Changes in cognition induced by social isolation in the mouse are restored by electro-acupuncture

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Social isolation by individual housing the mice eliminates social interaction and induces pathophysiological changes including decreased learning capabilities. Acupuncture with the manipulation of the needles according to traditional Chinese medicine or with the electrical stimulation applied on needles inserted into the acupoints (referred as electro-acupuncture, EA) may modulate stress response, mood, learning and memory process. We investigated whether or not EA could reverse memory impairments induced in the male mouse by social isolation. We also studied any changes due to EA or social isolation in neurotrophic factors as nerve growth factor (NGF) or brain-derived neurotrophic factor (BDNF) known to have a role in regulating memory and learning processes. We found that 30 min daily session of EA for a period of 4 days at the acupoint Zusanli (low burst frequency of 2 Hz, each pulse was a square electric wave and had a duration of 180, length of 0.1, and internal burst frequency of 80 Hz; intensity 1.0–1.5 mA) reverses the changes in the passive avoidance responses of isolated mice. These findings were associated with decreased NGF and BDNF in the hippocampus and decreased NGF in the striatum of isolated mice exposed to EA. In conclusion the present data in the mouse show that EA may modulate cognition in mice subjected to social isolation.

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1. Introduction

Social isolation by individual housing the animals eliminates social interaction and induces pathophysiological changes in rodents: for example, impaired response in the hypothalamus–pituitary–adrenal (HPA) axis and sympathetic nervous system [32,43]. Furthermore, social isolation has been reported to alter learning in a battery of behavioral tests. Passive avoidance learning is impaired in social isolated senescence-accelerated mice [12]. Isolation impairs place preference conditioning to morphine but not aversive learning in mice [14]. It has been also shown that in the mouse social isolation has effects on emotional behavior and impairs memory [26,52,53].

Acupuncture is a therapeutic technique, part of the Traditional Chinese Medicine (TCM) and has been used to treat stress conditions, depression and mood disorders. In modern medicine acupuncture is considered to be a modality of sensory stimulation of several classes of sensory afferent fibers [5]. Acupuncture with electrical stimulation (electro-acupuncture, EA) applied on needles inserted into so called "acupoints", releases endogenous opioids likely modulating the activity in different organ systems [27,30,51]. However, other systems and mediators, including neurotrophic factors, may be involved in the acupuncture modulation of stress response, mood, learning and memory process [13,18,19,42,49,56]. That neurotrophic factors may play a role is supported by studies showing that EA modulates these factors in the central nervous system [10,57]. Also neurotrophic factors as nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) play a subtle role in regulating behavior [9]. They are members of the family of proteins known as neurotrophins, including neurotrophin-3 (NT-3), and NT-4/5. NGF and BDNF are the most thoroughly studied neurotrophic factors, playing a crucial role in the survival and development of specific peripheral and brain neurons [1]. Both are produced and released by a variety of cells localized in the central and peripheral nervous systems and by cells of the immune and endocrine systems [6,9,23,36]. Limbic NGF and BDNF play also a key role in the fine tuning of learning and memory performances and in some behavioral processes associated with stressing situations [49]. In particular in the mouse intermale agonistic encounter following social isolation enhances serum NGF and promotes its synthesis in some hypothalamic areas [2].

Our working hypothesis is that EA may have a role in modulating memory impairments elicited by social isolation in the laboratory mouse throughout hippocampal and/or hypothalamic NGF and BDNF. We used the passive avoidance learning task since it represents conditioning memory (associative memory), in which certain