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EFFECTS OF PROLONGED PRENATAL EXPOSURE TO MILD LEVELS OF CARBON MONOXIDE ON SEXUAL BEHAVIOR OF RAT PROGENY

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The developing brain seems to be markedly vulnerable to chronic, relatively mild, decrease in oxygen availability induced by carbon monoxide (CO), an air pollulant which is also one of the costituents of the cigarette smoke. Previous findings have demonstrated notable success in identifying neurochemical markers of developmental CO toxicity and suggest that neurotrasmitter systems may be particularly sensitive to early CO exposure. In particular, abnormalities in the development of dopamine- and serotonine-containing neurons have been found in brain areas of rats exposed to CO during prenatal and/or postnatal life (Storm and Fechter, 1985; Fechter et al., 1987).

Since both dopamine and serotonin play an important role in the regulation of rat sexual behavior (Gessa and Tagliamonte, 1975), the purpose of the present study was to investigate the influence of prenatal exposure to mild but chronic CO levels (75-150 ppm from day 0 to day 20 of pregnancy) on the copulatory activity and related ultrasonic vocalization of adult male rats during copulation. This last behavioral pattern is a sensitive indicator of subtle changes in sexual motivation produced by neuroactive compounds. The results showed a significant increase in mount-intromission latency in 80 day old rats exposed to the highest concentration of CO ($p<0.005$).This behavioral parameter did not seem to be affected by prenatal CO exposure in 200 day old rats, even though a trend toward an increase in mount-intromission latency was exhibited by 150 ppm CO-exposed animals. However, 365 day CO 150-treated rats still showed a significant increase in mount-intromission latency ($p<0.05$). Individual comparisons between groups showed a significant decrease in mount-intromission frequency in 80 day old rats prenatally exposed to CO (150 ppm)($p<0.002$). A marked decrease in this behavioral parameter was observed in 200 day old rats prenatally exposed to both 75 ppm ($p<0.05$) and 150 ppm ($p<0.02$) of carbon monoxide. Finally, the percentage of rats reaching ejaculation after six consecutive 10 min sessions was significantly ($p<0.01$) decreased by prenatal exposure to CO (150 ppm). The latency to the first 50 KHz call of the treated animals was not significantly different with respect to controls and, due to low number of ejaculating animals in treated groups, we couldn' t statistically evaluate the latency to the 22 kHz call.

The present data, showing that prenatal exposure to CO, at concentrations below those associated with overt signs of toxicity, induces long lasting alterations in sexual behavior of male rats, further confirm that the offspring of mothers who smoke during pregnancy may be at notable higher risk than epidemiological findings on birthweight and neonatal mortality suggest. Furthermore, the results of ultrasonic emissions during the copulatory behavior seem to exclude that sexual motivation could be involved in the alteration of sexual behavior of rats induced by prenatal exposure to CO.

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CANAVESE B. and COLITTI M. Department of Animal Production Sciences. University of Udine, ITALY. Observations under L.M. and SEM of opercle malformations in sea bream (*Sparus auratus*)

The externalisation of the gills in fish with opercle is caused by opercle disgenesis which compromises the anatomical integrity. The malformation is already known in Vertebrate teratology; now fish farmers have become aware of this problem because it seems to be associated with specific teratogenic sensibilities, poorly described to exogenous and endogenous factors, and considerable economic damage. The anomaly is very frequent in the sea bream (5-35%) and is not life-threatening. The characteristic anomalies were observed under L.M. and SEM during young and adult life. We studied 150 sea bream with opercle anomaly aged between 35 and 600 days. The malformation was two-sided in 41 cases (27%), one-sided on the right in 44 cases (30%) and one-sided on the left side in 65 cases (43%). When the malformation was two-sided it was the same on both sides in 58.3% of cases. Four kinds of opercle malformations were observed by stereomicroscopy and SEM from 70 day old subjects; the different degrees of teratological severity could be described as: (I) folding of the opercle edge from the superior corner toward the gill chamber and extension to 1/3 inferior part; (II) concave groove of opercle which discovers the gill chamber between 1/3 medial and superior part; (III) partial lack of opercle bone from the edge to the 1/3 inferior part; (IV) partial lack of opercle bone in the 1/3 inferior part and hypogenesis of branchiostegal rays. The *in toto* skeleton staining with methylene blue and red alizarin-sulphate in subjects aged between 35-70 days showed which opercle bones were involved in the malformation: folding and hypogenesis of branchiostegal rays, and of the opercle bones, the opercle and interopercle. The structural study of the malformation, carried out with serial sections, showed that the folding of the opercle edge occured very early and it is very important in the teratogenic process. The anomaly was also characterised by tissue modifications including agenesis of specific muscolar fibres and tissue junctions in the fold.

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Methods to Reduce Stress in Nose-Only Rodent and Head-Only Rabbit Reproductive Toxicity Studies. Christian, M.S., Hoberman, A.M., Rothenberg, S., Foss, J.A. and Parker, R.E. Argus Research Laboratories, a Genzyme Transgenics Company, Horsham, PA, USA.

Whole-body inhalation exposure procedures may cause eye and skin irritation that results in maternal stress. Use of nose- or head-only inhalation exposure procedures more closely controls exposure levels and causes less skin irritation but may cause stress associated with restraint, eye irritation and/or exposure to high ambient temperatures during restraint. Stress factors may result in altered maternal weight gain, heat prostration and increased corticosteroid levels, maternal perturbations associated with reduced embryo-fetal viability, reduced fetal body weights, increased fetal alterations and/or altered postnatal behavior/function. We have developed several ways to reduce maternal stress in nose-only and head-only exposure inhalation systems including: 1) training the animals; 2) cooling of the exposure chamber; and 3) application of eye ointment and wearing protective goggles. Use of these methods resulted in nose-only or head-only exposed animals having values similar to historical control values for oral, intravenous or topical maternal body weight data (daily body weight changes) and standard Caesarean-sectioning and morphological evaluations for rats and rabbits (embryo-fetal number and viability, fetal body weight, sex, and external, soft tissue and skeletal alterations) and postnatal evaluations for rats. Training was accomplished by an initial, short period when animals are placed in an appropriate restraint apparatus, followed by an approximately 48-hour period during which the animals are not re-exposed to the restraint procedures. This interval is followed by daily restraint intervals in the apparatus; the intervals are increased daily from approximately 15 minutes to a full daily exposure interval. Cooling of the exposure chamber is accomplished by circulating iced water and/or lowering room temperature; the exposure chamber is constantly monitored for temperature to ensure that ambient temperature requirements are maintained. Eye ointment is applied in each animals eyes, and pediatric swimming goggles (Spedo® Goggles) are worn by each rabbit during training and all exposure intervals. Maternal stress levels were monitored by continual observation and recording of rectal temperatures, while the animals were in the restraint apparatus. Maternal rectal temperatures remained stable. Maternal weight loss generally associated with the first day of restraint and eye irritation were essentially eliminated. Fetal evaluations identified comparable viability, body weights, morphologic alteration incidences and postnatal observations in litters obtained from trained pregnant dams/does and litters obtained from control dams/does in studies employing other routes.