Research Interests Stress and Cognitive Electroimaging lab, Department of Physiology, AIIMS, New Delhi. Prof Ratna Sharma Email: ratnaaiims@gmail.com

Research interests:

The Stress and Cognitive Electroimaging Lab aims at assessing the Physiological, psychological, biochemical and electrophysiological correlates of stress and cognitive functions in normal individuals and neurodegenerative & psychiatric disorders.

The key areas of research include:

- 1. Neurophysiology of Stress and Cognitive Behaviour
- 2. Quantitative EEG Changes as a tool to assess specific conditions: awake, sleep, cognitive functions, psychological stress, neurodegenerative and psychiatric disorders etc
- 3. Explore the neurophysiological correlates of qEEG
- 4. Effect of psychological stress on cognitive functions in health and disease

National Mental Health Survey reports that about one in 10 adults in India experiences a clinically significant mental health problem which has stimulated efforts towards providing mental health care and more so towards research for diagnosis of the mental disorders. It is logical that the underlying neurophysiological impairments in mental disorders should be detected well before the severe clinical symptoms appear. It is therefore pertinent to develop tools for functional assessment of healthy brain development and behavioral states that are the key for understanding abnormality in psychiatric and neurodegenerative disorders. The need to identify reliable functional markers includes studying the electrical activity of the functional brain networks in terms of neuronal activity in time and space that forms the basis of brain function. This understanding is of obvious significance for developing tools for diagnosis as well as prognosis of various mental disorders. Electroencephalography (EEG) is emerging as a powerful functional imaging tool to study the electrophysiology of brain non-invasively with high temporal as well as spatial resolution. Its superiority to fMRI or PET is being reported in literature.

With funding from Department of Science and Technology, Government of India, Stress and Cognitive Electroimaging Lab was established by Prof Ratna Sharma in the Department of Physiology at AIIMS in 2011. In the last 6-7 years we have attempted to make substantial contributions towards understanding the neural underpinnings of various cognitive domains, in healthy individuals as well as in neuropsychiatric and neurodegenerative disorders. Quantitative EEG data of more than 380 healthy adults, 65 children, 55 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 group has been collected and analyzed during baseline and during testing of varied cognitive domains. These domains range from perception, memory (verbal and picture), working memory, interference, attention (both auditory and visual) to emotions. This has enabled us to standardize the age related cognitive changes in either gender across cognitive domains. Fundamental phenomena like changes due to stress, meditation, language, audio-visual integration, motor imagery and binocular rivalry have also been targeted as core areas for research. So far, the

neural correlates in terms of networks activated, their neural sources and coherent activation compared to baseline conditions has been achieved 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, connectivity measures, causality measures and graph theory 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. One of the notable contributions of the lab in understanding mental disorder is the identification of brain sources at left inferior parietal lobule and left temporal gyri for the microstate Schizophrenia shortened resting EEG in (https://doi.org/10.1016/j.schres.2018.06.020). EEG microstates are the momentary spatial configuration of brain electric field at the scalp that reflect quasi-stable "functional microstates" caused by activity of different intracranial generators. Lab has also identified an EEG microstate in healthy individuals that predicts the outcome in a visuospatial working memory task in young adult subjects with increasing memory load (http://dx.doi.org/10.1016/j.bbr.2016.08.020). We are in the process of publishing an important EEG biomarker based on brain source connectivity measures that has shown good sensitivity and specificity in distinguishing the Alzheimer's disease, mild cognitive impairment and healthy aged controls. We are currently exploring graph theory to study the dynamics of brain networks by measuring the clustering coefficient, characteristic path length and small world coefficient. These graph theory measures would help us in identifying brain regions that function as hubs and nodes of the brain networks in health and disease states. Many complex real-world phenomena including EEG signals are characterized by nonlinear dynamics and the chaos theory. Therefore, we have plans to incorporate the non-linear dynamical measures of complexity and stability to quantify critical aspects of brain dynamics.

QEEG data of patients has been collected and analyzed using these analysis strategies. The Lab has collaboration with Department of Neurology, Psychiatry, Deaddiction Centre, Paediatric Neurology and Ophthalmology of AIIMS, New Delhi.

With the aid of superlative data analysis software, the importance of EEG/MEG lies in picking up of neural changes in a time resolution of few milliseconds as compared to fMRI. Thus, EEG/MEG will indeed be an invaluable tool for novel perspectives to understand the dynamicity of cognitive processes in healthy as well as patient population and to generate algorithms for diagnosis of psychiatric and neurodegenerative diseases.

We aim to develop 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, ADHD, Autism, Depression wherein there is no objective gold standard for diagnosis, which often leads to over/under diagnosis.

The research group includes One Professor (Prof Ratna Sharma) three Assistant Professors (Dr Simran Kaur, Dr Prashant Tayade, Dr Suriya Prakash), ten PhD, five MD, four MSc students and

one ICMR RA. 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) and other research grants from various funding agencies (DST, DBT, DHR, Ayush, AIIMS).

We aim to accelerate our research in both fundamental and clinical neurosciences. In addition to above aim, we plan to provide EEG as a preoperative tool for neurosurgery in order to map and localize the areas of important functions like language, movement, vision etc. in order to protect these functions during tumor resection.

Finally, could this research be the underlying basis for possibly augmenting mental capabilities of a healthy subject in the event of higher work load or stress or restoring mental and physical capabilities in disease. To make these possibilities a reality, we are working towards using EEG to direct computers/ machines. A study is being conducted to create a brain computer interface based on EEG data of motor imagery using machine learning algorithm and mu rhythm based feedback training for rehabilitation purposes.

The laboratory has the Dense Array (128 electrodes) EEG and Polygraph recording system through which quantitative analysis of EEG, ECG, EMG and various bio-signals are done. Some of the key quantitative analysis carried out in the laboratory includes:

- Quantitative EEG analysis:
 - Source Localization
 - sLORETA based source localization of the neural correlates of cognitive behavior with milliseconds temporal resolution in the health and diseased states.
 - Source data computed from the Dense Array EEG is reconstructed over the Montreal Neurological Institute (MNI) MRI pane to view as 2D and 3D whole brain mapping.
 - Source montages are created for analysis by selecting particular group of source electric dipoles depending on the brain regions of interest for the cognitive task.
 - Wavelet transformation based Joint Time-Frequency Analysis (JTFA) Temporal and frequency bands are analyzed simultaneously in the EEG signals.
 - Wavelet co-efficient computes phase and magnitude of correspondence of frequency bands in relation with time, which facilitates analysis of the frequency band changes in the EEG signals with milliseconds temporal resolution.
 - Circular variance computes phase stability of the frequencies across trials and between various brain states. High phase stability means higher correlation between brain regions.
 - Fast-Fourier Transformation (FFT) based frequency spectral analysis
 - Power spectral analysis Frequency band changes in resting state and while performing cognitive task are analyzed in health and diseased state.

- Coherence analysis Frequency band coherence between brain regions are analyzed which signifies communication between brain regions.
- Connectivity measures, causality measures and graph theory measures
- Quantitative ECG, EMG and GSR are recorded simultaneously with EEG recording to assess the effect of psychological stress on cognitive functions in health and disease.
- Along with quantitative bio-signal analysis, behavioral parameters are also assessed. The laboratory has the E-PRIME platform based stimulus presentation system in which cognitive function test are created and administered to the subjects, from which various behavioral cognitive parameters like reaction time and decision making are assessed.

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