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Editorial

Calling for a Paradigm Shift: Physical Activity is the Way Life was Meant to be Lived, even in Experimental Animals

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By now, it has become widely accepted, albeit not as widely practiced, that when rodents are raised in a complex, enriched environment, complete with running wheels and peers, cognitive function and memory are enhanced, compared to those raised in isolation, with only food and water to sustain them. In our own *in vivo* studies, in which we were evaluating the effects of antidepressant medications and/or physical running exercise on the levels of hippocampal brain-derived neurotrophic factor (BDNF) transcripts [1-3] or protein [4,5], as well as various other cell survival signaling cascades, such as PI-3K and MAPK, and the transcription factor, CREB [6], the usual experimental design consisted of four treatment groups: (i) sedentary control rats, (ii) rats that received only antidepressant drugs, (iii) rats that were allowed access to a running wheel in their cages and (iv) rats that were administered both antidepressant medications and allowed to run. At that time, this kind of design was standard operating procedure. Few of us recognized that these "control rats", who were sedentary and provided with only food and water, were actually a stressed group, socially isolated, without any mental or physical stimulation at all. Although the other three groups were also singly housed, socially isolated, at least they had some stimulation of either the drug and/or running exercise. Although the experimental design was well enough conceived and implemented, there was a fallacy in our thinking, if not merely in the labelling of the groups: in such an experiment, the group of rats allowed to run were actually the controls, as their lifestyle most closely mimicked that of their wild counterparts. In our paradigm, therefore, although the purpose of our studies was to evaluate the effects of exercise, they also evaluated the effects of stress. After working with both rats and mice for a good number of years, I have come to recognize that as a form of stress, social isolation is highly individualized. Although as a species, both rats and mice may be considered to be "social" animals, not all individuals crave the company of others. Thus, the stress level (e.g., increased plasma corticosterone) in some rats may be higher when placed in the same cage as peers, such as that which would occur in the well-known model of social defeat stress [7,8], while other individuals may exhibit higher stress levels in isolation [9,10].

To make sure that experimental rats live the lives that they were meant to, the concept of environmental enrichment [11,12] and more recently, "enviromimetics" [13], was practiced so as to study the impact that an environment complete with all the manner of stimulation (e.g., running wheel access, an assortment of toys/objects to play with, access to climbing ladders and burrows in which to hide and, of course, peers) that wild rats would experience on neurogenesis [14], growth, morphology and maintenance of circuitry in the hippocampus [15,16], olfactory bulb [17,18] and cortex [19], while potentially warding off disease [13,20]. Indeed, environmental enrichment, but especially the running exercise component, has even been shown to be restorative following the deleterious effects of stress [21]. And in transgenic animals designed to exhibit decreased dentate gyrus neurogenesis [22], physical exercise promoted it, while environmental enrichment maintained it [16]. It should be noted that although several investigators did observe neurogenesis in the olfactory bulb as a result of being exposed to a rich tapestry of varying odours, an olfactory version of environmental enrichment [17,18], earlier investigators [23], who exposed their animals to only environmental enrichment did not.

Although providing such an environment may be financially prohibitive, "control" rats should at least have access to a running wheel, regardless of the specific aims and scope of the study. Indeed, it has been shown that of all the available stimuli in an enriched environ-

ment (above), running has the greatest influence on physical and cognitive health [11,16]. In fact, environmental enrichment alone, without the running component, had earlier been shown to actually correlate with the appearance of amyloid-precursor protein, a putative hallmark of Alzheimer's Disease [24].

Future studies should, therefore, include an exercise control group to mimic as closely as possible the conditions that their wild counterparts would experience. Inclusion of such a group would make any study internally and externally valid.

Bibliography

1. Garcia C., *et al*. "The influence of specific noradrenergic and serotonergic lesions on the expression of hippocampal brain-derived neurotrophic factor transcripts following voluntary physical activity". *Neuroscience* 119.3 (2003): 721-732.

2. Garza AA., *et al*. "Exercise, antidepressant treatment, and BDNF mRNA expression in the aging brain". *Pharmacology Biochemistry and Behavior* 77.2 (2004): 209-220.

3. Russo-Neustadt AA., *et al*. "Hippocampal brain-derived neurotrophic factor expression following treatment with reboxetine, citalopram, and physical exercise". *Neuropsychopharmacology* 29.12 (2004): 2189-2199.

4. Chen MJ and Russo-Neustadt AA. "Running exercise- and antidepressant-induced increases in growth and survival-associated signaling molecules are IGF-dependent". *Growth Factors* 25.2 (2007): 118-131.

5. Chen MJ and Russo-Neustadt AA. "Running exercise-induced up-regulation of hippocampal brain-derived neurotrophic factor is CREB-dependent". *Hippocampus* 19.10 (2009): 962-972.

6. Chen MJ and Russo-Neustadt AA. "Exercise activates the phosphatidylinositol 3-kinase pathway". *Brain Research. Molecular Brain Research* 135.1-2 (2005): 181-193.

7. Finnel JE., *et al*. "Physical versus psychological social stress in male rats reveals distinct cardiovascular, inflammatory and behavioral consequences". *PLoS One* 12.2 (2017): e0172868.

8. Schöner J., *et al*. "Post-traumatic stress disorder and beyond: an overview of rodent stress models". *Journal of Cellular and Molecular Medicine* (2017).

9. Gómez-Galán M., *et al*. "Running opposes the effects of social isolation on synaptic plasticity and transmission in a rat model of depression". *PLoS One* 20.11 (2016): e0165071.

10. Pisu MG., *et al*. "Sex differences in the outcome of juvenile social isolation on HPA axis function in rats". *Neuroscience* 320 (2016): 172-182.

11. van Praag H., *et al*. "Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus". *Nature Neuroscience* 2.3 (1999): 266-270.

12. van Praag H., *et al*. "Neural consequences of environmental enrichment". *Nature Reviews Neuroscienc*e 1.3 (2000): 191-198.

13. Pang TY and Hannan AJ. "Enhancement of cognitive function in models of brain disease through environmental enrichment and physical activity". *Neuropharmacology* 64 (2013): 515-528.

14. Redolat R and Mesa-Gresa P. "Potential benefits and limitations of enriched environments and cognitive activity on age-related behavioural decline". *Current Topics in Behavioral Neurosciences* 10 (2012): 293-316.

15. Kempermann G., *et al*. "Neurogenesis in the adult hippocampus". *Cold Spring Harbor Perspectives in Biology* 7.9 (2015): a018812.

16. Clemenson GD., *et al*. "Enrichment recues contextual discrimination deficit associated with immediate shock". *Hippocampus* 25.3 (2015): 385-392.

17. Johnson MC., *et al*. "Odor enrichment sculpts the abundance of olfactory bulb mitral cells". *Neuroscience Letters* 541 (2013): 173-178.

18. Bonzano S., *et al*. "Odour enrichment increases adult-born dopamineric neurons in the mouse olfactory bulb". *European Journal of Neuroscience* 40.10 (2014): 3450-3457.

19. Landers MS., *et al*. "Synapse formation in adult barrel cortex following naturalistic environmental enrichment". *Neuroscience* 199 (2011): 143-152.

20. Hannan AJ. "Environmental enrichment and brain repair: harnessing the therapeutic effects of cognitive stimulation and physical activity to enhance experience-dependent plasticity". *Neuropathology and Applied Neurobiology* 40.1 (2014): 13-25.

21. Bhagya V., *et al*. "Short-term exposure to enriched environment rescues chronic stress-induced impaired hippocampal synaptic plasticity, anxiety, and memory deficits". *Journal of Neuroscience Research* (2016).

22. Sakalem ME., *et al*. "Environmental enrichment and physical exercise revert behavioral and electrophysiological impairments caused by reduced adult neurogenesis". *Hippocampus* 27.1 (2017): 36-51.

23. Brown J., *et al*. "Enriched environment and physical activity stimulate hippocampal but not olfactory bulb neurogenesis". *European Journal of Neuroscience* 17.10 (2003): 2042-2046.

24. Teather LA., *et al*. "Environmental conditions influence hippocampus-dependent behaviours and brain levels of amyloid precursor protein in rats". *European Journal of Neuroscience* 16.12 (2002): 2405-2415.

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