BIOGRAPHICAL SKETCH

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NAME: I-Wei Shu MD PhD

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

POSITION TITLE: Associate Clinical Professor

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
Northwestern University	BA	1994-1997	Molecular and Cell Bio.
Mount Sinai Sch. of Medicine	n/a	1998-2000	Medical school years 1-2
Mount Sinai Sch. of Medicine	PhD	2000-2004	Neurosciences
Univ. of Ca. Davis Sch. of Medicine	MD	2004-2006	Medical school years 3-4
Univ. of Ca. San Diego (UCSD) Sch. of Medicine	n/a	2006-2010	Psychiatry residency
Veterans Affairs (VA) San Diego Healthcare System	n/a	2010-2013	Psychiatric research fellow

A. Personal Statement

I have over 15 years of biosignal processing experience, including extracting clinically-specific electroencephalographic (EEG) features from patients with neuropsychiatric disorders. I currently lead brain-computer interface (BCI) development and EEG data acquisition/analysis for UCSD Center for Mental Health Technology's Functional Neuroscience Laboratory. More specifically, my team and I have developed and maintain multiple EEGLAB/MATLAB-based technologies for assessing and targeting prefrontal neural signatures of learning and memory.

These technologies include a novel EEG neurofeedback protocol specifically-designed to target high-frequency (e.g., gamma) neural activity critical for optimal memory performance. We currently have NIH support to test this protocol in 2 clinical trials, aiming to improve memory function in patients with schizophrenia or mild cognitive impairment (MCI).

In addition to my scientific expertise, I have extensive experience managing small to medium size scientific and clinical teams. I previously served as Lead Psychiatrist for a Department of Defense clinical trial of the blood pressure medication losartan for PTSD, which involved 6 sites and over 280 consented participants. I have also served as Medical Director for VA San Diego's South County Posttraumatic Stress Disorder (PTSD) programs, helping to manage 3 fulltime psychiatrists, 1 fulltime nurse and 1 fulltime psychiatric resident serving over 5000 veterans.

Publications and projects that I would like to highlight include:

Lin YY, **Shu IW**, Singh Fiza. Frontal gamma as a marker of effective training during neurofeedback to improve memory in patients with mild cognitive impairment. 11th International IEEE EMBS Conference on Neural Engineering, 2023, *in press*

Lin YY, **Shu IW**, Hsu SH, Pineda JA, Granholm EL, Singh Fiza. Novel EEG-Based Neurofeedback System Targeting Frontal Gamma Activity of Schizophrenia Patients to Improve Working Memory. 44th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), 2022, pp. 4031-4035, doi: 10.1109/EMBC48229.2022.9870878

Shu IW, Granholm EL, Singh F. Targeting frontal gamma activity with neurofeedback to improve working memory in schizophrenia. Curr Top Behav Neurosci, 2022, https://doi.org/10.1007/7854_2022_377

Singh F, **Shu IW**, Hsu SH, Link P, Pineda JA, Granholm E. Modulation of frontal gamma oscillations improves working memory in schizophrenia. Neuroimage Clin. 2020;27:102339. doi: 10.1016/j.nicl.2020.102339. Epub 2020 Jul 10. PMID: 32712452; PMCID: PMC7390812.

Singh F, **Shu IW**, Granholm E, Pineda JA. Revisiting the Potential of EEG Neurofeedback for Patients With Schizophrenia. Schizophr Bull. 2020 Jul 8;46(4):741-742. doi: 10.1093/schbul/sbaa033. PMID: 32133510; PMCID: PMC7345762.

Gandara V, Pineda JA, **Shu IW**, Singh F. A Systematic Review of the Potential Use of Neurofeedback in Patients With Schizophrenia. Schizophr Bull Open. 2020 Jan;1(1):sgaa005. doi: 10.1093/schizbullopen/sgaa005. Epub 2020 Mar 2. PMID: 32803157; PMCID: PMC7418870.

NIMH 4R33MH112793 May 2020- Dec 2023
Enhancing Gamma Band Response in Schizophrenia to Improve Working Memory. Follow-up 12-week, randomized, double blind, placebo-controlled trial of EEG neurofeedback based on R61 parameters to improve gamma band response and working memory in patients with SCZ. Role: Co-Investigator

NIA 1R01AG065252 Mar 2020 – Feb 2025
Enhancing gamma band response to improve working memory in individuals with mild cognitive impairment.12-week, randomized, double-blind, placebo-controlled trial of EEG neurofeedback to improve cognitive endpoints in patients with MCI. Role: Co-Investigator

NIMH 1R61MH112793 Dec 2017-Apr 2020
Enhancing Gamma Band Response in Schizophrenia to Improve Working Memory. Exploratory Treatment grant to explore the use of EEG neurofeedback to improve gamma coherence in schizophrenia patients, and to determine the effects of neurofeedback on working memory. Role: Co-Investigator

B. Positions and Honors

Positions and Employment

2020-present	Acting CEO, Co-Founder/Member, BioSignal Solutions LLC
2019-present	Associate Clinical Professor, Dept. of Psychiatry, UCSD
2018-present	Co-Investigator, Functional Neuroscience Laboratory, UCSD Center for Mental Health Technology
2016-2020	PTSD Medical Director, VA San Diego South County Services
2015-2019	Assistant Clinical Professor, Dept. of Psychiatry, UCSD
2015-2017	Owner, Coastal Neurotherapeutics
2010-2015	Clinical Instructor, Dept. of Psychiatry, UCSD

Other Experience and Professional Memberships

2019-present	Member, UCSD Dept. of Psychiatry Senior Clinical Faculty Committee
2011-present	Diplomate (Psychiatry Certificate #62051), American Board of Psychiatry and Neurology
2010-present	Member, American Psychiatric Association
2008-present	Licensed Physician (License #A103813), Medical Board of CA
2022	Member, IEEE Engineering in Medicine and Biology Society
2022	Member, Institute of Electrical and Electronics Engineers (IEEE)
2018-2022	Member, Society for Neuroscience
2017-2022	Ad Hoc Reviewer, *Clin EEG Neuroscience*
2015-2020	Member, International Society for Traumatic Stress Studies
2020	Ad Hoc Reviewer, *Eur J Psychotraumatol*
2019-2020	Member, VA San Diego Tele-Mental Health Workgroup

2019-2020	Member, UCSD Dept. of Psychiatry Professional Development Series Committee
2019	Member, VA San Diego IU6 Clinic Improvement Committee
2013-2019	Ad Hoc Reviewer, *Depress Anxiety*
2019	Panelist, UCSD Dept. of Psychiatry Faculty Mentorship Seminar Series
2017-2019	Faculty Discussant, UCSD Dept. of Psychiatry Resident Rounds on PTSD/Trauma
2015-2017	Ad Hoc Reviewer, *Biol Psychology*
2017	Organizer/Presenter, Research Section, VA San Diego Psychiatry Retreat
2014-2016	Ad Hoc Reviewer, *Psychiatry Res*
2016	Invited Speaker, VA San Diego Quarterly Nurse Practitioner/Clinical Nurse Specialist
2015	Invited Discussant, International Society for Traumatic Stress Studies; Student Luncheon Meeting; Retreat
2013-2014	Consultant, Primary Care and Mental Health Integration, VA San Diego
2013-2014	Ad Hoc Reviewer, *Front Hum Neurosci*
2013	Organizer, 9th Annual Lewis L. Judd Young Investigators Research Symposium
2012	Invited Speaker, Naval Medical Center San Diego Mental Health Grand Rounds
2011-2012	Ad Hoc Reviewer, *Int J Psychol*
2010-2011	Member, Ethics Committee, San Diego Psychiatric Society

Honors

2018	VA San Diego Leadership Award Honorable Mention
2015	VA San Diego Excellent Care/Service HIGH Five Award
2013	Scholar, American Psychosomatic Society 2013 Young Investigator Colloquium
2013	Keynote Speaker, Dept. of Psychiatry 8th Annual Junior Faculty and Postdoctoral Research Symposium, UCSD

News/Media

Madhusoodanan J. Better brain training for treating psychological conditions. Nature. 2021 June 24: doi: https://doi.org/10.1038/d41586-021-01664-x [*expert source*]

C. Contribution to Science

1. Pathophysiology of neurodegenerative disorders

As a PhD candidate at Mount Sinai School of Medicine (Neurosciences PhD awarded 2004), I contributed to our understanding of how specific neurons exhibit unique vulnerabilities to oxidative damage. More specifically, my dissertation demonstrated that ventromedial hypothalamic neurons are especially sensitive to damage from glucose toxicity. I also contributed to a project demonstrating how oxidative stress produces axon damage in a mouse model of amyotrophic lateral sclerosis.

Morrison BM, **Shu IW**, Wilcox AL, Gordon JW, Morrison JH. Early and selective pathology of light chain neurofilament in the spinal cord and sciatic nerve of G86R mutant superoxide dismutase transgenic mice. Exp Neurol. 2000 Oct; 165 (2): 207-20.

Shu IW, Lindenberg DL, Mizuno TM, Roberts JL, Mobbs CV. The fatty acid synthase inhibitor cerulenin and feeding, like leptin, activate hypothalamic pro-opiomelanocortin (POMC) neurons. Brain Res. 2003 Sep 19; 985 (1): 1-12.

2. Developing novel methods for assessing and treating neurobiological and clinical abnormalities related to trauma and stress

Together, anxiety and stress-related disorders are the most common mental health disorders affecting American adults. Current treatments are only about 35% effective; thus, providers urgently need additional options to improve outcomes for their patients. EEG is a portable, widely-available and cost-effective modality with high temporal resolution. During my VA San Diego Research Fellowship (2010-2013), we tested the general hypothesis that, since PTSD is associated with increased fear responses, EEG markers of excessive limbic activity may serve as markers of PTSD symptomology. We were able to confirm this hypothesis under various conditions – appraising ambiguous facial features (Shu et al, 2014a), error processing (Shu et al, 2014b).

Shu IW, Onton JA, Prabhakar N, O'Connell RM, Simmons AN, Matthews SC. Combat veterans with PTSD after mild TBI exhibit greater ERPs from posterior-medial cortical areas while appraising facial features. J Affect Disord. 2014a Feb; 155: 234-40.

Shu IW, Onton JA, O'Connell RM, Simmons, AN, Matthews SC. Combat veterans with comorbid PTSD and mild TBI exhibit a greater inhibitory processing ERP from the dorsal anterior cingulate cortex. Psychiatry Research: Neuroimaging. 2014b Aug; 224: 58-66.

Furthermore, as PTSD Medical Director for VA San Diego South County clinics and Lead Psychiatrist for a multi-site Department of Defense clinical trial of the blood pressure medication losartan for PTSD, I helped identify specific metabolic complications related to PTSD, and biopsychosocial predictors of PTSD treatment response to the angiotensin receptor blocker losartan.

Stein MB, Jain S, Simon NM, West JC, Marvar PJ, Bui E, He F, Benedek DM, Cassano P, Griffith JL, Howlett J, Malgaroli M, Melaragno A, Seligowski AV, **Shu IW**, Song S, Szuhany K, Taylor CT, Ressler KJ; LOSe-PTSD Investigators. Randomized, placebo-controlled trial of the angiotensin receptor antagonist losartan for posttraumatic stress disorder. Biol Psychiatry. 2021 May 21: S0006-3223(21)01328-7. doi: 10.1016/j.biopsych.2021.05.012

Palmer BW, Shir C, Chang H, Mulvaney M, Hall JMH, **Shu IW**, Jin H, Lohr JB. Increased prevalence of metabolic syndrome in veterans with PTSD untreated with antipsychotic medications. International Journal of Mental Health. 2021 Aug 25: https://doi.org/10.1080/00207411.2021.1965398

3. Developing novel EEG methods to better assess and improve cognitive function for patients with neuropsychiatric difficulties

Optimal working memory (WM), the mental ability to internally maintain and manipulate task-relevant information, requires coordinated activity of prefrontal cortical (PFC) neurons. More specifically, during delay periods of tasks with WM features, PFC microcircuits generate persistent, stimulus-specific higher-frequency (e.g., gamma) activity. This activity largely depends on recurrent connections between parvalbumin positive inhibitory interneurons and pyramidal neurons in more superficial PFC layers. Due to the size and organization of pyramidal neurons (especially apical dendrites), local field potentials generated by PFC microcircuits are strong enough to pass outside the skull, and can be detected using electroencephalography (EEG). Since many patients with neuropsychiatric difficulties, e.g., schizophrenia or MCI, exhibit both PFC and WM abnormalities, EEG markers of PFC microcircuit activity during WM may serve as effective treatment targets.

A safe, clinically-feasible way to target PFC activity is EEG neurofeedback (EEG-NFB), a form of operant conditioning where an EEG signal of interest (e.g., frontal gamma activity) is coupled, in real time, to positive and negative reinforcement signals – e.g., the modulation of digital content (e.g., video game, slideshow). While EEG-NFB is a well-tolerated, non-invasive, non-pharmacologic treatment modality that can be rapidly disseminated at low cost, widespread institutional acceptance has, to date, been limited due to concerns about specificity of observed effects and discrepancies with current models of brain function. With specific regards to frontal gamma activity, however, for reasons discussed above, using EEG-NFB to modulate frontal gamma activity would likely directly modulate PFC gamma activity and improve WM and related cognitive functions.

Gandara V, Pineda JA, **Shu IW**, Singh F. A Systematic Review of The Potential Use of Neurofeedback in Patients with Schizophrenia. Schizophr Bull Open. 2020 Jan;1(1):sgaa005. doi: 10.1093/schizbullopen/sgaa005

Singh F, **Shu IW**, Granholm EL, Pineda JA. Revisiting EEG-Neurofeedback for Schizophrenia. Schizophr Bull. 2020 Jul 8;46(4):741-742. doi: 10.1093/schbul/sbaa033

Singh F, **Shu IW**, Hsu SH, Link P, Pineda JA, Granholm EL. Modulation of Frontal Gamma Oscillations Improves Working Memory in Schizophrenia. Neuroimage Clin. 2020;27:102339. doi: 10.1016/j.nicl.2020.102339

Shu IW, Granholm EL, Singh F. Targeting frontal gamma activity with neurofeedback to improve working memory in schizophrenia. Curr Top Behav Neurosci, 2022, https://doi.org/10.1007/7854_2022_377

Lin YY, **Shu IW**, Hsu SH, Pineda JA, Granholm EL, Singh Fiza. Novel EEG-Based Neurofeedback System Targeting Frontal Gamma Activity of Schizophrenia Patients to Improve Working Memory. 44th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), 2022, pp. 4031-4035, doi: 10.1109/EMBC48229.2022.9870878

Lin YY, **Shu IW**, Singh Fiza. Frontal gamma as a marker of effective training during neurofeedback to improve memory in patients with mild cognitive impairment. 11th International IEEE EMBS Conference on Neural Engineering, 2023, *in press*

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https://www.ncbi.nlm.nih.gov/myncbi/1X5MFQEWdvc/bibliography/public/

Foreign Disclosures

None