



Research paper

Early mood behavioral changes following exposure to monotonous environment during isolation stress is associated with altered hippocampal synaptic plasticity in male rats



Saroj Kumar Das^a, Iswar Baitharu^b, Kalpana Barhwal^a, Sunil Kumar Hota^a, Shashi Bala Singh^{c,*}

^a Defence Institute of High Altitude Research, DRDO, Jammu and Kashmir, India

^b Department of Environmental Sciences, Sambalpur University, Odisha, India

^c Defence Institute of Physiology and Allied Sciences, DRDO, New Delhi, India

HIGHLIGHTS

- Monotony during social isolation stress leads to early alteration of mood state.
- Hippocampal pyknosis and apical dendritic loss was augmented during monotony.
- Monotony stress altered the hippocampal asymmetric and symmetric synapse density.
- Fluoxetine improved the mood status by augmenting hippocampal serotonin level.
- Monotony stress altered the expression of pCREB and synaptophysin in hippocampus.

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ABSTRACT

Social isolation stress and its effect on mood have been well reported, but the effect of monotony (a state of repetition of events for a considerable period of time without variation) on mood and hippocampal synaptic plasticity needs to be addressed. Present study was conducted on male Sprague–Dawley rats. Singly housed (SH) rats were subjected to monotony stress by physical, visual and pheromonal separation in specially designed animal segregation chamber. Fluoxetine (a selective serotonin reuptake inhibitor) was administered orally. Behavioral assessment showed anxiety and depression like traits in SH group. Monotony stress exposure to SH group resulted in increased pyknosis, decreased apical dendritic arborization and increased asymmetric (excitatory) synapses with the corresponding decrease in the symmetric (inhibitory) synapses in the hippocampal CA3 region. Monotonous environment during isolation stress also decreased the serotonin level and reduced the expression of synaptophysin and pCREB in the hippocampus. Fluoxetine administration to singly housed rats resulted in amelioration of altered mood along with improvement in serotonin and decrease in excitatory synaptic density but no change in altered inhibitory synaptic density in the hippocampus. These findings suggest that monotony during isolation contributes to early impairment in mood state by altering hippocampal synaptic density and neuronal morphology.

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1. Introduction

Social communication serves as an evolutionarily significant source of behavioral response which is practically omnipresent

among mammalian species. An animal representation of social stress is diverse, ranging from an acute, intermittent or chronic exposure to social stress and social isolation stress [1]. It has been reported that many of the symptoms induced by isolation stress resemble symptoms of depression and anxiety disorder [2]. Social isolation stress has been shown to induce changes in brain structure, neurotransmitter function and behavior [3]. Chronic absence of novelty, repetition of events for a considerable period and no change in inhabiting environment over time leads to monotony.

* Corresponding author at: Defence Institute of Physiology and Allied Sciences, DRDO, New Delhi–110054, India. Fax: + 91 1 23914790.

E-mail addresses: drshashisingh@gmail.com, drshashibalasingh@outlook.com (S.B. Singh).

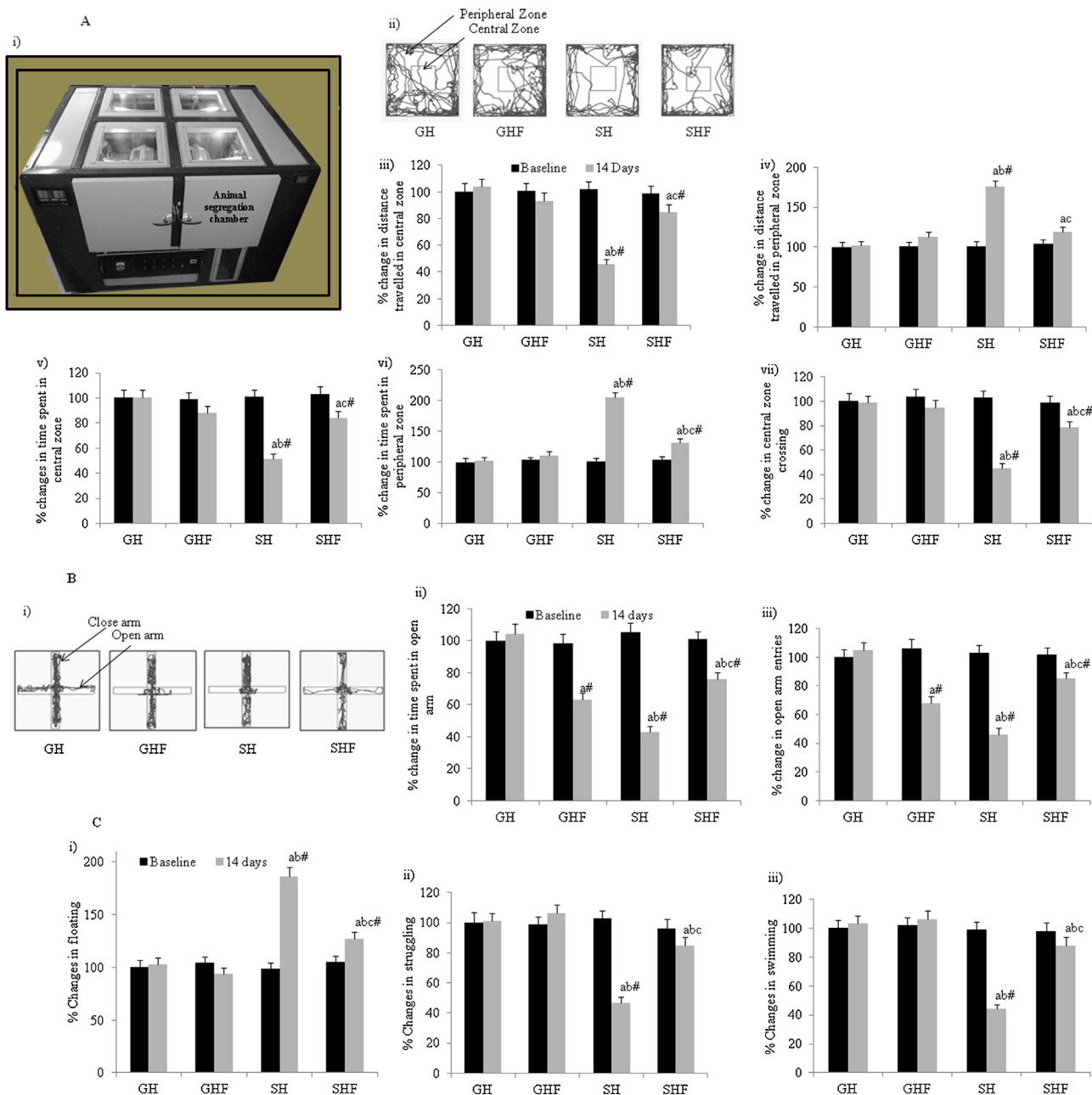


Fig. 1. Behavioral study. A: Figure showing animal segregation chamber A(i). Representative tracksheets of open field test A(ii). Graphs showing change in distance traveled in central A(iii) and peripheral zones A(iv) time spent in central A(v) and peripheral zones A(vi) and number of line crossing in central zone A(vii). B: Representative tracksheets of elevated plus maze test B(i). Graphs showing change in open arm time spent B(ii) and open arm entries B(iii). C: Graphs representing change in floating C(i), struggling C(ii) and swimming C(iii) time in force swim test. Values are expressed as mean \pm SEM. 'a' denotes $p < 0.001$ when compared to GH, 'b' denotes $p < 0.001$ when compared to GHF, 'c' denotes $p < 0.001$ when compared to SH and '#' denotes $p \leq 0.001$ when compared with baseline of the respective group.

However, the effect of monotonous environment (monotony) on mood alterations and its association with synaptic plasticity of sensitive brain regions need to be explored.

Social environment in early life significantly influences the neurochemical development of the brain. Isolation rearing also results in impaired presynaptic serotonergic function [4]. Since serotonin (5-HT) serves as maintenance factor for neuronal differentiation in adult brain [5], altered serotonergic system imparts profound effect on brain functioning [6]. Prolonged social isolation is known to be associated with decrease in hippocampal neurogenesis leading to altered mood behavior [7,8]. Previous report from our laboratory suggest that monotony stress can independently mediate mood behavioral changes [9]. Further, involvement of transcription fac-

tor CREB in mood behavior and depression is well established [10] and antidepressants treatment has been reported to increase CREB expression in rat hippocampus [11]. In the present study, we aimed at investigating the effect of monotony during isolation on mood state of adult male rats and its association with serotonin and altered hippocampal synaptic plasticity.

2. Materials and methods

2.1. Chemicals and reagents

The investigative chemicals including HPLC grade serotonin standard and fluoxetine hydrochloride were purchased from

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