OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 09/30/2024)

BIOGRAPHICAL SKETCH

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NAME: Khaleel A. Razak

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

POSITION TITLE: 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 |
| --- | --- | --- | --- |
| College of Engineering, Anna University, Madras, India | B.E. | 05/1992 | Electronics and Communications Engineering |
| University of Wyoming, Laramie, Wyoming | M.S. | 07/1997 | Bioengineering |
| University of Wyoming, Laramie, Wyoming | Ph.D. | 072001 | Zoology/Physiology/ Neuroscience |
| Georgia State University, Atlanta, Georgia | Post-Doctoral | 12/2003 | Developmental Neuroscience |
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1. **Personal Statement**

The long-term focus of my research program is to understand mechanisms of auditory processing and plasticity. My academic background is in Bioengineering and Neuroscience. For my senior undergraduate thesis, I developed a telephone for the hearing impaired (a 1990’s texting device). Testing the prototype at a school for the hearing impaired raised my interest in the auditory system. After college, I worked in a company that manufactured medical ultrasonic scanners. This kindled my interests in biosonar. Early exposure to topics in hearing and sonar led me to pursue training in auditory neuroscience. This was the beginning of ~25 years of experience working on the auditory system. My post-doctoral training was in auditory and visual system development. This interest in plasticity of sensory systems led to the major projects of my own research program at UC Riverside. Our current NIH and DOD funded projects focus on auditory cortex and midbrain plasticity during development and aging. In terms of disorders that affect auditory communication, humans with Fragile X Syndrome (FXS) and other autism spectrum disorders show significant auditory processing deficits. One major emphasis in the lab is to understand the structural and functional bases of developmental deficits in FXS. By focusing on basic sensory processing and circuit level processing, the goal is to identify neural pathways and mechanisms underlying auditory disorders in neurodevelopmental disorders. In fact, we are on the leading edge of understanding mechanisms that cause hypersensitivity in FXS across the auditory system (see reviews cited below). We showed evidence that abnormal parvalbumin neuron development and the perineuronal nets that cover these neurons lead to auditory hypersensitivity. We have also identified multiple EEG-based phenotypes in the *Fmr1* KO mice (an FXS mouse model) that are remarkably similar to those seen in humans with FXS. Together, these studies have identified novel mechanisms of sensory processing disorders in an autism model, and identified biomarkers for which underlying circuit mechanisms are becoming established.

I have collaborated with Dr. Pedapati for nearly 6 years now as investigators on a recently renewed NIH Centers for Collaborative Research on FXS. In particular, we have coordinated on studies and analysis of human and mouse EEG recordings. Through monthly meetings and reciprocal lab visits, we have created an environment of clear communication of paradigms and data sharing that have benefited both groups, and form a highly intellectually rewarding aspect of my career. I look forward to continuing this productive interaction. The research expertise that I will provide for the applicant’s project is in the area of cortical processing and electrophysiological responses, particularly those aligned with neurodevelopmental disorders such as FXS. The reviews cited below highlight our work on auditory processing in FXS within the context of sensory dysfunction in autism.

1. Razak KA, Binder, DK and Ethell IM. Mechanisms and biomarkers of auditory hypersensitivity in Fragile X Syndrome. Frontiers in Psychiatry – Child and Adolescent Psychiatry. *In Press*.
2. Razak KA, Dominick K and Erickson CA. Developmental studies in Fragile X Syndrome. J Neurodev Disord. 2020 May 2;12(1):13. doi: 10.1186/s11689-020-09310-9.
3. Rais M, Binder DK, Razak KA and Ethell IM. Sensory Processing Phenotypes in Fragile X Syndrome. *ASN neuro*, *10*, p.1759091418801092, 2018.
4. Sinclair D, Oranje B, Razak KA, Siegel SJ and Schmid S.Sensory processing in autism spectrum disorders and Fragile X syndrome-from the clinic to animal models. *Neurosci. & Biobehav. Rev*. 76:235-253, 2016.(doi: 10.1016/j.neubiorev.2016.05.029).
5. **Positions, Scientific Appointments, and Honors**

7/20-present Director, Graduate Neuroscience Program, University of California, Riverside

7/19-present Professor, Department of Psychology, University of California, Riverside

7/14-6/19 Associate Professor, Department of Psychology, University of California, Riverside

7/07-6/14 Assistant Professor, Department of Psychology, University of California, Riverside

08/13 NSF CAREER Award.

1/04-6/07 Research Scientist, Department of Zoology and Physiology, University of Wyoming

8/01-12/03 Post-Doctoral Associate, Department of Biology, Georgia State University

8/96-8/01 Research Assistant, Department of Zoology and Physiology, University of Wyoming

08/94 Tau Beta Pi, Engineering Honor Society.

03/93 National Technology Award from the President of India, Dr. S.D. Sharma, for the use of technology

in handicapped rehabilitation.

**C. Contributions to Science**

Full list of publications can be found at:

<https://www.ncbi.nlm.nih.gov/myncbi/10SpeYwV_axA0/bibliography/public/>

I. Mechanisms of auditory hypersensitivity in Fragile X Syndrome: My lab has studied the mouse model of Fragile X Syndrome (FXS) for nearly 10 years and has made significant discoveries on mechanisms of central auditory processing disorders. FXS is a leading genetic cause of intellectual impairment and autism. Symptoms include reduced IQ, repetitive behaviors, abnormal social and communication behaviors, increased anxiety and arousal and auditory hypersensitivity. We have identified neural correlates of auditory hypersensitivity in the Fmr1 knockout mouse model of FXS. These are the first studies to systematically evaluate the mechanisms of sensory processing abnormalities in an autism spectrum disorder. Ongoing studies examine the auditory system from the cochlea to the cortex using multiple transgenic lines of mice in which FMRP is removed from specific neurons, regions and time points.

1. Lovelace, J.W., Rais, M., Palacios, A.R., Shuai, X.S., Bishay, S., Popa, O., Pirbhoy, P.S., Binder, D.K., Nelson, D.L., Ethell, I.M. and Razak, K.A., 2020. Deletion of Fmr1 from forebrain excitatory neurons triggers abnormal cellular, EEG, and behavioral phenotypes in the auditory cortex of a mouse model of Fragile X syndrome. Cerebral Cortex, *30*(3), pp.969-988. PMCID: PMC7132927.

2. Wen TH, Afroz S, Reinhard SE, Tapia K, Binder DK, Razak KA and Ethell IM. Genetic Reduction of Matrix Metalloproteinase-9 Promotes Formation of Perineuronal Nets Around Parvalbumin-expressing Interneurons and Normalizes Auditory Cortex Responses in Developing Fmr1 Knock-out Mice. Cerebral Cortex. 28:3951-3964, 2018. PMCID: PMC6188540.

3. Lovelace JW, Binder DK, Ethell IM and Razak KA. Translation relevant EEG biomarkers in the mouse model of Fragile X Syndrome. Neurobiol. Dis. 111:39-48, 2018. PMCID: PMC5969806.

4. LovelaceJW, WenTH, ReinhardSE, HsuMS, SidhuH, EthellIM, BinderDK and RazakKA. Matrix metalloproteinase-9 deletion rescues auditory evoked potential habituation deficit in a mouse model of Fragile X Syndrome. Neurobiol. Dis. 89:126-135, 2016. PMCID: PMC4785038.

II. Developmental plasticity in the auditory cortex: I identified developmental changes in receptive field mechanisms that shape spectrotemporal changes in auditory cortex. In particular, I discovered the cortical mechanisms underlying selectivity for frequency-modulated sweeps, a class of sounds that is common in various vocalizations including human speech and showed how developmental changes in excitation-inhibition balance led to increased selectivity for these sounds. More recently, we have identified EEG phenotypes related to the development of auditory hypersensitivity in the *Fmr1* KO mouse, and how early sound exposure may reduce such symptoms.

1. Rais M, Lovelace JW, Shuai XS, Woodard W, Bishay S, Estrada L, Sharma AR, Nguyen A, Pirbhoy PS, Palacios AR, Nelson DL, Razak KA and Ethell IM. Functional consequences of postnatal interventions in a mouse model of Fragile X Syndrome. Neurobiology of Disease. *In Press.*
2. Kulinich AO, Reinhard SE, Rais M, Lovelace JW, Scott V, Binder DK, Razak KA and Ethell IM. Beneficial effects of sound exposure on auditory cortex development in a mouse model of Fragile X Syndrome. Neurobiol. Dis. 134:104622, 2020.
3. Razak KA, Richardson, MD and Fuzessery ZM. Experience is required for the maintenance and refinement of FM sweep selectivity in the developing auditory cortex. Proc. Natl. Acad. Sci. (USA) 105:4465-4470, 2008. PMCID: PMC2393755.
4. Razak KA and Fuzessery ZM. Development of inhibitory mechanisms underlying selectivity for the rate and direction of frequency-modulated sweeps in the auditory cortex. J. Neurosci. 27:1769-1781, 2007. PMCID: PMC6673737.

III. Cortical mechanisms of sound localization: The auditory cortex is necessary for sound localization behaviors. However, our understanding of how the auditory cortex represents 2D space is rudimentary. Sound localization is a broadly interesting problem because space is not directly encoded in the output of the auditory receptor epithelium (cochlea). Spatial information is computed based on integration of peripheral (ear shape) properties and neural responses to binaural cues. How the auditory cortex represents such integrated information remains unclear. The pallid bat (*Antrozous pallidus*) is an ideal model to study mechanisms of sound localization. This species listens passively to prey-generated noise and localizes prey with extraordinary accuracy, most of the time in very low-light situations. Based on neurobehavioral work in the pallid bat, I have published a specific hypothesis on how the auditory cortex of mammals represents 2D space that depends on overlapping maps of binaural and spectral processing.

1. Brewton D, Gutierrez V and Razak KA. Accurate sound localization behavior in a gleaning bat, *Antrozous pallidus*. *Scientific Reports* *8*(1):13457, 2018. PMCID: PMC6128894
2. Razak KA. Functional segregation of monaural and binaural selectivity in the pallid bat auditory cortex. Hearing Res. 337:35-45, 2016.
3. Razak KA, Yarrow S and Brewton D. Mechanisms of sound localization in two functionally distinct regions of the auditory cortex. J. Neurosci*.* 35:16105-16115, 2015. PMCID: PMC6605498.
4. Razak KA. Systematic representation of sound locations in the primary auditory cortex. J. Neurosci. 31:13848-13859, 2011.  PMCID: PMC3219787.