REPLY TO LUND:
Where does the gravitostat fit in?

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We appreciate the thoughtful reflection by Jens Lund (1) on different aspects of our recent article in PNAS (2). Lund is right to point out that results from studies of the effects of hypergravity on body mass and body fat in rodents support the gravitostat hypothesis (2). Hypergravity and increased loading may regulate body mass via several different mechanisms. Both hypergravity and loading most likely to some extent increase burning to provide energy for an inevitable increase in physical workload. Especially when moving upward animals must increase their burning to gain potential energy (PE). PE is proportional to the body mass (increased by loading) and acceleration of gravity (increased by hypergravity), given that PE = mass × acceleration of gravity × height. This mechanism involving increased burning could be regarded as a part of the gravitostat as it senses the body weight and adjusts the body mass. In our study on loading (2) we did not notice any significantly increased energy expenditure but instead a clearly reduced food intake. Thus, the gravitostat may have the capacity to regulate both food intake and energy burning to maintain a constant body mass.

Investigation of astronauts exposed to microgravity during space travel may have limited relevance for the physiological effects of the gravitostat on Earth. Confounding factors peculiar to space travel include, besides those initiating psychological stress mention by Lund (1), disturbance of the vestibular system and so-called space sickness, with symptoms including nausea and probably affected appetite (3). Another factor seen during space travel, but not on Earth, is a constant shift of blood volume from the legs to the upper part of the body (4).

As pointed out by Lund (1), evidence is accumulating that fat mass may be regulated by two different systems that act at different levels of the body fat (5, 6). This assumption is in line with the model of "a dual intervention point system." This hypothesis predicts a middle range of fat mass that can be altered without major effects on fitness and therefore may be subjected to less strict regulation (7). If the fat mass is decreased more drastically a regulatory system intervenes to increase appetite and/or decrease energy burning. This regulatory signal could be low levels of leptin (5, 8). This is well in line with the observation that the effects of leptin are more pronounced in lean individuals (5, 9, 10). If leptin is a starvation signal acting mainly in the lean there is a need for a complementary antiobesity signal in individuals with high levels of fat mass, as discussed in refs. 5 and 6. As noted by Lund (1), the gravitostat is active in obese animals (2). Therefore, the gravitostat might initiate the unknown catabolic signal in the overfed state sought after by several authors (5, 6). To test this hypothesis, the effects of increased loading and leptin treatment on body weight should be directly compared in lean, modestly obese, and severely obese rodents.

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