Available online at www.sciencedirect.com
ScienceDirect
Hormones and Behavior 51 (2007) 306–312
Hormones and Behavior
www.elsevier.com/locate/yhbeh

Cortisol controls the pubertal development of agonistic behavior in male golden hamsters via type II corticosteroid receptors

Joel C. Wommack *, Yvon Delville

Psychology Department and Institute for Neuroscience, The University of Texas at Austin, Austin, TX 78712, USA

Received 21 April 2006; revised 12 November 2006; accepted 13 November 2006
Available online 24 December 2006

Abstract

In male golden hamsters, agonistic behavior undergoes a pubertal transition from play fighting to adult aggression. Previous studies have shown that this aspect of behavioral development is associated with pubertal increases in glucocorticoids and that daily social stress or injections of a synthetic glucocorticoid accelerate the transition. The goals of this study were to confirm the effects of cortisol on the development of agonistic behavior and to investigate the role of type II corticosteroid receptors in this process. First, animals treated with cortisol during early puberty [from postnatal days 31 (P-31) to P-36] showed an accelerated transition from play fighting to adult aggression. In a second experiment, the behavioral effects of cortisol were blocked by a co-treatment with a type II corticosteroid receptor antagonist. These findings are the first to show a facilitating role for type II corticosteroid receptors in the pubertal development of a social behavior. As such, these findings provide new insights into the neuroendocrine mechanisms controlling behavioral development during puberty.

Keywords: Play fighting; Aggression; Corticosteroid receptors; RU486; Adolescence; Hamster

Introduction

Puberty is characterized by a maturation of agonistic behavior from play fighting to adult aggression (Fagen, 1981; Delville et al., 2003, 2005; Pellis et al., 2005). Recent studies in golden hamsters have focused on the peri-pubertal development of the offensive component of agonistic behavior (Delville et al., 2003, 2005). In hamsters, play-fighting and adult attacks can be differentiated through the area on the body of the opponent first targeted by the aggressor. Play-fighting attacks are directed towards the face and cheeks of an opponent, while adult attacks are focused on its belly and rear (Wommack et al., 2003; Taravosh-Lahn and Delville, 2004). While much is known about the neuroendocrine control of adult aggression (Albers et al., 2002; Simon, 2002), little is known about the control of play fighting and the transition between both forms of agonistic behavior (Delville et al., 2005; Sisk and Foster, 2004).

Contrary to what one would expect, the transition from play fighting to adult aggression is not controlled by gonadal steroids. While testosterone facilitates offensive aggression in adult male rodents, the relationship between pubertal changes in androgen levels and agonistic behavior is not as clear (Payne, 1974; Albers et al., 2002; Simon and Lu, 2005; Grimes et al., 2006). For example, hamsters and rats start engaging in play fighting prior to the pubertal increases of testosterone levels, suggesting that the onset of agonistic behavior is independent of gonadal steroids (Goldman and Swanson, 1975; Schoenfeld and Leonard, 1985; Pellis and Pellis, 1993; Vomachka and Greenwald, 1979). Additionally, increasing testosterone levels do not appear to be associated with the transition from play fighting to adult aggression (Sisk and Foster, 2004). While significant increases in plasma testosterone levels coincide with the transition from play fighting to adult aggression in male golden hamsters, preweaning castration does not affect this behavioral shift (Pellis and Pellis, 1988; Romeo et al., 2003; Vomachka and Greenwald, 1979; Wommack et al., 2003). The failure to establish a link between the hypothalamic-pituitary-gonadal (HPG) axis and the maturation of

* Corresponding author. Psychology Department, Florida State University, Tallahassee, FL 32306-1270, USA. Fax: +1 850 644 7739.
E-mail address: wommack@psy.fsu.edu (J.C. Wommack).

0018-506X/$ - see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.yhbeh.2006.11.007

offensive responses suggests that this behavioral transition is controlled by a separate neuroendocrine axis.

Recent studies have reported pubertal changes in the hypothalamic–pituitary–adrenal (HPA) axis with considerable variation between species. In rats, the early pubertal development of the HPA axis is characterized by prolonged adrenocorticotropin releasing hormone (ACTH) secretion and corticosterone responses without changes in baseline hormone levels (Gomez et al., 2002; Vazquez, 1998). In tree shrews (Van Kampen and Fuchs, 1998) and humans (Elmlinger et al., 2002; Jonetz-Mentzel and Weideman, 1993; Kiess et al., 1995), glucocorticoid levels gradually increase over the course of puberty. Additionally, male golden hamsters show increases in both baseline and post-stress glucocorticoid levels during puberty that are synchronized with the transition from play fighting to adult aggression (Wommack et al., 2004, 2005).

Studies on social stress during puberty gave us our first insight into the relationship between glucocorticoids and the pubertal development of agonistic behavior. Specifically, social defeat is a stressor to which juvenile hamsters do not fully habituate, thus subjugation results in a daily increase in plasma cortisol levels (Wommack and Delville, 2003; Wommack et al., 2004). Interestingly, socially subjugated juvenile male hamsters show an accelerated transition from play fighting to adult aggression (Wommack et al., 2003). As such, it was previously hypothesized that glucocorticoids controlled the transition from play fighting to adult aggression. This hypothesis was confirmed in an initial study as male hamsters that received daily injections of dexamethasone, a type II agonist (Sutanto and De Kloet, 1987), showed an accelerated transition from play fighting to adult aggression (Wommack et al., 2005). The goals of the current study were to further investigate the relationship between cortisol and the development of offensive responses and confirm the role of type II corticosteroid receptors in behavioral development.

Materials and methods

Animals and treatment

Male golden hamsters were obtained from a breeding colony housed within the laboratory derived from animals originally purchased from Harlan Sprague Dawley (Indianapolis, IN). Approximately a week after birth, all litters were culled to 6 pups including males and females. The males were weaned on postnatal day 25 (P-25) and individually housed in Plexiglas cages (20×33×13 cm). Animals were kept in an AALAC-accredited facility. All procedures were carried out according to NIH guidelines for laboratory animals and approved by the Institutional Animal Care and Use Committee of the University of Texas at Austin. Within 2 days, each animal was briefly (a few seconds) observed in the presence of an adult intruder. Individuals that immediately fled from the adult were considered to be inherently fearful (approximately 1 in 12) and were removed from the experiment. All animals received food and water *ad libitum* and were housed under a reversed light/dark cycle (14L–10 D, lights off at 9:00 am).

Experimental design

The hypothesis that cortisol accelerates the development of offensive responses was tested through a series of experiments. First, animals received repeated injections with different doses of cortisol to determine whether this hormone was capable of accelerating the transition from play fighting to adult aggression. Once a sufficient dose of cortisol for accelerating behavioral development was found, a second study was carried out to confirm the role of type II corticosteroid receptors. Animals received repeated injections of a dose of cortisol sufficient to accelerate behavioral development combined with RU-486, a selective type II receptor antagonist in hamsters (Gray and Leavitt, 1987).

Cortisol and offensive responses

Male golden hamsters were repeatedly injected with cortisol (hydrocortisone, Sigma Chemical Co., St. Louis, MO) during early puberty. On P-31 male golden hamsters were weighed and screened for offensive responses using a resident–intruder paradigm (Payne, 1973; Ferris et al., 1997). Smaller (10–20%) and younger animals were placed in the home cage of experimental animals for 10 min. The size difference between the resident and intruder favors offensive responses (Delville et al., 2003). After confirmation that each resident readily performed play fighting offensive responses, animals were separated into experimental and control groups balanced for litter and body weight. Animals received daily subcutaneous injections of cortisol in propylene glycol (0, 10, or 40 μg/100 g; n=6–7 per dose) from P-31 to P-36. All injections were administered in the second half of the dark phase. On P-37, the offensive responses of experimental animals were observed in the presence of an unfamiliar and smaller intruder. Offensive responses such as attacks and pins (see below for a detailed description) were video recorded for later review. This time period corresponds to early puberty in golden hamsters, as defined by plasma testosterone levels and testicular weights (Vomachka and Greenwald, 1979; Wommack et al., 2004). Body weights were recorded prior to testing. All behavioral tests were conducted in the middle of the dark phase with experimenters blind to the treatment groups.

RU-486/Cortisol and offensive responses

To test the involvement of type II corticosteroid receptors in the development of offensive responses, a second experiment was performed using a combination of cortisol and RU-486. In golden hamsters, RU-486 is a corticosteroid type II receptor antagonist and not a progestin receptor antagonist (Gray and Leavitt, 1987; Benhamou et al., 1992). To test the possible effects of each substance on offensive responses, a total of four groups were included in this study: Vehicle/Vehicle, Vehicle/Cortisol, RU-486/Vehicle, and RU-486/Cortisol. A similar paradigm as the previous cortisol experiment was used. On P-31, male golden hamsters were weighed and screened for offensive responses using a resident–intruder paradigm (Payne, 1973; Ferris et al., 1997). Smaller (10–20%) younger animals were placed in the home cage of experimental animals for 10 min. The size difference between the resident and intruder favors offensive responses (Delville et al., 2003). After confirmation that each resident readily performed play-fighting offensive responses, animals were separated into experimental and control groups balanced for litter and body weight. From P-31 to P-41, animals received subcutaneous injections of 0 or 1.0 mg RU-486 (a generous gift from Roussel Uclaf, France) suspended in 0.3 ml sesame oil. Similar or higher doses of RU-486 have been used to block corticosteroid type II receptor activation in golden hamsters and prairie voles (Jimenez et al., 1999; Curtis and Wang, 2005). One hour later, animals received daily subcutaneous injections of cortisol in propylene glycol (0, 10 μg/100 g; n=9–10 per dose). All injections were administered in the second half of the dark phase after behavioral testing on P-37 to ensure that the behavioral effects were due to repeated hormone injection rather than the acute effects of cortisol offensive aggression (Hayden-Hixson and Ferris, 1991). Body weights were recorded across the study. As stated above, animals were tested for offensive responses in the presence of an unfamiliar and smaller intruder for 10 min on P-37 and P-42. Offensive responses such as attacks and pins (see below for a detailed description) were video recorded for later review. Body weights were recorded prior to behavioral testing. Additionally, locomotor activity was recorded the days following tests for offensive responses, on P-38 and P-43 (see below for a detailed description). All tests were conducted during the middle of the dark phase under dim red light illumination and the experimenters were blind to the treatment groups.