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Influence of a single treatment with vitamin E or K (hormonal imprinting) of neonatal rats on the sexual behavior of adults

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The effect of a single neonatal treatment (imprinting) with vitamin E or vitamin K_1 on the sexual activity of three-month old rats, was studied. In female animals vitamin E treatment significantly lowered the Meyerson index and lordosis quotient, among males there were significantly more inactive animals and no multiple ejaculations could be observed. Vitamin K_1 treatment caused only slight changes in the same direction, in both sexes. Considering also earlier results concerning vitamin A and D neonatal treatments (alterations in receptor binding capacity, sex hormone levels and sexual behavior), and receptorial changes caused by neonatal vitamin E and K_1 treatments, the present experiment also calls attention to the lifelong effects of perinatal treatment with lipid soluble vitamins.

Keywords: vitamin E, vitamin K, receptors, sexual behavior, perinatal treatments

Hormonal imprinting takes place at the first encounter of the maturing receptor and the appropriate hormone during the critical – neonatal – period of development [3]. As a consequence of imprinting the receptor accomplishes its maturation and reaches the binding capacity characteristic to the adult age [4, 5]. Without imprinting there is no complete receptor maturation [6]. However, in that time the excess of the appropriate hormone, or presence of such molecules which are chemically different from the appropriate hormone, nevertheless able to bind to the maturing receptor (members of

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the same hormone family, hormone analogues, environmental pollutants) can cause faulty imprinting with lifelong alterations in the receptor's binding capacity and the response of the receptor bearing cell [3–5]. Neonatal treatment with steroid hormone analogues disturbs not only the maturation of their target receptors, but they influence the binding capacity of other members of the steroid receptor superfamily, for life. Allylestrenol, a synthetic steroid hormone with a protecting effect in endangered pregnancy, or benzpyrene, which has a steroid-like structure decrease both estrogen and glucocorticoid receptor binding capacity [3–5] after neonatal treatment and dramatically influence sexual behavior [7] in adulthood. Neonatal treatments with other steroids [15, 21] or with molecules having receptor in the steroid receptor superfamily [8], cause lifelong morphological, biochemical, even genetic [15] changes.

The steroid receptor superfamily has two members, which bind vitamin A or D. These molecules cause faulty imprinting of steroid receptors [8]. Considering these observations, the imprinter effect of other two members of lipid soluble vitamin group (vitamin E and K) was found in studies on receptor kinetic analysis of adult animals. In the present experiments the functional (sexual behavioral) effect of neonatal treatments with these vitamins was observed.

Materials and methods

Newborn male and female (Charles River originated) closed bred Wistar rats were treated with 1.5 mg vitamin E (tocopherol acetate, Sigma, St.Louis USA) or 50 μg vitamin K_1 (phytomenadione, Konakion MM, Roche, Switzerland) subcutaneously (controls were injected with the vehicle only) and the sexual behavior was studied in three-month old animals.

The receptivity of *female rats* was measured by the help of indicator (experienced) males. The Meyerson index and the lordosis quotient were studied. The former gives a binary answer for the appearance of the lordotic response as a result of the primary mounting by males [17]. The latter is a ratio of the percentual lordosis number in ten mountings (L/M). For comparable results the females within the two-week study were screened only during estrus (the timing was checked by vaginal smears).

In each group five-six animals were tested a day. During the two-week testing period one animal was tested four times (in four consecutive days) as a mean.

The average of the daily data were used for evaluating significance with Student "t" and χ^2 tests.

Twenty control and twenty neonatally treated three-month old female animals were tested in each group.

Three-month old *males* (ten treated and ten controls) were tested in a 4-week period, once a week for 30 min, with receptive (ovariectomized and hormone treated) females. Five different patterns of behavior were distinguished [12], as inactivity, mounting, intromission, ejaculation and multiple ejaculation. Significances were evaluated as above.

Results and discussion

In the case of *female animals* the controls showed an acceptable activity in both indexes. In the neonatally vitamin E treated animals the Meyerson index as well, as the lordosis quotient was significantly lower, than in the control. In the neonatally vitamin K_1 treated animals these values were also lower, than in the appropriate controls, however without any significance (Fig. 1).

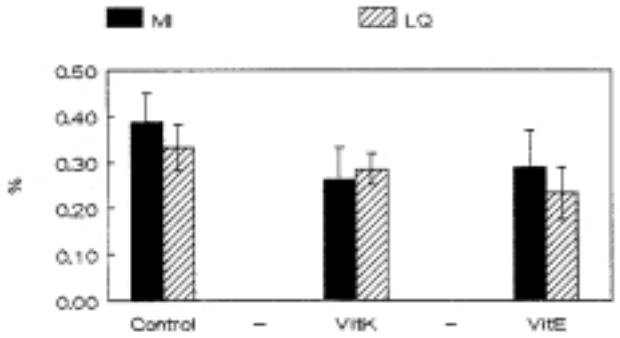

Fig. 1. Meyerson index (MI) and lordosis quotient (LQ) of control and neonatally vitamin E or K treated female animals. Significance: $p<0.01$ between control and vitamin E treated groups

In the case of *male animals* the activity of the controls was as usual. In the neonatally vitamin E treated group the number of inactive animals significantly increased and the number of intromissions dramatically decreased. No multiple ejaculation occurred at all. A not significant reduction of mounting was also observed. In the neonatally vitamin K_1 treated group there were no significant changes related to the controls, however a non-significant increase of inactivity, and decrease in the number of intromissions were observed (Fig. 2).

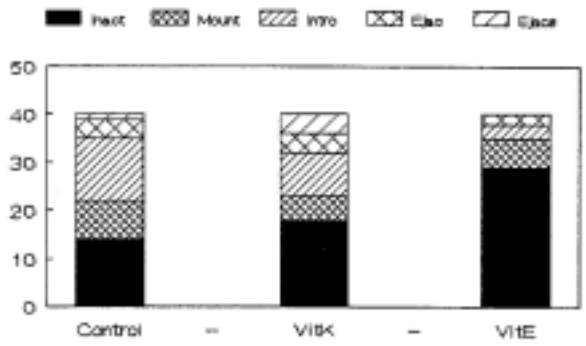

Fig. 2. Sexual activity of control and vitamin K or E treated male animals. Inact=inactive; Mount=mounting; Intro=intromission; Ejac=ejaculation; Ejacs=multiple ejaculations. Significance: $p<0.01$ between the control and vitamin E treated groups

Vitamin E (tocopherol) and K_1 (phytomenadione) are lipid soluble vitamins. Vitamin E is an antioxidant, however it has certain effects on sexuality [14]. For example, prolonged deficiency produces irreversible sterility due to degeneration of the germinal epithelium. In vitamin E deficient females, pregnancy terminates in about ten days with fetal death and resorption of the uterine content. However, in our experiments tocopherol was administered neonatally and only in a single dose, which could be enough for imprinting, but the molecule given is not present three months later. This points to the receptorial effect of neonatal tocopherol treatment. Only very scarce data are available on the receptorial effect of vitamin E. Catignani [2] and later Donchenko et al. [13] found specific receptor-like binding protein in rat liver cytoplasm and nucleus, respectively. Kitabchi et al. [16] and later Bellizzi et al. [1] demonstrated the presence of cell surface receptors. In our earlier experiments glucocorticoid receptor affinity was influenced by neonatal vitamin E treatment [9]. The present results show that neonatal tocopherol treatment deeply influenced sexual parameters, which used to be adjusted perinatally at receptorial level. This means, that vitamin E (administered neonatally), like the other lipid soluble vitamins, A and D [8] can influence steroid receptor mediated processes, such as sexual activity.

In case of vitamin K_1 (which is a blood clotting influencing factor) there are no data on the direct effect to sexuality in adult age, though it can influence indirectly some (glucocorticoid or vitamin D_3) receptors [18–20]. In our earlier experiments it had effect on the binding capacity of thymic glucocorticoid and uterine estrogen receptors, after single neonatal treatment [10]. The negativity of results in the present experiments shows that its imprinting effect is not general and the sexual sphere (brain's sexual centers) are hardly touched by it.

In earlier experiments perinatal vitamin A and D treatments (imprinting) caused strong changes in the receptor binding capacity and sexual behavior of adult animals [8, 11]. The present experiment also calls attention to the durable effect of vitamin E. Though the perinatal imprinting with vitamin K_1 did not cause alteration in sexual behavior, the administration of lipid soluble vitamins in the perinatal critical period seems to be worth considering.

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