correspondence

Of mice and men

We would like to compliment, and complement, the recent Opinion in *EMBO reports* by Stuart Peirson and Russell Foster (2011), which calls attention to the potential obstacles associated with linking observations on light and circadian rhythmicity made on nocturnal mice to diurnally active humans. Pitfalls to consider include that qualitative extrapolations from short-lived rodents to long-lived humans, quantitative extrapolations of very different doses (Gold *et al*, 1992), and the varying sensitivities of each species to experimental optical radiation as a circadian stimulus (Bullough *et al*, 2006) can all have a critical influence on an experiment. Thus, Peirson & Foster remind us that “humans are not big mice”. We certainly agree, but we also thought it worthwhile to point out that human studies have their own interesting pitfalls, of which all researchers should be mindful.

Many investigations with humans—such as testing the effects of different light exposures on alertness, cognitive performance, well-being and depression—can suffer from what has been coined as the ‘Hawthorne effect’. The term is derived from a series of studies conducted at the Western Electric Company’s Hawthorne Works near Chicago, Illinois, between 1924 and 1932, to test whether the productivity of workers would change with changing illumination levels. One important punch line was that productivity increased with almost any change that was made at the workplaces. One prevailing interpretation of these findings is that humans who know that they are being studied—and in most investigations they cannot help but notice—might exhibit responses that have little or nothing to do

with what was intended as the experiment. Those who conduct circadian biology studies in humans try hard to eliminate possible ‘Hawthorne effects’, but every so often, all they can do is to hope for the best and expect the Hawthorne effect to be insignificant.

Even so, and despite the obstacles to circadian experiments with both mice and humans, the wealth of information from work in both species is indispensable. To exemplify, in the last handful of years alone, experimental research in mice has substantially contributed to our understanding of the retinal interface between visible light and circadian circuitry (Chen *et al*, 2011); has shown that disturbances of the circadian systems through manipulations of the light–dark cycles might accelerate carcinogenesis (Filipski *et al*, 2009); and has suggested that perinatal light exposure—through an imprinting of the stability of circadian systems (Ciarleglio *et al*, 2011)—might be related to a human’s susceptibility to mood disorders (Erren *et al*, 2011a) and internal cancer developments later in life (Erren *et al*, 2011b). Future studies in humans must now examine whether, and to what extent, what was found in mice is applicable to and relevant for humans.

The bottom line is that we must be aware of, and first and foremost exploit, evolutionary legacies, such as the seemingly ubiquitous photoreceptive clockwork that marine and terrestrial vertebrates—including mammals such as mice and humans—share (Erren *et al*, 2008). Translating insights from studies in animals to humans (Erren *et al*, 2011a,b), and vice versa, into testable research can be a means to one end: to arrive at sensible answers to pressing

questions about light and circadian clockworks that, no doubt, play key roles in human health and disease. Pitfalls, however, abound on either side, and we agree with Peirson & Foster that they have to be recognized and monitored.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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