Physiology & Behavior 119 (2013) 130–136

Contents lists available at SciVerse ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Review

A review of seasonal/circannual effects of laboratory rodent behavior

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HIGHLIGHTS

- The effect of seasons on lab rodent behavior is reviewed.
- Few consistent effects were described for activity, learning or sex behavior.
- Statistical issues are discussed and power analyses are conducted for sample studies.

ARTICLE INFO

Article history:
Received 4 January 2013
Received in revised form 13 May 2013
Accepted 5 June 2013

Keywords:
Seasonal effects
Circannual effects
Endogenous oscillator
Rodent behavior

ABSTRACT

The existence of seasonal or circannual effects on laboratory rodent behavior has been the subject of much debate in recent conversations with colleagues. If such effects are real, they could explain poor replicability or hinder the detection of treatment effects. Here, we review the literature in which seasonal or circannual rhythms were examined under typical 12:12 h photoperiods and present our historical data of locomotor activity of male and female Sprague–Dawley rats across several seasons and years. In general, there was little evidence to indicate significant effects on the locomotor activity of rats or mice, while studies of depression behaviors were somewhat inconsistent in their findings. Results of the few anxiety behavior assessments were fairly consistent, at least in rat studies. Two studies of pain-related behaviors indicated decreased responses during spring or summer testing. If such seasonal effects are real, this would imply that laboratory rodents have a type of internal Type 2 circannual clock or endogenous oscillator. However, photoperiod, temperature, or humidity cannot be the zeitgeber. Further, the need for a circannual clock in a short-lived rodent is debatable.

Published by Elsevier Inc.

Contents

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0031-9384/$ – see front matter. Published by Elsevier Inc.
http://dx.doi.org/10.1016/j.physbeh.2013.06.007

1. Introduction

Relatively good evidence exists for seasonal or circannual effects on certain toxicological, physiological, and reproductive parameters in laboratory rodents (e.g., [1–9]); however, there appears to be much less known or reported regarding such effects on behavioral endpoints, even in those vivariums with 12:12 h photoperiods and held under strict environmental conditions. In our discussions with colleagues, this issue seemed to generate relatively strong opinions. For example, one colleague noted that they did not conduct behavioral studies in their laboratory during the autumn and winter seasons as rodents were extremely inactive during those times. Comments such as those motivated us to critically examine the scientific literature. If seasonal effects have been documented on other endpoints (e.g., toxicological, physiological, and reproductive), such influences could extend to behaviors as well. Thus, here we review studies in which seasonal or circannual effects on behavior were explored as well as data from our laboratory in which the behavior of control rats was measured at various times over 3 years.

We had several reasons for collating this literature. The first was that such a review of behavioral endpoints was not currently available and thus, our goal was not only to assemble the existing literature, but also to stimulate others to examine and report their own historical and future data for similar effects. Further, if seasonal or circannual effects do substantially impact behavioral endpoints, the likelihood of occurrence in typical studies could be high. In order to attain sufficient group sizes, most experimental laboratories must perform studies in replicates or cohorts. For example, for many behavioral endpoints, a minimum of 10/sex/group is recommended [10]. This can result in 40 subjects if both sexes and only two experimental groups are assessed. While some laboratories may be capable of testing 40 subjects in a single day, the strong evidence for circadian rhythms on behavior would advise against such a strategy for those assessments which are of a longer duration. Further, most laboratories have a limited number of behavioral apparatus (e.g., open fields or water mazes) and thus, there is a maximum number of subjects that can be assessed each day. This can lead to assessments being conducted over an extended period of time that could potentially introduce seasonal effect variations into the results. Replicate or cohort is often included as a factor in statistical analyses, but rarely is a significant effect ascribed to seasonal effects.

2. Search strategy

An initial comprehensive PubMed search was conducted in December 2012. Because our focus was on behavior, we selected those endpoints that are most commonly reported as it was assumed that those would be the most likely to have been investigated with regard to season. Those endpoints were activity, anxiety, depression, learning, and memory. In an effort to be as thorough as possible, we also included the terms for the most commonly used apparatus to assess these endpoints. Thus, the search used the following terms and Boolean operators: (annual variation OR annual effect OR annual effects OR seasonal variation OR seasonal effect OR circannual effects OR circannual variation) AND (rats OR rat OR mouse OR mice) AND (open field OR locomotor activity OR elevated plus OR Barnes maze OR zero maze OR anxiety OR depression OR learning OR memory). This primary search yielded 158 publications. To accurately classify season, hemisphere (i.e., northern or southern) of the laboratory in which the study was conducted was determined.

Certain studies were not included in this review and the following criteria were used for exclusion. Day length or photoperiod governs many of the circadian effects on behavioral endpoints [11]. Thus, in order to fully evaluate seasonal effects without the influence of altered photoperiod, those studies in which the behavioral effects may have been due to changes in the vivarium photoperiod were excluded (e.g., [12]). Publications studying species other than the typical strains of laboratory rats or mice were also excluded (e.g., studies of the reproductively photoperiodic Siberian hamster [13]). Any study not fully available in English was excluded. Studies not reporting õbehavioral endpoints were not included. Any study, in which the vivarium photoperiod was other than 12:12 h or temperatures were not consistent, was not included nor were studies which did not detail the light cycle under which the assessments were conducted as this can substantially affect behavior [14]. Finally, studies that did not directly include season in the analyses or did not address the potential effect(s) of season were excluded.

A small number of additional studies not in the original PubMed search were located from our review of other studies; thus, the final number of relevant publications was 14. These were categorized with regard to behavioral function and each is summarized below. Table 1 lists age, sex, strain, test lighting conditions, and endpoints measured for these studies.

3. Results

3.1. Seasonal/circannual effects on activity levels

Activity is one of the most frequently measured behaviors in laboratory rodents and such assessments are included in many first tier preclinical test guidelines (e.g., [15,16]). Measurement of activity levels provides a global test of CNS function [16,17] and, if altered by an experimental manipulation, can potentially confound interpretations of cognitive tests. Thus, it is not surprising that more studies measuring activity levels are reviewed here than those measuring any other endpoint.

Table 1
Studies reviewed in this paper.

Reference number	Species/strain/sex	Photoperiod of assessment	Endpoint
[36]	Sprague–Dawley male rats	Light	Depression (forced swim test)
[37]	Wistar female rats	Light	Depression (forced swim test)
[24]	Sprague–Dawley male rats	Light	Latency to leave home cage (exploratory behavior)
[34]	Wistar male rats	Light	Anxiety (elevated plus maze), depression (forced swim test)
[31]	CF No. 1 male mice	Not stated	Learning (passive avoidance)
[21]	Swiss male mice	Light	Activity
[35]*	Wistar male rats	Light	Anxiety (elevated plus maze)
[22]	N/Nih-HS male and female rats	Light	Activity, anxiety (zero maze)
[18]*	C57BL/6J male mice	Light	Activity
[23]	Wistar male rats	Light and dark	Activity
[19]*	CBA/J male and female mice	Light and dark	Activity, nociceptive behavior
[20]	Mixed strain of C57BL/6J and 129 female mice	Dark	Activity, learning, anxiety (light–dark box), depression (sucrose intake), sex behavior
[42]	Sprague–Dawley male and female rats	Light and dark	Nociceptive behavior
[38]	NMRI male mice (sex interpreted from photo)	Light (assumed, not directly stated)	Depression (forced swim and tail suspension tests)

* Indicates that the study compared two timepoints in a single year. See Section 4, "Statistical issues and retrospective power analyses" for more explanation.