Brain-heart Connections in Spinocerebellar Ataxia: Role of Central Autonomic Network

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1. Aobstact

More than a century ago, C. Bernard stated the connection between the brain and the heart. Here, we have emphasized on the central autonomic network (CAN) based on our previous pioneering work of structure-function connectivity in spinocerebellar ataxia (SCA) patients. In order to study the correlation, SCA was the suitable disease model as being neurodegenerative disorder with frequent autonomic manifestations. The prefrontal cortex, bilateral middle temporal, left cuneus, left lingual and left caudate were the key brain areas of CAN for top down regulation of autonomic function assessed as heart rate variability and severity scoring. We have evaluated CAN to know parasympathetic and sympathetic autonomic brain areas vis-a-vis parasympathetic and sympathetic autonomic function in SCA which may shed light on putative pathophysiology.

Central autonomic network (CAN) is the internal regulatory system which controls and coordinates the autonomic nervous system. Animal experimental studies have revealed the cortical and subcortical areas of CAN comprised of insular cortex, hypothalamus, amygdala, parabrachial complex, periaqueductal gray, nucleus of tractus solitarius and ventrolateral medulla [1-3].

Yet with the advancement of neuroimaging techniques, the studies intriguing CAN were performed in human [6]. By the task based activation method of autonomic control, a large number of studies have found the areas of brain in autonomic control [17]. Although the autonomic nervous system regulates a wide range of physiological aspects in our body like – cardiovascular, respiratory, endocrine and digestive [4], amongst all, heart rate variability (HRV) has been widely used as cardiovascular autonomic marker to know the state of heart and brain as well [5-7]. The neuroimaging studies were performed to identify the brain areas associated with HRV revealed that insula, prefrontal and cingulate cortices were activated during autonomic task and thus, related to HRV [5,6,8].
In our earlier pioneering work, we have assessed a correlation between the brain areas and autonomic function parameters in spinocerebellar ataxia (SCA) patients [7]. To study this association, SCA disease model was found to be suitable as SCA being a neurodegenerative disorder with autonomic dysfunction. Our neuroimaging study revealed the cortical brain atrophy in all the four lobes (frontal, parietal, occipital and temporal) along with the volumetric loss in subcortical brain areas in SCA [9]. On the other hand, literature suggested 60% dysautonomia in SCA patients [10-12]. We have also reported autonomic dysfunction in SCA patients [13,14]. We more intrigued to know about the structural atrophy goes hand in hand with the loss of functional attributes of autonomic regulation in SCA patients.

Thus, in one hand, we had volume brain areas achieved by whole brain scanning and in other hand, we had autonomic parameters performed by comprehensive autonomic function tests. In order to correlate the structure-function parameters, we have selected the autonomic parameters such as HRV, being the commonly used cardiovascular parameter. While choosing other autonomic biomarkers, baroreflex sensitivity (BRS) has been used as surrogate marker for short term blood pressure regulation [14]. Actually, baroreflex lowers the blood pressure fluctuations by regulating the heart rate and vascular tone [15]. The modulation is occurred by the baroreflex arc in medulla along with the inputs from higher cortical and subcortical brain areas of CAN [7,14]. Nevertheless, composite autonomic severity score (CASS) is a comprehensive method to quantify autonomic function [16].

The strength lied in that we had able to differentiate the parasympathetic and sympathetic autonomic brain areas based on the correlation of parasympathetic and sympathetic autonomic correlates in the patients of SCA [14]. Priorly, Beissner et al. described the brain areas involved in parasympathetic and sympathetic autonomic control in their meta-analytic review based on activation likelihood method [17].

This structure-function comprehensive correlation approach is on priority for the understanding on the pathophysiology of autonomic abnormalities in SCA patients.

### 2. Brain structures associated with components of autonomic correlates in SCA

All the brain areas associated with the components of autonomic correlates were important parts of the CAN (Table 1). The common brain area associations were as follows:

- Left cuneus which was usually correlated with HRV and systolic BRS may regulate parasympathetic component of BRS by regulating the response of heart rate in the SCA patients.
- Similarly, left lingual, the common area associated with HRV and systolic BPV was responsible for parasympathetic modulation while left caudate, a significant area of association was related to both parasympathetic and sympathetic autonomic control.
- The right lateral orbitofrontal cortex and bilateral medial orbitofrontal cortex, both were the part of prefrontal cortex, the area of sympathetic modulation. The prefrontal cortex was commonly connected between systolic BRS and systolic BPV.

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<tr>
<th>Brain areas</th>
<th>Autonomic correlates</th>
<th>Brain areas</th>
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<td>Parasympathetic brain areas</td>
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<td>Sympathetic brain areas</td>
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<td>Right lateral orbitofrontal cortex</td>
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<td>Left cuneus</td>
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<td>Right cuneus</td>
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<td>Bilateral medial orbitofrontal cortex</td>
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<td>Bilateral middle temporal</td>
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Table 1: Correlation of brain areas with autonomic function parameters in SCA patients.
Moreover, the prefrontal cortex (included bilateral caudal middle frontal, right lateral orbitofrontal cortex and bilateral medial orbitofrontal cortex) appeared as the connecting link between CASS and autonomic tone parameters in SCA reveals the associations of CAN and autonomic attributable [7].

3. Conclusion

The comprehensive assessment of autonomic dysfunction strongly appraised the top down regulation by the central autonomic network in SCA patients. Therefore, the holistic brain structure and autonomic function correlation study may provide the probable pathophysiological insight of dysautonomia in SCA patients.

4. Abbreviations

HRV- heart rate variability, BPV – blood pressure variability, BRS – baroreflex sensitivity, CASS – composite autonomic severity score

8. References