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Rodent rhythmicity studies: Use of unfavorable light regimes

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In a recent issue of the journal Neuron, DeBruyne et al. [1] reported the quite unexpected finding that mouse transcription factor CLOCK is not required for circadian oscillator function in whole-mouse knockouts. Their study illustrates the highly sophisticated techniques currently helping to unravel the mechanisms of biological time keeping. A caveat, however, is that the ancillary procedures used by DeBruyne et al. [1] to assess locomotor rhythmicity in exercise wheels were not 'state-of-the-art' for that purpose, unlike their employed molecular biology techniques. In essence, mice in pre-tests were provided with a choice between the 'lesser of two evils' for ambient illumination for their rest and running activity, namely bright light and darkness. Following that they were tested in constant darkness: The results obtained are no less remarkable, despite this shortcoming, in having revealed periods of intense and lesser activity, and established the inessentiality of the transcription factor in conditions of constant darkness. The shortcoming to which I refer is the unnatural ambient lighting conditions used in the tests, both during the cycles and the following constant conditions. More clear-cut results can be expected using ecologically appropriate lighting conditions (dim-dark cycles and constant dim light) for such studies [2].

Thus, given the means to control their ambient illumination, several species of wild nocturnal mice (genus *Peromyscus*) in exercise wheels select dim light (say,

0.0002–0.0009 ft-c = a clear moonless night) for activity, and darkness or very much dimmer light for sleep, corresponding roughly to the light exposure during these phases of existence in the wild [2]. These preferences remind us that, at night, wild nocturnal rodents forage in various phases of moonlight and/or starlight, but very infrequently in darkness. During the day they sleep in their nests in very dim light or darkness, but never in bright light.

The use of bright light in the laboratory for studies of nocturnal rodents is tolerable to the animals only if a shaded or dark nesting area is available. Extended exposure to bright light destroys the visual cells of both pigmented and albino rats [3]. DeBruyne et al. [1] obtained positive results with their cyclic bright-dark regime only because active nocturnal rodents avoid bright light much more than darkness. This choice was between the two most unfavorable ambient illumination conditions for vision during locomotion, namely, that in which visual cells would be destroyed versus that in which vision is impossible. During the test phase in constant darkness, the only choice was between remaining inactive or being active in an unfavorable, otherwise avoided, condition for locomotion [4].

Supporting the latter assertion, darkness usually has very deleterious effects on wheel-running parameters, compared to those in dim light: learning takes longer, animals run less and much more slowly, running sessions are much shorter, and otherwise highly consistent directional running tends to become haphazard [4, Figs.4–6]. On more nearly natural dim-dark light cycles, nocturnal rodents, including domesticates, become active in the dim-light phase and sleep in the dark [2].

If the bright light used by DeBruyne et al. [1] were to be replaced by sufficiently dim light (i.e., if they were to employ dim-dark light cycles followed by constant dim

light), conditions would be ecologically appropriate. On the cyclic dim-dark regime, the mice would adapt readily, becoming active in the dim light and sleeping in darkness. Locomotor performance would be greatly improved, with the animals being more active and running faster and more consistently. Such improvements also would be expected in the following constant dim light tests. Active and inactive periods would be much more sharply demarcated, with little or no wheel running in darkness or between successive active periods in constant dim light. Such results would not be surprising in rodents whose biological clocks can program wheel-running periods from night to night at elapsed times accurate to within 1% [5, 6].

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