Zhou X. Generation and Characterization of Humanized Mice Carrying COMT158 Met/Val Alleles. *Neuropsychopharmacology.* 2014; 39:1823-32. PMC4059890

5. I am also interested in the interaction of mechanisms between traumatic brain injury and PTSD symptoms, as our Marine Resiliency Study team were the first to report that TBI more than doubles risk for development of PTSD in Active Duty Marines. We are the first group to show that TBI-related changes in fear learning mediate increases in PTSD symptoms, and we are working with Dr. Ming Huang to use MEG to delineate circuitry, and consequent psychophysiological abnormalities that differentiate between PTSD and TBI. Important for this application, our group has also developed a blast model of TBI in rats, to follow up our findings in Marines.

1. Glenn D, Acheson DT, Geyer MA, Nievergelt C, Baker DG, **Risbrough VB** (in press) MRS-II Team Fear learning alterations after traumatic brain injury and their role in development of posttraumatic stress symptoms. *Depression and Anxiety.* 2017; 34:723-733*.* PMID:28489272
2. Huang MX, Harrington DL, Robb Swan A, Angeles Quinto A, Nichols S, Drake A, Song T, Diwakar M, Huang CW, **Risbrough VB**, Dale A, Bartsch H, Matthews S, Huang JW, Lee RR, Baker DG. Resting-State Magnetoencephalography Reveals Different Patterns of Aberrant Functional Connectivity in Combat-Related Mild Traumatic Brain Injury. *J Neurotrauma.* 2017; 34(7):1412-1426. PMID:27762653

3: Acheson DT, Geyer MA, **Risbrough VB**. Psychophysiology in the study of psychological trauma: where are we now and where do we need to be? *Curr Top Behav Neurosci*. 2014; 21:157-83. PMID:25158622

4: Huang MX, Nichols S, Baker DG, Robb A, Angeles A, Yurgil KA, Drake A, Levy M, Song T, McLay R, Theilmann RJ, Diwakar M, **Risbrough VB**, Ji Z, Huang CW, Chang DG, Harrington DL, Muzzatti L, Canive JM, Christopher Edgar J, Chen YH, Lee RR. Single-subject-based whole-brain MEG slow-wave imaging approach for detecting abnormality in patients with mild traumatic brain injury. *Neuroimage Clin*. 2014; 5:109-19. PMC4087185

Complete List of Published Work in MyBibliography (99 peer reviewed manuscripts):
http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/40543988/

D. Research Support

Ongoing Research Support

1 I01 BX002558-01 Risbrough, V. (PI) 10/1/2014-9/30/2018
BLR&D MERIT REVIEW AWARD FOR DEPLOYMENT HEALTH RESEARCH (OEF/OIF/OND)
Role of COMTval158met in PTSD risk and treatment response
Major Goals: Determine mechanism of COMTval158met effects on fear extinction and fear learning using humanized mice for COMTVal158Met SNP and examine this SNP's association with treatment response to extinction based therapy in veterans with PTSD.

R01 AA026560-01 Risbrough V, Der-Avakian A (Multi-PI) 10/1/2017-9/30/2021
NIH/NIAAA
Developing rodent models of PTSD/AUD: leveraging clinic-based strategies
Goals/Aims: Identify inflammatory and sleep contributions to excessive alcohol use after trauma.
Role: Corresponding-PI

CESAMH 07/01/2007 - Continuing
Veterans Affairs Center of Excellence for Stress and Mental Health
The major goals of the Center are the advancement of the understanding and care provided for military veterans who are exposed to stressful or traumatic events. Dr. Risbrough receives funding as the PI of the CESAMH Biorepository to study PTSD treatment response and to maintain her Psychophysiology Laboratory, as well as for administrative duties as the Associate Director of Neuroscience for the Center.
Role: PI of CESAMH Biorepository Core, Associate Director of Neuroscience Research

NIDA 1R43DA041760 Wang, Yu, (PI) 05/01/2017 - 08/31/2019
Web Application and Services for Methodologically Rigorous Animal Study Design
Goals: Design a website and software suite to aid in development of rigorous and adequately powered model organism experiments for research scientists.
Role: Site PI (UCSD)

1 UH2 MH109334-01 Pizzagalli DA (PI) 04/01/16 – 03/31/21
National Institute of Mental Health (NIMH)
Novel Cross-Species Neurophysiological Assays of Reward and Cognitive Domains
The major goals of this project are to develop, optimize, and validate cross-species (rat/human) EEG measures linked to behaviors related to reward learning, cognitive flexibility, and error processing in rats.
Role: Co-Investigator

MR141217 Baker, D (PI) 10/01/2015- 09/30/2018
CDMRP/DOD
Patterns of Tinnitus and Hearing Loss Secondary to Blast Injury
Major Goals: Identify neural substrates of tinnitus symptoms due to blast exposure in active duty Marines.
Role: Co-Investigator

1 I01 CX001542 (Simmons, PI) 04/01/2017-3/31/2021
CR&D MERIT REVIEW AWARD
Title: Anti-depressant response in neurobiologically defined psychiatric veteran groups
Major goals: To determine genetic, physiologic and circuit predictors of SSRI treatment response in PTSD.
Role: Co-Investigator

Pending

1 I01 BX004312-01 Risbrough, V; Rissman R (Multi-PIs) 10/1/2018-9/30/22
BLR&D Merit Review Award
Neuronal exosomes to identify biomarkers and pathology of deployment-related TBI
Goals: To examine exosome cargo to develop novel biomarkers of cognitive decline associated with combat-related TBI.
Role: Corresponding PI
NOTE: Received notice of intention to fund 2/9/2018.

DM102425 Risbrough V (PI) 10/01/2018-09/30/2021
DOD
Impact of Operational Sleep Disruption on PTSD-Relevant Fear Learning Processes
Goals and specific aims: Investigate the role of REM and slow-wave sleep deprivation in fear extinction acquisition, consolidation, and recall in humans.
Role: PI
NOTE: Received notice of intention to fund April 2018 from CDMRP- now in pre-award negotiation process

Recently completed

5 R01 MH074697-08 Risbrough, V. (PI) 07/01/2005-02/28/2015
NIMH
Stress and CRF System Effects on Information Processing
Major goals: Use rodent experimental systems to elucidate the mechanisms underlying the behavioral effects of stress and the neuropeptide corticotropin releasing factor (CRF) on information processing.
Over the 8 years of funding this grant produced 32 manuscripts in high impact journals such as *Journal of Neuroscience*, *Neuropsychopharmacology* and *Nature*.

Marine Resilience Study II Baker, D., Geyer, M., Risbrough, V (Multi-PI) 10/01/2012-09/30/2015
U.S. Marine Corps – NIMH/Army STARRS collaboration
Prospective Study of the Psychological, Social, and Biological Markers of Risk and Resilience for Operational Stress in Marines (Marine Resilience Study II)
Project 1: To provide long term follow-up to the Marine Resiliency Study (MRS).

Project 2: Conduct a pre-post deployment study to identify neurocognitive predictors of PTSD vulnerability.
Role: Multi-PI – Directed project 2
Over the 3 years of funding this grant produced >25 articles in high impact journals such as *JAMA Psychiatry* and *Molecular Psychiatry.*