

A study of girls with PMLD in the special school: a possible involvement of estrogen-induced release of serotonin in the subfornical organ

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(Keywords: Profound and Multiple Learning Difficulties/Disabilities, serotonin, subfornical organ)

1. Introduction

Children with Profound and Multiple Learning Difficulties/Disabilities (PMLD) belong to special schools dealing with physical difficulties in Japan and almost of them have cerebral palsy. Typical symptoms are spasticity, epilepsy, mental retardation, learning disabilities and ataxia. Sometimes they have a strong behavioral disorder (Bellamy et al, 2010)⁽¹⁾. PMLD are defined as those who have extremely delayed intellectual and social functioning, may have limited ability to engage verbally, they require others to interpret their communication intent and frequently have associated medical conditions, which may include neurological problems, and physical or sensory impairments.

It was well known that many neurotransmitters and neuromodulators in the brain play vital functional roles in animals. Rapid changes in serotonin (5-HT) levels in the brain often induce some disorders (Takada & Curzuon, 1995)⁽²⁾. Indeed, a previous observation revealed, in the rat, that low 5-HT levels attenuate the effects of discrimination test.

Our current studies show that the subfornical organ (SFO), a circumventricular structure lacking a normal blood-brain barrier and is located above the third ventricular. SFO neurons contains both estrogen and angiotensin II (ANG II) , and that estrogens regulate the 5-HT release through the alteration of numbers of ANG II receptors and binding ANG II (Kisley, Sakai, Fluharty, 1999)⁽³⁾. Thus, it might be expected that the neurotransmitters/modulators release from the SFO may be influenced on the brain regions, resulting in a behavioral disorder.

In this study, we attempt to speculate that the 5-HT release from the SFO may participate in the cases of behavioral disorders of three PMLD girls who belong to a special school. Our speculation also may offer to explain the relationship between their behavioral disorders and changes in plasma 5-HT and/or estrogen.

2. Case Study

The human care and the experiments were performed according to the guiding principles of the Japan Neuroscience Society.

Girl A: 15 years old ; cerebral palsy, spasticity, epilepsy, mental retardation, learning disabilities, and ataxia ; weight, 105 lb; Tall, 5 ft and 2.2 inch. Eating, needing assistance, sometimes she eat food greedily with her fingers; Communication, no words. Teachers guess her feelings from her emotion. Bathing, needing assistance; Dressing, needing assistance; going to the toilet, needing assistance. She can stand assisted near by toilet bowl and sit assisted on toilet bowl. She has got her period, but not so regularly. Transferring, all by her wheelchair needing assistance, she cannot walk but she can sit with her knee up, and her foot on the floor. Continence, needing assistance.

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Suddenly, she screams and hits her chest or the side of her wheel chair. Teachers in the special school fix her a proneboard by the belt.

Girl B: 16 years old; cerebral palsy, spasticity, epilepsy, mental retardation, learning disabilities, and ataxia; weight, 110 lb; Tall, 5 ft and 2.99 inch. Eating, needing assistance, sometimes she holds the spoon; Communication, she can say only 'Yes'; Bathing, needing assistance; Dressing; needing assistance; going to the toilet, needing assistance. Diaper changing on the bed in toilet. She has got her period, but not so regularly; Transferring, all by her wheelchair needing assistance, she cannot walk but can sit by w-sitting; Continence, needing assistance. She has striking the head, self-injurious behavior. She is always wearing her headgear.

Girl C: 14 years old; periven-tricularleukomalacia, spasticity, epilepsy, mental retardation, learning disabilities, and ataxia; weight, 90 lb; Tall, 4 ft and 11 inch. Eating, needing assistance, sometimes she holds the spoon. She can eat by her hand; Communication, she can say words about her families, likely mam and dad; Bathing, needing assistance; Dressing, needing assistance; going to the toilet, needing assistance. She can stand assisted near by toilet bowl and sit assisted on toilet bowl. She has got her period, but not so regularly; Transferring, she can walk a little. Teachers assist her body; Continence, needing assistance. She has rocking and striking the head, self-injurious behavior. She is always wearing her headgear. Sometimes she kicks others and throws goods, then she goes into the special classroom. Teachers admonish her doing wrong behavior.

In all the cases, teachers in the special school respond to strong behavioral disorders using equipment or by admonishing the student.

3. Discussion

In three cases of PMLD children, it is necessary to care for the children, especially, when they cause strong behavioral disorders. It might be expected the possibility that explosive excitability of brain neurons may provoke the strong behavioral disorders. The disorders may be involved in the some neurotransmitters and neuromodulators. In this study, we focused on the participation of estrogen and 5-HT levels in the disorder.

Experimental observations revealed that several brain regions are innervated by 5-HT projections, and that 5-HT has various functional roles. The 5-HT release is regulated by complex mechanisms. For example, Fig.1 obtained from our previous data show a possible mechanism of 5-HT in the SFO is implicated in important for body fluid homeostasis and blood pressure control in response to circulating ANG II. In the SFO, decreases in the 5-HT release reduce the drinking and pressor responses to ANG II, while enhanced release of 5-HT causes thirst and pressor response. Although the price mechanism is known, SFO neurons sensitive to ANG II serve to inhibit the 5-HT in the SFO. SFO neurons contain both ANG II AT 1 and estrogen receptors, and the estrogen decreases ANG II binding to AT 1 receptors and number of SFO neurons that express AT 1 receptors (Kisley, Sakai, Fluharty, 1999)⁽³⁾.

Thus, high estrogen level (ovariectomized (OVX) female rats are treated with estrogen benzoate) elicits the elevated release of 5-HT. Low estrogen level (OVX female rats treated with propylene glycol), on the other hand, causes the reduced 5-HT release in the SFO (Tanaka et al. 2003)⁽⁴⁾. Taken together, estrogen may modulate the release of 5-HT through SFO neurons having both ANG II and estrogen receptors (Fig.1).

From the three cases, the role of estrogen that modulate the release of 5-HT through SFO neurons should be considered for PMLD children's care.

From the three cases and previous findings lead to the hypothesis that the levels of 5-HT levels regu-

lating by estrogen in the PMLD children brains may be implicated in the any disorder. In addition, our speculations imply that it may necessary to measure regularly the either plasma 5-HT or estrogen levels in the PMLD children for controlling a wrong behavior.

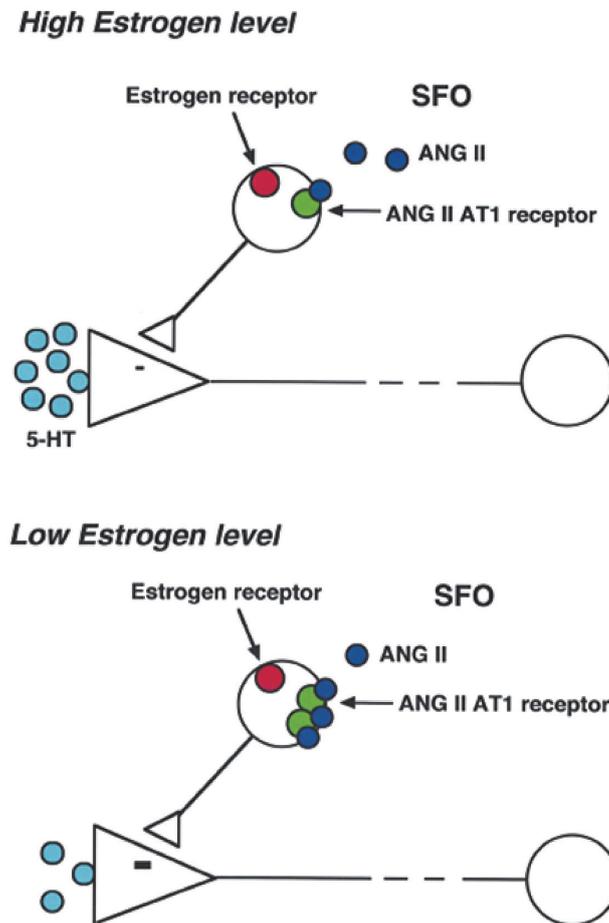


Fig. 1. estrogen may modulate the release of 5-HT

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