‘AN ANALYSIS OF SERUM CALCINEURIN ACTIVITY IN DRUG NAÏVE SCHIZOPHRENIA PATIENTS’

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ABSTRACT
Calcineurin is a Ca-calmodulin dependent protein phosphatase, which plays as connecting link between dopaminergic and glutamatargic neurotransmitter systems and their dysregulation in schizophrenia. The main objective of this study was to examine the potential role of calcineurin in schizophrenia. Calcineurin levels were estimated in 15 schizophrenia patients in the age group of 18-45 who were attending outpatient department of psychiatry, Dharwad institute of mental health and Neurosciences, Dharwad in Karnataka, India. The results of the present study showed significant (P<0.001) decreased activity of serum calcineurin in schizophrenia patients compared to those of normal subjects. The observations thus suggest impaired calcineurin activity in schizophrenia patients.

KEYWORDS:
Schizophrenia, calcineurin, drug naïve, PANSS score, calmodulin

INTRODUCTION
Schizophrenia is a complex neuropsychiatric disorder which characterized by an array of spectrum of symptoms, which includes delusions, hallucinations, disorganized speech or behavior and impaired cognitive ability. This disease occurs at an early age and becomes chronic and devastates the life style of the affected person and becomes disabling disorder for many patients and their families. The prevalence of schizophrenia is 4.3 to 8.7 million people in India and 2.2 million in USA and 6 to 12 million in china. Males tend to experience their first episode of schizophrenia in their late 20’s or early 30’s. While in women the mean age of onset of schizophrenia is 25-35. However the women seem to have two peaks in the age of onset of disease the first after menarche and the second once they are over 40. Recent hypothesis of schizophrenia pathophysiology model describes the role of protein phosphatases in schizophrenia which regulate the cellular processes by dephosphorylating the proteins particularly the calcineurin the protein phosphatase 2B which is a key regulatory molecule involves in numerous signaling pathways by removing phosphate groups that have been added to proteins by various kinases and involves in turning on and off the cellular processes and there by controls the cellular processes. Particularly in neurons, calcineurin regulates phosphorylations elicited by both glutamatergic and dopaminergic signaling making it particularly interesting molecule in schizophrenia since it acts as a connecting link between the dopaminergic and glutamatergic neurotransmitter systems which are dysfunctional in schizophrenia. An attempt is made to investigate the serum calcineurin in Schizophrenia patients and evaluate the potentiality of calcineurin as biomarker for the schizophrenia.
Socio demographic details:

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Male</th>
<th>Female</th>
<th>Age (Male)</th>
<th>Positive symptoms</th>
<th>Negative symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>8</td>
<td>7</td>
<td>30.21±6.07</td>
<td>28.43±9.86</td>
<td>17.8±8.37</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(male)</td>
<td>(male)</td>
</tr>
<tr>
<td>15</td>
<td>18</td>
<td>5</td>
<td>15.18±5.27</td>
<td>15.18±5.27</td>
<td>26.68±6.87</td>
</tr>
</tbody>
</table>

| No. of controls | 15 | 08 | 07 | 25±7.08 | 30±8.75 | 6 |

Discussion:
Calcineurin is a calcium and calmodulin dependent serine/threonine protein phosphatase and is also known as phosphatase 2B which involves in various cellular processes. It is also involved in cognition and working memory. Dysregulation of calcineurin leads to impairment in working memory, attention deficit, aberrant social behavior and several other abnormalities which are the characteristics of schizophrenia. Calcineurin directs the control of the cAMP response element binding protein (CREB) which plays an important role in the cognition and memory. It regulates Growth associated protein 43 (GAP43) dephosphorylation which is involved in neuronal plasticity and memory. Genetic association studies of several population showed that genetic variation in PP3CC gene encoding for a gamma unit of catalytic subunit of calcineurin leads to Schizophrenia. In calcineurin Knockout mice model, Calcineurin deficiency impairs the ability of neurons in Prefrontal cortex (PFC) to efficiently mobilize and recycle synaptic vesicles during high-frequency activity, leading to a disruption of high-frequency neuronal and network activities in PFC that are required for working memory leads to impairment in working memory of Schizophrenia. In our study the serum calcineurin activity has been measured, as per our knowledge this is the first report which is based on the peripheral, blood based estimation of calcineurin in schizophrenia since the calcineurin has been estimated in the other pathological conditions such as diabetes mellitus, mental retardation, Down’s syndrome, leukemia, ischemia, and found to be significantly decreased in all pathological conditions, we have excluded the co-morbid psychiatric, and other diseased conditions to avoid the factors which might responsible for the decrease in the calcineurin activity and reflects the activity of calcineurin in Schizophrenia disorder condt ions.

Conclusion:
These findings provide further evidence for the systemic nature of schizophrenia and give added validity to the concept that calcineurin in peripheral system also varied in schizophrenia and this can be used to develop blood based biomarker for the schizophrenia.

Acknowledgement:
The author Nivedita Shireshi acknowledges the financial assistance provided by UGC in the form of RGFNF fellowship to her and also acknowledges the contributions of Dr. Raghavendra B. Nayak of Dharwad Institute of Mental Health and Neurosciences (DIMHANS) for providing the blood samples of Schizophrenia patients. The author sincerely thanks all the volunteers who participated in this study.

References: