

## Control of adiposity by environment enrichment

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### INTRODUCTION

Environmental enrichment is of increasing interest in terms of animal welfare in biological research. However, the impact of environmental enrichment on the data obtained in the study of animals models of disease has remained largely unexplored. One such environmental enrichment method is the voluntary use of running wheels in the cage. In this study, the influence of the availability of running wheels on adiposity and bodyweights was studied in C57BL/6 mice, the background strain for a range of transgenic models. Mice are very motivated to use running wheels [1,2] and voluntary exercise has been shown to lower bodyweights and total body fat in mice [3]. These studies were however relatively short-term and observations were made at the end of the interventional period. In the present study, serial measurements were taken throughout the 24-week observation period to assess adiposity in mice with and without voluntary access to running wheels.

### METHODS

**Animals and Treatment:** Three weeks old mice (C57BL/6, male) were obtained from Harlan UK and divided into two groups of 9. Animals from the two groups, I and II, were similarly housed in groups of 3. However, from the age of 4 weeks old, group II animals had access to a running wheel in the cage. Whole body <sup>1</sup>H MRS was recorded to assess adiposity prior to and at 3, 5, 8, 15, 22 and 24 weeks after start of voluntary exercise. Bodyweights, food and water intake measurement from the two groups were recorded at these times.

**MR Scanning:** Anaesthesia was induced and maintained by inhalation of 1-2% isoflurane/oxygen mix. Mice were scanned individually after placement in a <sup>1</sup>H tuned volume coil and MR performed on a 4.7T Unity Inova MR spectrometer (Varian Ltd, USA). <sup>1</sup>H MRS spectrum was collected using a pulse-collect sequence (TR 20s, 45° pulse angle, 4 averages). An exponential line broadening of 5Hz was applied prior to baseline correction and peaks (water referenced at  $\delta$ 4.8ppm) integrated using SpecNMR (JEOL, UK). The total percentage adiposity was calculated by multiplying the lipid peak by 0.38 to correct for the ratio of total body water compared to total fat free mass [4].

**Statistical Analysis:** All data values are quoted as mean  $\pm$  standard deviation and significant difference between the two groups was tested using the t-test.

### RESULTS AND DISCUSSION

Bodyweight and percentage adiposity data for the two groups are shown in Tables 1 and 2, respectively.

**Table 1: Bodyweight data**

	0 (g)	3 weeks* (g)	5 weeks (g)	8 weeks (g)	15 weeks (g)	22 weeks (g)	24 weeks (g)
control	20.26 $\pm$ 2.00 (n=9)	22.58 $\pm$ 1.82 (n=9)	27.93 $\pm$ 1.78 (n=9)	29.99 $\pm$ 1.73 (n=9)	31.43 $\pm$ 1.84 (n=9)	32.61 $\pm$ 2.00 (n=9)	31.06 $\pm$ 1.90 (n=9)
exercise	19.55 $\pm$ 1.76 (n=9)	20.78 $\pm$ 1.11 (n=9)	26.77 $\pm$ 2.19 (n=8)	28.29 $\pm$ 2.55 (n=8)	30.25 $\pm$ 1.84 (n=8)	31.35 $\pm$ 1.67 (n=7)	39.64 $\pm$ 1.26 (n=6)

\*significance observed between the control and exercise groups at the 0.05 significance level.

**Table 2: Percentage adiposity data**

	0 (%)	3 weeks (%)***	5 weeks (%)**	8 weeks (%)*	15 weeks (%)*	22 weeks (%)**	24 weeks (%)
control	20.26 $\pm$ 2.00 (n=9)	22.58 $\pm$ 1.82 (n=9)	27.93 $\pm$ 1.78 (n=9)	29.99 $\pm$ 1.73 (n=9)	31.43 $\pm$ 1.84 (n=9)	32.61 $\pm$ 2.00 (n=9)	31.06 $\pm$ 1.90 (n=9)
exercise	19.55 $\pm$ 1.76 (n=9)	20.78 $\pm$ 1.11(n=9)	26.77 $\pm$ 2.19 (n=8)	28.29 $\pm$ 2.55 (n=8)	30.25 $\pm$ 1.84 (n=8)	31.35 $\pm$ 1.67(n=7)	29.64 $\pm$ 1.26 (n=6)

\*, \*\*, \*\*\* significance observed between the control and exercise groups at the 0.001, 0.01 and 0.05 significance levels, respectively.

N. B., the decrease in the numbers of the exercise group arises from euthanasia due to fight-induced damage and one from impaired heating during the MR experiment.

Bodyweights between the control and exercise groups were similar throughout the study. However, percentage adiposity as measured by MRS was significantly different between the groups at 3, 5, 8, 15, and 22 weeks. Apparently, both control and exercise groups gain the same amount of weight during this period but the weight gain in the latter group arises from lean mass rather than adipose tissue. At the end of the experiment, the percentage adiposity are comparable between the two groups suggesting that at this stage in life, either voluntary exercise is insufficient to lessen adiposity in the whole body and other mechanisms determine adipose tissue metabolism.

### CONCLUSION

We have shown that environmental enrichment through the use of voluntary running wheels leads to a significant modulation in body composition of control mice under standard laboratory conditions. Further studies are required to assess the impact of similar environment enrichment protocols on body function in various models of disease.

### REFERENCES

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