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Experimental evolution of the thrifty and spendthrift genotypes, and its consequence for susceptibility to adverse effects of "Western diet": insights from a selection experiment on bank voles

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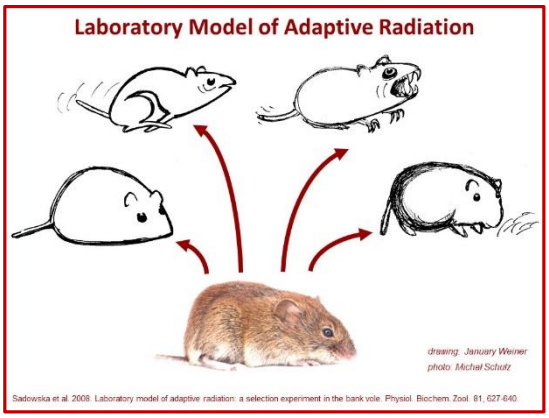
The background: Obesity and co-occurring disorders have become major medical issues in a large and rapidly increasing part of the World. The immediate reasons seem obvious: a practically unlimited access to calorie-rich food, although often nutritionally deficient (so called "Western diet"), combined with reduced physical activity. However, the question why humans are so vulnerable to these conditions, remains subject of debate and intensive research. The question is important not only from biomedical, but also from the evolutionary biology perspective, and, remarkably, the evolutionary perspective contributed to the progress in medicine. According to the "thrifty genotype" hypothesis, the ultimate cause is a history of past selection for the ability to cope with the food scarcity combined with energy-costly locomotory demands. This hypothesis, and related hypotheses concerning phenotypic mechanisms (epigenetic and developmental), have been supported by results of many studies. However, its logical counterpart, the "spendthrift genotype" hypothesis, which predicts ability to avoid the detrimental effects of calorie excess in animals adapted to perform best under no energy limitation, received much less attention and the results are inconsistent.

The experimental evolution model system and hypotheses: The project is based on a unique model system - lines of a common rodent, the bank vole, selected for three distinct physiological and behavioral performance traits: ability to grow on low-quality food (*Herbivorous* lines), high capability of aerobic exercise (*Aerobic* lines), and eagerness to hunt crickets (*Predatory* lines). In the *Herbivorous* lines, the selection required coping with temporary malnutrition, so it favored evolution of the thrifty genotype. In contrast, in the *Aerobic* and *Predatory* lines, the selection resulted in an increased metabolic rate, so it favored evolution of the spendthrift genotype. Therefore, we predict that the *Herbivorous* voles will be more susceptible, whereas the *Aerobic* and *Predatory* ones less susceptible to the adverse effects of the "Western diet", compared to voles from unselected *Control* lines.



The experiments: We will perform a series of experiments based on the *nature* (selection direction) *vs. nurture* (diet type) principle. We will monitor changes of body mass, fat content and blood glucose level during the growth of the voles, and measure several traits characterizing their vigor, physiological performance, and energy balance – such as the locomotor activity and its daily pattern, running performance, the aerobic exercise capacity (the gold standard in the assessment of physical fitness), basal metabolic rate, daily food consumption, and body temperature. Eventually, biochemical analyses of blood will be performed, such as in a typical medical diagnostics, and tissue samples will be preserved for further analyses (in future projects). We will also measure females reproductive success and their offspring performance.

The expected outcome: The immediate outcome of the project will be a comprehensive verification or falsification of predictions of the thrifty and spendthrift genotype hypotheses on the unique animal model, at the level whole-animal (organismal) performance. The project will also provide a basis for further investigation of biochemical and molecular mechanisms underlying the expected differences between the lines selected in distinct directions. The collected tissue samples will be immediately ready for such analyses, and the results can be interpreted jointly with the results of genomic analyses, which are already under way.

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