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Stress and Cognitive Electroimaging Lab

Stress and Cognitive Electroimaging Lab, established by me in the Department of Physiology at AIIMS in 2011, has made substantial contributions towards understanding the neural underpinnings of various cognitive domains, in healthy individuals as well as in neuropsychiatric and neurodegenerative disorders. QEEG data of patients is collected and analyzed using various analysis strategies. The lab has collaboration with Departments of Neurology, Psychiatry, Deaddiction Centre, Pediatric Neurology and Ophthalmology of AIIMS, New Delhi.

Quantitative EEG data of more than 450 healthy adults, 165 children, 90 elderly and 250 patients (including Parkinson's & Alzheimer's disease, mild cognitive impairment, Schizophrenia, Autism, Attention deficit Hyperactive disorder, Glaucoma and Addiction) across wide range of age groups has been collected and analyzed during baseline and during testing of varied cognitive domains and published.

Various cognitive domains being studied range from perception, memory (verbal and picture), working memory, interference, attention (both auditory and visual) to emotions. This has enabled us to study the age-related cognitive changes in either gender across cognitive domains.

Neural basis of alteration of functions due to cognitive load, stress, emotions, meditation, attention, language, audio-visual integration, motor imagery and visual perception in binocular rivalry paradigm have also been targeted as core areas for research. The neural correlates in terms of networks activated, their neural sources as well as connectivity and coherent activation compared to baseline conditions is being studied using Quantitative EEG.

Quantitative EEG (QEEG) is the methodological analysis of EEG to derive the quantitative measures that reflect the underlying physiology and pathophysiology. QEEG measures such as spectral power, coherence, EEG microstates, source localization and connectivity measures, are being used in our laboratory to study the brain activity of patients and healthy controls. One of the main strengths of our lab is dense array EEG acquisition using 128-channel EEG that provides greater precision and accuracy in localizing the brain sources of EEG activity across 6239 voxels that are correlated directly to structures revealed by MRI.

We aim to develop QEEG signatures of stress & cognitive functions and a platform for screening and profiling of patients with psychiatric and neurodegenerative disorders that can be used as a neural signature /biomarker in these disorders. This of utmost importance in conditions such as dementia (in Alzheimer's, Parkinson's), ADHD, Autism, Depression where there is no objective gold standard for diagnosis, which often leads to over/ under diagnosis.

Further, research in SCEL aims to understand the underlying basis for possible augmention of mental capabilities of a healthy subject in the event of higher work load or stress or restoring mental and physical capabilities in a disease.

The research group includes one Professor (Prof Ratna Sharma), two Additional professors (Dr Simran Kaur, Dr Prashant Tayade) and one Assistant Professor (Dr Suriya Prakash). Thesis work of fourteen PhD, 14 MD, 8 MSc, 4 DM, students and two ICMR RA has been done in the lab. Research publications (published and under publication) includes international and national original articles, that have also been applauded by the institute (received AIIMS Excellency award 2017) and other forums (APPI awards) as well as research grants from various funding agencies of Government of India (DST, DBT, DHR, Ayush, AIIMS).

Brief Summary of research work done by Prof Ratna Sharma, Stress and Cognitive Electroimaging Lab, Department of Physiology, AIIMS, New Delhi:

- 1. In healthy individuals, exposure to high-arousing emotional stimuli improves verbal working memory by directing the attentional resources toward the task and decreasing the decision-making time through suppression of DMN areas, thus making faster and correct responses (doi.org/10.3758/s13415-018-00661-4).
- 2. Brain microstate preceding a trial influences the outcome (error or success) in a memory task (doi: 10.1016/j.bbr.2016.08.020).
- 3. Visual perception: Studies on neural processing of congruency and affective valence in a binocular rivalry paradigm during revealed that visual perception shows perceptual bias towards incongruence when the associated valence was negative (doi:10.1007/s10339-020-00957-9). Pre-stimulus microstates influence the perception and perceptual reversals in addition to other stimulus attributes (doi:10.1016/j.neulet). Frontal lobe showed sensitivity to both valence and incongruence associated with the visual stimuli (doi:10.101A/j.bandc). Increased error rates when faced with incongruity and negative affect during visual tasks could be due to lower functional connectivity between the brain area pairs which process emotion, attention, memory, and semantic relations. In conclusion, scene incongruence has an attentional advantage which is greatly influenced by the valence.
- 4. Studies have been published identifying QEEG based biomarkers (specific microstates, spectral power and brain connectivity) for screening and profiling of patients with psychiatric and neurodegenerative disorders that can be used as a neural signature /biomarker for Alzheimer's, Parkinson's, Glaucoma, Autism, Schizophrenia and depression (doi:10.4103/0028-3886.349604; doi.org/10.1016/j.neulet.2021.136036; doi:10.1007/s11571-020-09643-0).
- 5. Specific QEEG parameters that could serve as state/trait markers of schizophrenia providing objectivity to the diagnosis of schizophrenia: Patients and first-degree relatives displayed higher power spectral density than controls for all frequency bands in left parahippocampal gyrus. Left deep parahippocampal gyrus distinguished patients from first-degree relatives and controls (lower power in higher frequency bands). Functional connectivity was lower in patients and higher in relatives compared to controls between resting-state network areas (doi.org/10.1016/j.schres.2020.03.066).

Shortened Microstate Map 5 duration (with hyperactivation in left inferior parietal lobule and temporal gyri) distinguished patients with schizophrenia from controls (<u>https://doi.org/10.1016/j.schres.2018.06.020</u>).

Pre-trial microstate map 1 (intracranial generator localized to right inferior frontal gyrus) distinguished controls from patients and pre-response microstate map 4 distinguished controls from first-degree relatives (which could be considered an endophenotypic marker) (doi.org/10.1016/j.bbr.2019.111964). Patients deactivated Default mode network, resting state networks and auditory cortex more compared to controls during search period to perform VSWM task. Relatives showed altered activation of right medial and inferior frontal gyrus during different events and loads of the task in lower frequencies compared to controls. Relatives also showed hyperactivity in right cingulate and parahippocampal gyrus compared to controls (doi.org/10.1016/j.pscychresns.2022.111530).

- 6. Cognitive deficits in Parkinson's, (doi.org/10.1016/j.jocn.2018.08.016); Alzheimer's (DOI: 10.4103/0028-3886.349604); Schizophrenia (doi.org/10.1111/appy.12333) and acute and chronic anxiety/stress and depression scores in health, neurodegenerative and psychiatric disorders as biomarkers have been evaluated (doi:10.4103/aian.AIAN_341_18).
- 7. The practice of meditation for a period of one month improved IQ and cognitive functions; reduced baseline stress and reactivity to a stressor, suggesting that the practice of meditation may benefit subjects in reversing the effects of stress (PMID: 23251943).

Research done (from 1994-2010)

- Neurophysiology of Self-Aggressive Behaviour
- Neurophysiology of Sleep-Wakefulness
- Endogenous Analgesic Mechanisms in Brain
- Yoga in Health and Disease

Honors and awards

- 1. Best Research paper Published in Physiology instituted in the name of Dr B K Anand, in APPICON 2022 entitled "State-dependent perception and perceptual reversals during intermittent T binocular rivalry: An electrical neuroimaging study"
- 2. AIIMS Excellence Research Award 2017, Certificate for Commendation awarded to Dr Ratna Sharma in recognition of her outstanding publication under the category: Basic Research titled "Functional brain microstate predicts the outcome in a visuospatial working memory task".
- 3. The Dev Raj Bajaj Research Prize for the year 2017 was awarded to Dr. Siju George Chacko, PhD Student, Stress and cognitive electroimaging lab, Dept. of Physiology, AIIMS, New Delhi by Association of Physiology and Pharmacology of India in 2017, for the best paper on the development of newer techniques/instrumentation in Physiology entitled "Surface Laplacian of spherical spline improves the classification accuracy for mu rhythm based Brain Computer Interface"
- 4. Oral presentation (Medical Sciences category) won 2nd Cash prize Rs.15000/- at (NBRCom-2019) Dr Sunaina Soni, PhD student, Stress and cognitive electroimaging lab, entitled: "Altered parahippocampal gyrus activation and its connectivity with resting-state network areas in Schizophrenia: A QEEG Study" in the 2nd National Biomedical Research Competition (NBRCom-2019) 17th November, 2019 PGIMER, Chandigarh
- First prize in oral presentation. Rupesh Samanchi PhD student, Stress and cognitive electroimaging lab, entitled. "Pre-stimulus alpha power in verbal visual Sternberg task: An EEG based state marker of primary angle closure glaucoma". FIPS congress 2019. 29th September 2019. ESIC Faridabad

- 1st Prize for poster presentation in the 1st National Biomedical Research Competition held in AIIMS, Rishikesh, Oct 2018.
 Samanchi R, Muthukrishnan SP, Dada T, Sihota R, Kaur S, Tayade P, Sharma R; Paper titled "Lower Gamma Band Power generation in Limbic Cortex and Medial Temporal Lobe: A potential EEG Biomarker for Neurodegeneration in Glaucoma"
- 1st Prize for poster presentation in Physiology Update 2018 held in MAMC, New Delhi,
 Samanchi R, Muthukrishnan SP, Soni S, Dada T, Sihota R, Kaur S, Tayade P, Sharma

R; Paper titled 'Cortical Degeneration in Glaucoma as Reflected by Lower Frontal Activity of Resting EEG Microstates"

8. Suttee Nag Award in the Indian Neuroscience Academy, 2018, Batabyal T., Muthukrishnan S. P, Sharma, R, Tayade, P, Kaur S; Paper titled "Cortical diaspora of processing face and words as distractors during emotional interference: A quantitative EEG study"

Publications

Full length publications: 57 Abstracts: 118

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Details of Research experience

Research Projects as Chief Investigator: -

- 1. Microstate signatures and resting EEG sources of meditation and stress, Department of Science and Technology, Government of India, Funding sanctioned for 2020-2023; 53 lakhs
- 2. EEG microstates that favor perceptual reversal of emotional stimuli compared to perceptual stability in schizophrenia during binocular rivalry, STS project, India council for medical research, Government of India, 2020
- 3. QEEG correlates of Default Mode Network activity and its correlation with cognitive deficits in Multiple System Atrophy-Parkinsonian type and Multiple system Atrophy -Cerebellar Ataxia type" India council for medical research, Government of India, RA, 2019-2022
- 4. EEG microstate and phase coherence correlates of cognitive deficits in Parkinson's disease, India council for medical research, Government of India, SRF, 2016-2019
- 5. A study of EEG microstates and source connectivity as state and trait markers in schizophrenia with depression, India council for medical research, Government of India, RA, 2019-2022
- 6. Blood heavy metal levels and quantitative EEG correlates in children with autism, 2014-2019: India council for medical research, Government of India, in collaboration with Pediatric Neurology
- 7. Quantitative EEG correlates of Cognitive deficits in Parkinson Disease, Department of Biotechnology, Government of India, 2011-2014, Rs 22 lakhs
- 8. A study of quantitative EEG changes, cognitive function and stress in mild cognitive impairment and Alzheimer's disease, Department of Science and Technology, Government of India, 2010-2013, Rs 82 lakhs

- 9. Cognition induced changes in brain oscillations, Institute Research Grant, 2009-2010, Rs 2 lakhs
- 10. A study on stress reactivity of students as a function of their general and emotional intelligence and effect of meditation on the stress response, Institute Research Grant, 2007-2009, Rs 1.4 lakhs
- 11. A study to assess acute mental stress induced changes in EEG, cognitive behavior and neurosteroids across the menstrual cycle and effect of meditation on stress induced changes, CCRYN, Ministry of Health, Government of India, 2006-2009, Rs 15 lakhs
- 12. The effect of stress induced changes in theta and alpha bands during memory retrieval. Institute Research Grant, 2005-2007, Rs 1.4 lakhs
- 13. A randomized controlled trial on the efficacy of yogic intervention in premenstrual syndrome, India council for medical research, Government of India, 2003-2006, Rs 16 lakhs
- 14. Effect of prenatal auditory overstimulation with species-specific music sounds on postnatal learning in domestic chicks, Institute Research Grant, 2003-2005, Rs 80,000
- 15. Effect of meditation on Stress induced changes in cognitive functions. Institute Research Grant, 2002-2003 Rs 30,000
- 16. Pain mechanisms in autotomy: deafferentation vs pharmacological model. Institute Research Grant, 2000-200, Rs 25,000
- 17. Pain mechanisms in autotomy, Institute Research Grant, 1998-1999, Rs 25,000

As co-investigator:

- 1. Cortical sources of cognitive dissonance: A QEEG study. Institute Research Grant, 2014-2015
- 2. Emotion dependent modulation of interference: A QEEG study: Institute Research Grant, 2015-2016
- 3. Study of EEG microstates and resting state networks in relaxed wakefulness, Institute Research Grant, 2016-2018
- 4. QEEG based neural correlates of perceptual dominance, Institute Research Grant, 2016-2018
- 5. Correlation of cortical sources and brain iron during rest and visuospatial working memory in Attention deficit hyperactive disorder, Department of Health research, Government of India, (2017-2020)
- 6. QEEG based neural correlates and microstates of attention and interference in ADHD: An endophenotypic marker: Department of Science & Technology, Government of India, (2017-2020)
- 7. EEG microstates as a biomarker in addictive disorder, Institute Research Grant, 2019-2021
- 8. Cortical sources of working memory in opioid addicted patients: A Quantitative EEG study: STS project, India council for medical research, Government of India, (2019)
- 9. Study of EEG Microstates in OM chanting, Institute Research Grant, 2019-2020

PhD/ MD/ MSc/ DM work being conducted/ completed as chief guide: Phd Thesis

1. A Study of Quantitative EEG Changes, Cognitive Function and Stress in Mild Cognitive Impairment and Alzheimer's Disease.

- 2. Cognitive Control of Saccadic Eye Movements in Normal Subjects and Parkinson's Disease: A Behavioral, Event Related Potentials and Functional Magnetic Resonance Imaging Study.
- 3. Evaluation of reflexology as an adjunctive therapy in children with refractory Childhood Epilepsy including West Syndrome.
- 4. Quantitative EEG Correlates of Cognitive Deficits in Mild Cognitive Impairment and Alzheimer's Disease.
- 5. QEEG Correlates of Cognitive Deficits in Parkinson's disease.
- 6. Quantitative EEG Correlates of Emotion Induced Changes in Cognitive Performance in Healthy Volunteers.
- 7. Brain Computer based on EEG Data of Motor Imagery.
- 8. Neural Processing of Congruency and Affective Valence During Binocular Rivalry: A QEEG Study.
- 9. Neural Processing of Cognition in Glaucoma: A Quantitative EEG Study.
- 10. A study of Cortical Connectivity and EEG Sources in Autism Spectrum Disorder.
- 11. Microstates and Cortical Sources as QEEG Tool to Quantify and Classify Normal, Meditative, stressed and Psychiatric brain States.
- 12. Neural correlates of local sleep and its association with cognition: A QEEG study.

MD Thesis

- 1. Effect Of Meditation on Stress Induced changes in Cognitive Functions.
- 2. A Study to Assess the Effect of Meditation on General and Emotional Intelligence, their EEG Correlates and Stress Response.
- 3. Effect Of Working Memory Load on Visuospatial Task Performance as Assessed by Quantitative EEG.
- 4. Quantitative EEG Correlates of Perceptual Reversal of Emotional Stimuli During Binocular Rivalry.
- 5. Quantitative EEG Correlates of the Effect of Music on Cognitive Interference.
- 6. EEG Microstates of Perceptual Reversals of Emotional Stimuli in Schizophrenia During Binocular Rivalry.
- 7. EEG Microstates in Major Depressive Disorder.
- 8. Default Mode Network of Addictive Disorders: A QEEG study
- 9. Quantitative EEG Microstates and Cortical Sources of Changing Visuo-Spatial Working Memory Load in Patients with Schizophrenia.
- Impact of Transcendental Meditation (TM) on Acute and Chronic stress among surgeons in training: An open labeled randomized controlled trial (as co-guide) MSc
 - 1. EEG Microstates of Perceptual Reversals of Emotional Stimuli in Schizophrenia During Binocular Rivalry.

D.M. Thesis (as co-guide)

- 1. QEEG characteristics in 6–18-year-old ADHD and typically developing children and adolescents.
- 2. Analysis of predictors of response to hormonal therapy in children with treatment naïve West syndrome with QEEG, Serum biomarkers, fMRI and DTI: An observational study.
- 3. Development of visual cue induced craving paradigm alcohol dependence and study of its QEEG correlates

Dr Ratna Sharma Full length paper published in last 10 years Corresponding author in BOLD

 Sunaina Soni, Suriya Prakash Muthukrishnan, Mamta Sood, Simran Kaur, **Ratna Sharma**, Spectral perturbations of cortical dipoles during a dynamic visuo-spatial working memory task in schizophrenia, Psychiatry Research: Neuroimaging, 2022; 111530, ISSN 0925-4927,

https://doi.org/10.1016/j.pscychresns.2022.111530.

- Gurja JP, Muthukrishnan SP, Tripathi M, Mehta N, Sharma R. Multidomain Cognitive Testing: a Biomarker for Classifying the Cognitive Status of Mild Cognitive Impairment and Alzheimer's Disease. Neurol India 2022;70:1052-8. DOI: 10.4103/0028-3886.349604
- 3. Gurja JPK, Muthukrishnan SP, Tripathi M, **Sharma R**. Reduced Resting State Cortical Alpha Connectivity Reflects Distinct Functional Brain Dysconnectivity in Alzheimer's Disease and Mild Cognitive Impairment. Brain connectivity, 2022; 12(2). https://doi.org/10.1089/brain.2020.0926
- 4. Samanchi R, Muthukrishnan SP, Dada T, Sihota R, Kaur S, **Sharma** R. Altered spontaneous cortical activity in mild glaucoma: A quantitative EEG study. Neuroscience Letters, 2021; 759: 136036. https://doi.org/10.1016/j.neulet.
- Zacharia, A.A., Ahuja, N., Kaur, S., Sharma R Frontal activation as a key for deciphering context congruity and valence during visual perception: An electrical neuroimaging study, Brain and cognition, 2021; 150: 105711.
 - DOI: https://doi.org/10.1016/j.bandc.
- Gopal Chandra Janaa,*, Ratna Sharmab , Anupam Agrawala A 1D-CNN-Spectrogram Based Approach for Seizure Detection from EEG Signal from EEG Signal Procedia Computer Science 167 (2020) 403–412
- Anita Pal, Vinay Goyal, Madhuri Behari, Ratna Sharma. Study of EEG Microstates in Parkinson's disease: A potential biomarker? Cognitive Neurodynamics, 2021;15(3):463-471. DOI: 10.1007/s11571-020-09643-0
- Anita Pal, Nishi Pegwal, Madhuri Behari, Ratna Sharma. High delta and gamma EEG power in resting state characterise dementia in Parkinson's patients. Biomarkers in neuropsychiatrya. 2020; 3:100027.

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- 11. Zacharia, A.A., Ahuja, N., Kaur, S., Mehta N, **Sharma R**. Statedependent perception and perceptual reversals during intermittent T binocular rivalry: An electrical neuroimaging study, Neuroscience Letters 736 (2020) 135252, doi.org/10.1016/j.neulet.
- 12. Soni S, Muthukrishnan SP, Sood M, Kaur S, **Sharma R**. Altered parahippocampal gyrus activation and its connectivity with restingstate network areas in schizophrenia: An EEG study. Schizophr Res. 2020; 222:411-422.

doi: 10.1016/j.schres.2020.03.066.

- 13. Zacharia AA, Ahuja N, Kaur S, Mehta N, **Sharma R**. Does valence influence perceptual bias towards incongruence during binocular rivalry? Cogn Process. 2020 May;21(2):239-251. doi: 10.1007/s10339-020-00957-9.
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- Sunaina Soni, Suriya Prakash Muthukrishnan, Rupesh Samanchi, Mamta Sood, Simran Kaur, **Ratna Sharma** 'Pre-trial and pre-response EEG microstates in schizophrenia: An endophenotypic marker', *Behavioural Brain Research*, 2019; 371: 111964. doi.org/10.1016/j.bbr.
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- Chacko SG, P. Tayade, S. Kaur and R. Sharma, "Creation of a high resolution EEG based Brain Computer Interface for classifying motor imagery of daily life activities," 2019 7th International Winter Conference on Brain-Computer Interface (BCI), Gangwon, Korea (South), 2019; pp. 1-5. doi: 10.1109/IWW-BCI.2019.8737258
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- 23. Soni S, Muthukrishnan SP, Sood M, Kaur S, Sharma R. Hyperactivation of left inferior parietal lobule and left temporal gyri shortens resting EEG microstate in schizophrenia. *Schizophrenia Research*, 2018: 201, 204– 207.<u>https://doi.org/10.1016/j.schres.2018.06.020</u>
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- 29. Singh, Y., & **Sharma, R.** (2015). Individual Alpha Frequency (IAF) Based Quantitative EEG Correlates of Psychological Stress. *Indian Journal of Physiology and Pharmacology*, 59(4), 414–421.
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