**UGP-1 (BSE398A)**

# TITLE- STRESS AND EEG

## MIDTERM REPORT

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INDEX

| **Sr. No.** | **Title** | **Pg. No.** |
| --- | --- | --- |
| 1 | Introduction | 2 |
| 2 | Read Which Motivated the Topic | 2 |
| 3 | Time-Dependent Shifts in Neural Systems Supporting Decision-Making Under Stress | 3 |
| 4 | What is EEG and how does it work? | 4 |
| 5 | Origin of extracellular Fields- EEG, ECoG, LFP, and spikes | 5 |
| 6 | Cortisol and DHEA in development and psychopathology | 6 |
| 7 | Review of approaches to integrate EEG and behavior | 8 |

# Introduction

Hi, I am Shashank Katiyar and this is my mid-term report on my UGP-1. So, till now, I have read from 6 papers/sources about the topic, apart from watching a few youtube videos and reading short articles on basic background information on EEG and Stress Neuroscience. Below, I have written a short summary of every read of mine so far. I have also added the link to the original work below every heading. Thanks!

# Read Which Motivated the Topic

Title- **Protective and damaging effects of stress mediators: central role of the brain**

Link-<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3181832/pdf/DialoguesClinNeurosci-8-367.pdf>

Firstly, allostatic load and allostasis were discussed. How allostasis is necessary and how its overload over time causes various problems in the body, due to the interlinked action of various body systems in allostasis.

They told about the 4 types of faulty allostatic responses- repetitive, unadaptive, delayed inhibition, and no response. The various systems of the body are highly linked in reacting to stressful situations.

Then they talked about the role of good quality and quantity of sleep in preventing stress. This involved many experiments with rodents in which they were not allowed to sleep for different durations by disturbing them.

All the studies indicated the reduced ability of the brain when the organisms were not allowed to sleep for more than 6 hours.

Then, the physical effects of stress on the brain were discussed. Macroscopically, in most of the experiments, the hippocampus reduced in size under stress, and the amygdala increased. Microscopically, neurons in the amygdala were lengthened and in the hippocampus, their growth was checked under stress. Many molecular mechanisms due to which this was happening were also discussed.

The prefrontal cortex also showed similar changes under stress, like the hippocampus.

In the human brain, the effects of stress have been studied mainly with the help of analysis of patients with diseases associated with stress. The changes of the above-mentioned organs under stress were almost the same as in model organisms.

Then, the role of positive outlook of life, social connections, and self-esteem was discussed regarding stress. These are important indicators of a person’s vulnerability to stress.

In conclusion, many factors which are apparently simple but difficult to execute can result in a win-win situation for all by reducing the occurrence of stress in the world. For example- companies that focus on their employees’ work-life balance can expect less money spent on health insurance and also better loyalty from their employees. The employees will get a better-balanced life.

# Time-Dependent Shifts in Neural Systems Supporting Decision-Making Under Stress

Chapter 30 from the book- **Decision Neuroscience- An integrative perspective**

This paper dealt with neurocognitive systems, which are sets of parts of the brain, which have a similar function and act together. It talked of SN (Salience Network) and ECN (Executive Control Network).

The Salience Network is the network responsible for reflex and habitual activities, and regulation of various systems. It is the system, which requires less manual attention, but is faster. It consists of the amygdala, thalamus, hypothalamus, midbrain, etc.

The Executive Control Network is the network responsible for higher cognitive tasks, memory functions, and attention. It is the system, responsible for cautious, manual decisions, and is functionally slow. It consists of the dorsolateral and dorsomedial prefrontal cortex, frontal eye fields, etc.

The human brain, it has been observed, doesn’t consume a lot of extra energy, even in demanding/stressful situations. An explanation for this is that even in resting state, it consumes a lot of energy (20%) considering its weight (2%), so a further increase in that would lead to less energy for the remaining systems, so it needs to find other ways to distribute energy effectively.

A possible way is to reallocate energy from one neurocognitive system to the other according to the situation (Stress would cause reallocation from ECN to SN). The stress-sensitive neuromodulatory systems (catecholamines and corticosteroids) may be responsible for this reallocation of energy.

Upon action of the stressor, catecholaminergic responses are the first ones to act. Salience Network takes control at this stage. They are followed by non-genomic corticosteroid effects. ECN begins coming up with SN at this stage. Then, the genomic corticosteroid effects follow, which last till late after the stressor has been overcome. Now, again ECN control has taken over.

In conclusion, the chapter tries to simplify response to stress by dividing the activity of the brain into two broad neurocognitive systems and explaining response through energy reallocation between them. However, the real image is way more complex and will be found out hopefully in the future.

# What is EEG and how Does it work?

Link- <https://imotions.com/blog/what-is-eeg/>

So EEG is basically a measurement of the voltage generated by the electrical current flowing through the billions of neurons in the brain. It is done using small electrodes placed on the scalp of the head, at specific positions.

It is a really cheap and efficient method to measure brain activity with immense temporal precision. The data from the electrodes is amplified by an amplifier before reading, because of the weak magnitude of electric fields on the scalp.

Then we saw the various parts/lobes of the brain, responsible for certain activities. This knowledge is useful in placing the electrodes according to the experiment being conducted.

The Occipital Lobe is responsible for most of the visual processing in the brain. Thus, experiments involving visual cues focus on the electrodes placed near this area mainly.

The Parietal Lobe is responsible for combining all the information from external and internal sources and making sense out of it. It relates the body both spatially and contextually with the environment. It is the place that stores information for objects to be grasped and thus is useful for experiments involving catching objects, like the oddball task.

The Temporal Lobe is responsible for combining the input data with past associations and making useful conclusions out of it. It also contains areas required for language and speech. It is also associated with navigating tasks.

The Frontal Lobe is the region responsible for the ability of humans to make imaginary stories, the reason they have excelled way beyond all other species. It is a necessary part of cognitive processing.

Apart from this, the source also discussed the various frequency bands of EEG responsible for certain levels of awakeness. They include Delta (<4Hz), Theta (4-7Hz), Alpha (7-12Hz), Beta (12-30Hz), and Gamma (30-50Hz).

# Origin of extracellular Fields- EEG, ECoG, LFP, and spikes

Link- <https://www.nature.com/articles/nrn3241.pdf>

In this paper, we saw various methods of measuring the brain activity of different invasiveness. They were EEG, ECoG, LFP, MEG, and VSDI.

In EEG, the electrodes are placed on the scalp to measure the voltages due to electric fields in the brain neurons. In ECoG (Electrocorticogram), they are placed at the cerebral cortex, so that the barrier of the skull is avoided in the measurement. In LFP (Local Field Potential), the electrodes are inserted into the cortex, at the site, where measurement is to be taken. MEG (Magnetoencephalography) is basically the magnetic counterpart of EEG in which we measure the magnetic field due to electrical currents in the brain. VSDI (Voltage Sensitive Dye Imaging) involves expressing certain voltage-sensitive dyes into the cell and shining light on them to observe their color and estimate the voltage difference indicated by them.

We also looked at the various sources which contribute to the voltage reading observed in EEG, ECoG, and LFP. Synaptic currents are the most important contributors, as their influence is distributed over a comparatively longer time duration, so the activity of many synapses gets added up. Action potentials are deflections of the largest amplitude, but their short duration causes them to be rarely simultaneous and thus contribute lesser, but cannot be ignored. Other sources include NMDA receptor-triggered calcium spikes and Intrinsic currents due to HCN gated and T-type calcium channels. Gap Junction channels and neuron-glia interactions also contribute to the voltage readings.

Next, we discussed the role of the geometry of neurons in determining their contribution to voltage measurement. Pyramidal neurons have a shape such that the site of current input to the neuron is quite distant from the site of current output from the neuron. This causes a large dipole moment of it, resulting in more contribution to the voltage readings. The folds (gyri and sulci) in the brains of mammals also play an important role in influencing the readings and need to be modeled carefully.

Temporal properties are also an equally important contributor to how neuronal activity influences voltage reading. When multiple neurons fire simultaneously, they cause a much larger deflection, than firing at different instances. The power law dictates that the contribution of a given frequency to the voltage (power) is inversely proportional to the frequency value.

Then we discussed the inverse problem of LFP, which basically means that given the voltage reading, we have to find the neurons and everything about them (their location, orientation, time of firing connections, etc.) which caused such a reading. The inverse problem is difficult because there are too many unknowns and fewer knowns. It is usually solved by first solving the forward problem (neurons to voltage), and then establishing the relations between the two, and using them to solve the inverse problem. Finding sinks and sources (sites of origination and disposal of current) is an important step of the inverse problem and CSD (Current Source Density) is useful in it.

CSD employs the fact that if a dipole (source-sink pair) is far away from multiple voltage recording sites, then all the sites will have similar readings, but if the source is near, then their readings will be much more dissimilar. This way, an estimate can be made of the locations of dipoles.

Overall, EEG, ECoG, and LFP are methods of measuring brain activity in order of increasing invasiveness and spatial accuracy. EEG is the safest and cheapest of all, and thus, it becomes important to also improve its spatial accuracy, to pin down the source of activity accurately. For that, source localization is necessary. Improving EEG technology with time, with more number electrodes, with better sensitivity is paving the way forward for it.

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# Cortisol and DHEA in development and psychopathology

Link- <https://www.sciencedirect.com/science/article/pii/S0018506X1630215X>

In this paper, the main focus was to discuss the role of cortisol in combination/association with DHEA (dehydroepiandrosterone). Before this paper, there was quite less attention given to DHEA in researches compared to cortisol, even though both have equally important roles in regulating stress.

We first saw where and how both these molecules are produced. Upon activation of the HPA (Hypothalamus Pituitary Adrenal) axis, the neurons of the hypothalamus release CRH (Corticotropin-Releasing Hormone), which goes to the pituitary gland, to release ACTH (Adrenocorticotropic Hormone). ACTH travels to the adrenal gland through the bloodstream, where it triggers a chemical reaction pathway, to yield Cortisol and DHEA as products.

DHEA exists in both, its sulphated (DHEA-S) and non-sulphated forms in the body. Both together are referred to as DHEA(S) in the paper. DHEA-S has a longer half-life, and thus the majority of DHEA in the body is DHEA-S.

Then, we saw how these molecules function in the body. Cortisol when released acts on two molecules, MR (Mineralocorticoid Receptors) and GR (Glucocorticoid Receptor). MR is more sensitive to cortisol than GR. Thus, initially, when cortisol is released, MR gets activated, and GR shows its function only at high concentrations of cortisol. MR and GR are normally in the cytosol of the cell. Upon action of cortisol, these molecules are able to enter into the nucleus and influence the transcription machinery, by acting as transcription factors and binding to enhancers of specific genes. When cortisol levels rise, negative feedback loops are initiated by the action of cortisol on GRs in the hypothalamus and pituitary regions, which then stop making cortisol precursors.

Effects of DHEA(S) through genetic action haven’t been found yet. It has mainly been observed to show its effect by acting on membrane receptors and altering the biophysical properties of plasma.

The harmful effects of long-term exposure to cortisol on the immune, cognitive and metabolic machineries are well established. In many studies, DHEA(S) has been found to counter the harmful effects of cortisol on the various aspects of health. Thus, they have tried to talk in terms of cortisol/DHEA(S) ratio in the paper, as they have opposing functions.

It has been observed that short-term stress causes higher levels of cortisol in individuals, but long-term stress doesn’t. To explain this, it is theorized that early stress causes increased production of cortisol, but long-term activation of the HPA axis causes the adrenal gland to become difficult to stimulate by ACTH. Similar behavior of the adrenal gland is with respect to DHEA. The cortisol/DHEA ratio to some extent determines their resultant effect on the body.

Then we saw how the levels of these molecules change with a person’s age. After birth, both cortisol and DHEA(S) are increasingly produced, but during the second half of the first year of birth, DHEA(S) production reduces. Cortisol levels are quite stable throughout early childhood up to adolescence normally. DHEA(S) levels go up again at adrenarche. Though cortisol levels remain mostly stable throughout childhood, response to cortisol varies. It is low before adrenarche but increases thereafter.

Then we saw how the levels of these molecules are different from normal in various psychopathology. Internalizing disorders are associated with a higher cortisol/DHEA(S) ratio than normal while externalizing disorders are associated with a lower ratio than normal.

Overall, there is quite a low number of researches that deal with DHEA(S), even though this molecule seems to be equally important as cortisol, and can even be helpful in curing stress-related problems because of its counteracting role to cortisol.

# Review of approaches to integrate EEG and behavior

Link- <https://pubmed.ncbi.nlm.nih.gov/29632480/>

First, we saw some basic methods of filtering/enhancing the raw EEG data. These methods include frequency-wise sorting EEG, blind source separation, and deep learning.

Frequency-wise sorting of the EEG signal is an easy initial processing step that allows observing the frequencies associated with a specific type of action and may give useful insights to help further analysis.

Blind Source Separation refers to the removal of noise from the EEG signal, which is due to non-neural body functions in the neural frequency range. Eye movements and stimulations usually have this property, thus this method is named so. Examples include- data-driven methods like ICA (Independent Component Analysis) and PCA (Principal Component Analysis).

Deep Learning methods have the ability to make non-linear relations between input and output to observe patterns with great capability. CNN (Convolutional Neural Networks) and RNN (Recurrent Neural Networks) are two examples. These involve multiple hidden layers, which are responsible for making the relations.

Then we saw some methods of finding out latent variables from the behavior data, which help us connect it with EEG better (basically filtering/enhancing of behavioral data). For this, we saw two approaches- DDM (Drift Diffusion Modelling) and RL (Reinforcement Learning)

DDM is basically modeling the drift rate (information gathering rate), decision threshold, and non-decision time. RL involves calculating the way the individual’s decision changes with time, as he receives more information, and recalculates the weightage of the options he is given. After modeling, model fitting is done to find out the relevant latent variables.

After this, various approaches to finally correlate the simplified EEG and behavioral data were discussed. These include Single Trial Regression- which involved level 1 (within-subject trials) and level 2 (between-subject trials) analysis, Similarity Analysis- which involved comparing different types of data of same trial (involved use of Representational Dissimilarity Matrix, and visualization of multi-dimensional data using t-SNE) and Partial Least Squares- which is used to counter the problem of multicollinearity in regression.

In the end, we saw that HBM (Hierarchical Bayesian Modelling) is the best method currently available to draw correlation between EEG and behavior. As the name suggests, it involves computing reverse probability (Bayes’ Theorem), and uses Hierarchical method, to weigh variables correctly, rather than equally.