of review provided by Aboagye and colleagues is a good early step in this direction.

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Are drug targets missed due to lack of physical activity? – Reply ▲

Initial letter: Gurwitz, D. (2001) *Drug Discov. Today* 6, 342–343

Response from Brenda Anderson

David Gurwitz provides good justification for testing drug efficacy in exercising rodents. He rightfully points out that the genome is 'fine-tuned' for physical activity, and provides evidence that exercise influences many systems, including transmitter systems[1–3].

Despite the evidence, the use of exercising rats might not be appropriate for all drug testing. Numerous human conditions and disease states are associated with reduced levels of activity. Individuals that develop Alzheimer's disease are reported to lead more sedentary lives prior to disease onset relative to persons that do not go on to develop the disease[4]. Low levels of physical activity are associated with bouts of depression, and activity is reduced with age. Thus, specific conditions exist that might be modeled best with the standard lab cage.

Although it might be true (as Gurwitz points out) that drug efficacy could be better detected in exercising rats, sedentary rats might provide a better model for the detection of side effects. Exercise can be neuroprotective against ischemia[5] and epilepsy[6–7]. Exercising rats have less oxidative damage in the brain[8], and an increased capacity for oxidative metabolism in central motor structures[9]. Therefore, side effects related to excitotoxicity could be detected more easily in sedentary rather than in exercising rodents.

Strong arguments can be made for the use of exercise as a standard laboratory condition. However, the ultimate choice of animal housing should depend on the population being modeled, and the goal of the study.

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