

Summary of GM mice  
research conducted by  
Otago University.

Title

Summary of study of hormone influenced emotional behaviour and metabolism in  
genetically modified mice.

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Introduction:

The motivation for this research is that studying emotion and metabolism in  
genetically modified mice may increase understanding of obesity in humans.

Title of Study:

Leptin and insulin do not exert redundant control of metabolic or emotive  
function via dopamine neurons.

Source of Study:

"Hormones and Behavior" 106 2018 pp 93-104

Research laboratory:

Centre for Neuroendocrinology and Department of Anatomy, University of  
Otago School of Biomedical Sciences, Dunedin, New Zealand

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Approvals:

The University of Otago Animal Ethics Committee approved all animal protocols.

Funding:

The present study was funded by an Otago Medical Research Foundation Laurensen Award and one researcher was supported by The Health Sciences Career Development Program Postdoctoral Fellowship from the University of Otago.

Purpose:

To see whether the hormones leptin and insulin have overlapping influence on dopamine (DA) control of energy balance in mice.

Method:

Genetically modified (GM) mice were bred that had genes removed (“knocked out”) that were responsible for leptin and insulin influence on DA levels.

These mice were bred by cross breeding standard genetically modified mice types; four crosses were required to obtain a type that could be crossed with itself (back bred) to produce the four groups of mice with the required characteristics. After breeding was completed, about twenty mice were killed and tissue samples tested to confirm that the breeding program had delivered the wanted genetic modifications in each group. Confirmation was repeated at the end of the study.

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There were four mouse groups:

Leptin gene removed (single knockout)

Insulin gene removed (single knockout)

Leptin and insulin gene removed (double knockout)

Control mice, no GM modifications.

The knockout mice were then subjected to various experiments to see how they behaved compared to control mice. If a double knockout mouse had different behavioural characteristics to either of the single knockout mice, overlapping control by leptin and insulin was implied.

Energy balance was assessed, and also normal activity (walking around in their cages, using a running wheel). Additionally, anxiety and depression were assessed as no previous study had assessed this in mice with these particular genetic modifications.

Study 1: Feeding behaviour: four groups of about ten male mice. One group was allowed free access to food at regulated times. Subsequently a sugar preference test was conducted. The other group had continuous access to food. Body weight was measured.

Study 2: Depression: Four groups of about ten male and ten female mice were subjected to the forced swimming test. The mice were placed in a jar filled 2/3 with water and left for five minutes. The time taken before they stop swimming was recorded, as an measure of feelings of despair or helplessness.

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Study 3: Anxiety: The same groups were then given tests for anxiety, using a maze, a light/dark box, and an open field box. Their behaviours were recorded.

Study 4: Voluntary activity: Four groups of ten male and four groups of ten female mice had movement around their cages and on a running wheel recorded.

Results:

Statistical tools were applied to the data. There were no differences between any of the mice groups for any tests, except that male mice with the leptin gene removed used the running wheels more, consistent with previous studies.

Conclusion:

If a double knockout mouse had different behavioural characteristics to either of the single knockout mice, overlapping control by leptin and insulin would be implied. As no significant differences occurred, overlapping control does not occur.

END OF SUMMARY

Comments:

It is difficult to estimate how many mice were killed for this experiment, but a full test of all the groups would require eight groups of about ten mice (four groups of male and four of female mice). The breeding programme required four crosses before back breeding was commenced. Each cross will result in some mice that are kept, and others that are discarded. Twenty mice were killed for tissue testing before and after the study.