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Effects of pre- versus post-conceptional iron and n-3 fatty acid supplementation of deficient rat dams on neurodevelopmental outcomes in the offspring

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Periconception is the period spanning the weeks directly before and after conception and is a crucial window for optimising neurodevelopment in offspring[1-4]. Iron and omega-3 fatty acids (n-3 FAs) are two vital nutrients for the development of the nervous system however, little research has been conducted into their importance during the periconceptional window[5-8]. This study investigated whether supplementing iron and n-3 FA deficient (ID and n-3 FAD) rat dams before conception compared to after conception results in different neurodevelopmental outcomes in offspring. We hypothesised that initiating iron and n-3 FA supplementation in deficient dams after conception would not be as efficacious in preventing impaired offspring neurodevelopment induced by double- deficiency, compared to initiating supplementation before conception.

Female rats consuming an ID and n-3 FAD diet were randomly allocated to receive iron and DHA/EPA supplementation either 10 days before (Pre-Fe+DHA/EPA) or 10 days after conception (Post-Fe+DHA/EPA). Dams and offspring (Pre-: n = 24; Post-: n = 26) were subsequently maintained on supplemented diets throughout the experiment. Between postnatal days 31–41, cognitive and behavioural tests were conducted on offspring. Offspring were euthanised between postnatal day 42–45 and n-3 FAs, iron and monoamine concentrations were measured in the hippocampus, striatum and frontal cortex. All outcomes were compared to offspring who were either iron and n-3 FA deficient (ID+n-3 FAD: n = 24) or sufficient (Control+Fe+DHA/EPA: n = 22). One-way ANCOVA, with sex as a covariate, was used to determine between-group differences and two-way ANOVA was used to explore diet-sex interactions.

There were no differences in brain iron or n-3 FA levels between Pre- and Post-Fe+DHA/EPA offspring ($P > 0.05$). Female Post-Fe +DHA/EPA offspring had greater norepinephrine concentrations in the frontal cortex (Pre-: 3.21 ± 0.57 ng/mg vs Post-: 2.50 ± 0.55 ng/mg; $P = 0.014$) and consumed less sucrose in the sucrose preference test (Pre-: 96.16 ± 1.73%; Post-: 90.15 ± 1.66%; $P = 0.010$) compared to Pre-Fe+DHA/EPA offspring. Female Post-Fe+DHA/EPA offspring also had significantly lower liver iron concentrations compared to female Pre-Fe+DHA/EPA offspring (Pre-: 537 ± 47.13 µg/L vs Post-: 310 ± 45.28 µg/L; $P = 0.034$). There were no other significant differences in monoamine concentrations or behavioural tests.

Our results indicate that supplementing ID and n-3 FAD mothers both before and after conception is efficacious in preventing neurodevelopmental deficits associated with deficiency. However, ID and n-3 FAD during the periconceptional period may alter reward-based learning in female offspring[9-11]. Additionally, optimising iron provision during periconception may have important implications for the prevention of postnatal ID-anaemia, particular during early infancy[12].

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