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HIGH CAFFEINE EXPOSURE INCREASES OVARIAN ESTRADIOL PRODUCTION IN RATS

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Abstract

Chronic caffeine consumption exerts a negligible effect on the reproductive organs of normal adult females, but it is not known whether this is also true for children and adolescents. Here, we investigated the effects of high caffeine exposure on sexual maturation and ovarian estradiol production in immature female rats. Immature female SD rats were divided into controls and caffeine groups fed 120 and 180 mg/kg/day for 4 or 8 weeks. There was a significant delay in vaginal opening in the caffeine-fed groups. In addition, serum estradiol levels were elevated in the caffeine-fed animals after 2 and 4 weeks of exposure. Estradiol secretion as well as aromatase expression also increased significantly in the ovarian cells in response to caffeine. These results demonstrate that peripubertal exposure to high caffeine increases estradiol production in the ovary; this may disturb the coordinated regulation of the hypothalamo-pituitary-ovarian axis, thereby interfering with sexual maturation.

Keys words: peripubertal, hypothalamo-pituitary-ovarian axis, caffeine

Introduction Caffeine is now increasingly available in energy drinks whose unrestricted availability makes them easily accessible by younger children [1], [2], [3]. Approximately 75–95% of children and adolescents consume caffeine on a regular basis, and 12% can be classed as ‘high chronic’ users [3]. In general, daily caffeine consumption for children and adolescents is recommended not to exceed 2.5 mg/kg/day, equating to one small cup of coffee [4]. However, most current energy drinks have about 100 mg of caffeine per serving and a few of them have up to 500 mg per serving [2].It has been reported that caffeine caused a significant increase in estradiol secretion by H295R cells (a human adrenocortical carcinoma cell line) [6]. In addition, perturbation of steroid hormone balance at higher caffeine intakes has been documented in men and male rabbits [7], [8]. Similarly, there is suggestive evidence for a positive or negative association between caffeine intake and estrogen levels in postmenopausal [9], [10], or premenopausal women [10], [12]. As mentioned above, evidence from laboratory studies and human cases has raised concern that high caffeine exposure may alter sex hormone levels and interfere with the endocrine system.Adolescence is a critical period for the growth and maturation of the

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reproductive organs, and is characterized by extensive morphological and functional changes [13], suggesting that caffeine might have an even more pronounced impact on the reproductive system than it does in adults. Human studies have generally been of small size and flawed by inaccurate assessment of exposure levels because they relied on self-reporting of dietary data.

Animals and experimental design

Two-week-old female Sprague-Dawley rats (n = 60) were obtained from Samtako Biokorea (Kyunggi, South Korea) and allowed to acclimate. At weaning (21 days of age), the animals were assigned to groups according to bodyweight in order to eliminate variation in mean bodyweight among the groups and individual animals were housed in separate plastic cages under controlled conditions (22–24 °C, humidity 40–50%, 12 h light–dark cycle), with free access to food and water. Animal care was consistent with

Discussion

In the present study we have shown that peripubertal exposure to high caffeine delays sexual maturation, transiently reduces reproductive organ weights and stimulates ovarian E_2 secretion in immature female rats. To the best of our knowledge, there have been no reports in the world literature about the influence of caffeine exposure on ovarian hormone production, specifically in the peripubertal period.

We applied caffeine to 22-day-old rats for 4 or 8 weeks, during which the ovary develops and

Conflict of interest

None.

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YK, HC, and JB participated in the experiments, data collection and analysis; YYC, participated in the experiments; JR, contributed to the design of the study, data analysis, supervision and development of the manuscript. JR takes responsibility for the integrity of the data analysis. All authors read and approved the final manuscript. This study was supported by the Ministry of Education and Science (NRF-2014R1A1A2053601).

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