Restoration of Young Ovarian Function in Post-reproductive Female Mice Significantly Improves Quality of Life and Lifespan

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Background

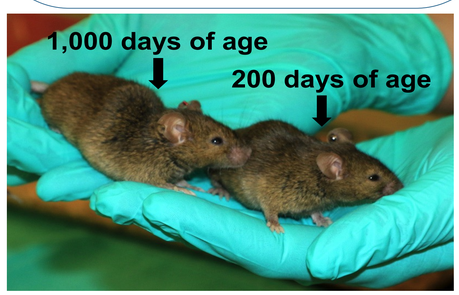
These studies were designed to elucidate the role of ovarian senescence in the increased susceptibility for postmenopausal females to become subject to disease when compared to premenopausal females. Current dogma hypothesizes that the inability of the senescent ovaries to produce hormones for the reproductively senescent female is responsible for the increase in disease.

Preliminary lab work has shown that depletion of germ cells from the ovaries of a young mouse, then a transplanting the germ cell depleted ovaries to a postreproductive mouse produced improved health shown through increased life span and decreased cardiovascular and orthopedic diseases.

Hypothesis

Transplantation of young ovaries to post-reproductive mice would restore cognitive function, improve body composition and increase lifespan relative to the age of the transplanted ovaries, independent of germ cell function.

Our objective was to determine if restoration of reproductive potential in post-reproductive female mice would positively affect the health of the mice specifically evaluating body composition, cognitive acuity and life span which typically decline in function with aging and especially during the menopausal transition.



Photos

The two mice depicted above show how the overall appearance of health for the 1,000 day old mouse with the young transplanted ovaries seems virtually the same as a mouse at the age of only 200 days.

Methods

In order to test our hypothesis female CBA/J mice received new (60d) ovaries at 12 months old and were reevaluated at 16 and 25 months old. The following was evaluated:

1) Body composition: Lean body mass, body fat and total body water were evaluated using MRI.

2) Cognitive behavior and sensory function: Olfactory identification (buried pellet test) and olfactory discrimination (novel recognition block test) was used to measure cognitive behavior in the mice. Burrowing was used as a measure of sensory function.

3) Germ Cell Depletion: Young ovaries with and without germ cells were transplanted to 12 month old mice. Recipients were evaluated at 16 and 25-months of age. Controls included 6mo and 16mo old mice.

Results

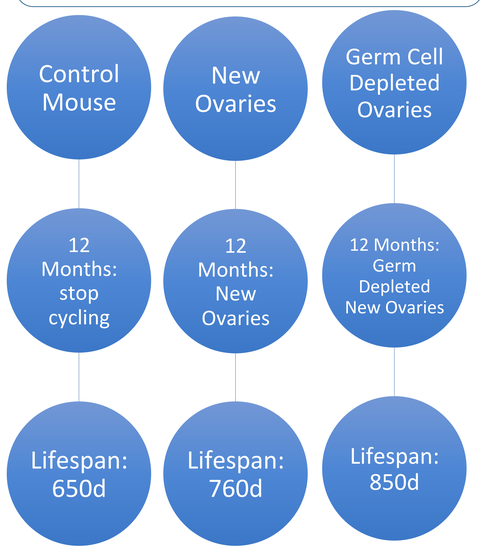
The results of the testing done on the mice receiving the young ovaries showed significant differences showing improved health in body composition, cognitive function, and lifespan. See graph descriptions for detailed results.

Graphs

The Graph to the right shows the relationship of the effect of the germ cell depletion on the mice.

These images and the graph below show VCD depletion of small follicles in CBA/J mice. A) oil-treated mice (B) VCD-treated mice and (C) primordial and primary follicle numbers. concentrations that the control.

Longevity Effects of Germ Cell Depletion



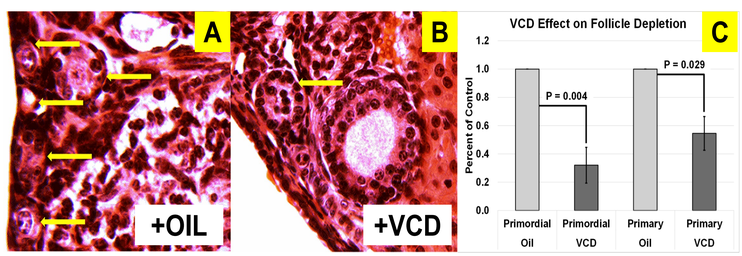
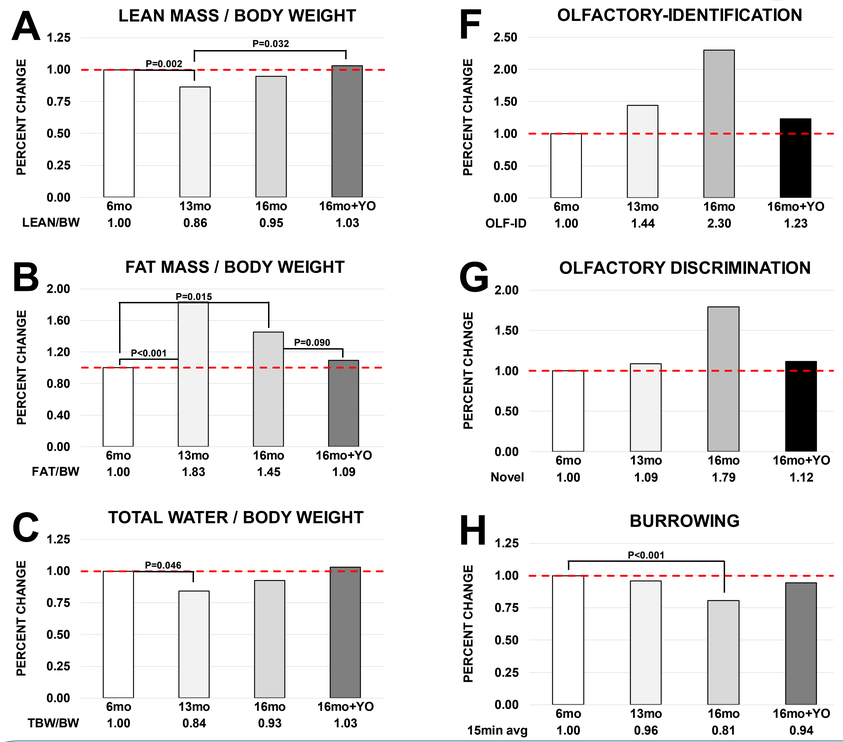


Figure 4. VCD depletion of small follicles in CBA/J mice. A) oil-treated mice **(B)** VCD-treated mice and **(C)** primordial and primary follicle numbers.



Graphs

Graphs F, G, and H (above) show Olfactory Identification, discrimination, and burrowing, respectively. In each case it shows a significant increase in speed to recover the buried pellet, exploring new blocks

Graphs A, B, and C show the effect on the ratio of lean mass, fat mass, and water weight, respectively. In each case, 16 month old mice with the young ovaries showed healthier ratios that are similar to the 6 month old control group. The numbers show significant improvements in health for the precipitants of the transplants.

Discussion

The tests have shows that young ovarian function restored many health benefits to post menopausal mice. These health improvements include less body fat, increased lean body mass, increased life span from depleted germ cells and increased cognitive function with quicker olfactory reaction. The results clearly show that the young ovaries transplanted to the older mice improve health in multiple aspects.

Acknowledgements

A special thanks to Kate Parkinson and Rhett Peterson and Ms. Sumira Phatak for assistance with the MRIs. Research was made possible by Utah State University Research Initiation Funds.

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