



Research report

Effects of environmental enrichment on anxiety-like behavior, sociability, sensory gating, and spatial learning in male and female C57BL/6J mice

Taylor R. Hendershott, Marie E. Cronin, Stephanie Langella, Patrick S. McGuinness, Alo C. Basu*

Department of Psychology, College of the Holy Cross, 1 College Street, Worcester, MA 01610, United States

H I G H L I G H T S

- Female mice showed greater preference for EPM open arms regardless of housing.
- EE attenuated sensory gating in male and female mice.
- EE enhanced spatial learning in male and female mice.
- EE resulted in greater use of spatially precise strategies in the water maze.
- Swim speed and escape latency in SE females were slow relative to the other groups.

A R T I C L E I N F O

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The influence of housing on cognition and emotional regulation in mice presents a problem for the study of genetic and environmental risk factors for neuropsychiatric disorders: standard laboratory housing may result in low levels of cognitive function or altered levels of anxiety that leave little room for assessment of deleterious effects of experimental manipulations. The use of enriched environment (EE) may allow for the measurement of a wider range of performance in cognitive domains. Cognitive and behavioral effects of EE in male mice have not been widely reproduced, perhaps due to variability in the application of enrichment protocols, and the effects of EE in female mice have not been widely studied. We have developed an EE protocol using common laboratory equipment that, without a running wheel for exercise, results in significant cognitive and behavioral effects relative to standard laboratory housing conditions. We compared male and female wild-type C57BL/6J mice reared from weaning age in an EE to those reared in a standard environment (SE), using common measures of anxiety-like behavior, sensory gating, sociability, and spatial learning and memory. Sex was a significant factor in relevant elevated plus maze (EPM) measures, and bordered on significance in a social interaction (SI) assay. Effects of EE on anxiety-like behavior and sociability were indicative of a general increase in exploratory activity. In male and female mice, EE resulted in reduced prepulse inhibition (PPI) of the acoustic startle response, and enhanced spatial learning and use of spatially precise strategies in a Morris water maze task.

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1. Introduction

Since Donald Hebb's original observations of increased spatial learning ability in rats reared in an enriched environment (EE) [1,2], laboratory controlled enrichment has been associated with widespread molecular and morphological changes through-

out the brain in rodents, mainly in comparison to subjects reared in isolation (for review see Ref. [3,4]). Further, these molecular and morphological changes have been associated with behavioral changes [5]. Although some effects on the nervous system have been replicated by different research groups, behavioral and cognitive effects of EE have not been widely reproducible (Table 1). The mechanisms of enrichment-related changes are of interest for the understanding of functional neuroplasticity, and the influence of housing conditions on rodent behavior is a serious concern for the reproducibility of pre-clinical research findings [6].

* Corresponding author.

E-mail address: abasu@holycross.edu (A.C. Basu).

Table 1
Variability in reports of EE effects on cognition and behavior.

Ref.	Species, strain	Sex	Number of Animals	Age at Enrichment	Age at Testing	Enrichment Duration	Running Wheel	EPM behavior	Sensory gating	Social behavior	MWM Spatial learning and memory
[8]	Mouse, C57BL/6J	F	SE = 13 EE = 14 EE _R = 14	3 weeks	12 weeks	40 days	Yes, No	↓, ↓ % time in open arms	↑, ↓ PPI		n.c.
[9]	Mouse, 129SvJ/C57BL/6 hybrids	F	SE = 8 EE _R = 7	3 weeks	25 weeks, 51 weeks	~22 weeks, 48 weeks	Yes	↓ % open arm entries			
[10]	Mouse, NMRI	M	SE = 8 EE _R = 8	4 weeks	17 weeks	~13 weeks	Yes	n.c.			
[16]	Mouse, ICR	M	SE = 12 EE _R = 12	4 weeks	6 weeks	2 weeks, 4 weeks	Yes		↑, ↓ PPI		
[17]	Mouse, NMRI	M	SE = 16 EE _R = 16	4 weeks	8 weeks	4 weeks	Yes			↑social behavior ↑aggressive behavior	n.c.
[18]	Mouse, C57BL/6J, 129S6/SvEv/Tac	M	SE B6 = 8 EE _R B6 = 8 SE 129 = 8 EE _R 129 = 8	3 weeks	10 weeks	7 weeks	Yes				
[19]	Mouse, C57BL/6J	M and F (combined)	SE = 24 EE _R = 24	8 weeks	14 weeks	40 days	Yes				↓ latency
[21]	Mouse, C57Bl/6	Female	SE = 10 EE _R = 11	3 weeks	20 weeks	17 weeks	Yes				↑ probe
Present Study	Mouse, C57BL/6J	M and F (sex as factor)	SE-M = 11 SE-F = 12 EE-M = 10 EE-F = 11	4 weeks	8 weeks	4 weeks	No	↑ latency to enter open arm ↑ open arm entries	↓ PPI	n.c.	↓ latency* ↓ duration ↓ thigmotaxis ↑ spatial precision

Change in EE housed mice relative to SE housed mice: n.c. no change; ↓ decrease; ↑ increase; *interaction of housing and sex, R running wheel.

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