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Maternal dairy fat diet does not influence neurotrophin levels and cognitive performance in the rat offspring at adult age

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ABSTRACT

Cognitive development may be influenced by maternal nutrition especially fats. Indian population is vegetarian and main source of fat is dairy. This study investigates the effect of dairy fat consumption during pregnancy in an animal model on fatty acids, brain neurotrophins (brain derived neurotrophic factor: BDNF; and nerve growth factor: NGF) and cognitive performance in adult offspring. Pregnant Wistar rats were assigned to control (Control C) and four treatment groups: High fat diet (HFD); High fat diet supplemented with omega-3 fatty acids (HFDO); High fat diet deficient in vitamin B_{12} (HFBD); High fat deficient in vitamin B_{12} supplemented with omega-3 fatty acids (HFBDO). Half the dams were dissected on d20 of gestation, and the brains of their pups were collected. The remaining dams delivered on d22 of gestation and were assigned to a control diet. The cognitive performance of these adult offspring was assessed at 6 mo of age. Brain fatty acids were comparable to control in the pups at birth and offspring at 6 mo of age. The protein levels of BDNF in the pup brain at birth were lower in both the HFD ($p < 0.01$) and HFBD ($p < 0.05$) groups as compared to control. The mRNA levels of TrK B were lower ($p < 0.05$) in the pup brain at birth in the HFD as compared to control group. In the offspring at 6 mo of age the protein levels of BDNF and NGF in all the treatment groups were similar to that of control. However, the mRNA levels of only BDNF ($p < 0.01$ for both) were higher in the HFBD group as compared to both control and HFD groups. The cognitive performance of the adult offspring from various dietary groups was similar to control. In conclusion, consumption of a maternal high dairy fat diet although lowered the levels of brain BDNF in the pup at birth it does not affect the cognitive health of the adult offspring.

1. Introduction

Reports suggest that twelve percent of the global burden of diseases is due to mental and behavioral disorders and the majority is from low and middle income countries (Venkatashiva Reddy et al., 2013). It is reported that these disorders may have a neurodevelopmental origin and one of the key factors influencing neurodevelopmental outcome of the fetus is maternal nutrition (Marques et al., 2015).

The quantity and quality of dietary fats consumed during pregnancy have profound health implication during and after pregnancy (Schwab et al., 2014). The components of fats are fatty acids which provide energy and are required for the formation of cell membranes, hormones (Cerf and Herrera, 2016) and also proper brain development. Amongst the fatty acids the importance of omega-3 fatty acids like docosahexaenoic acid (DHA) in cell membrane functioning, brain and nervous system development is well established (Sugasini and Lokesh, 2015).

Omega-3 fatty acids regulate neurotrophins like brain derived neurotrophic factor (BDNF) (Zugno et al., 2015) and nerve growth factor (NGF) (Ikemoto et al., 2000). These neurotrophins play an important role in the development of neurological system and are essential for survival and protection of neurons throughout lifespan (Sofroniew et al., 2001). BDNF is important for learning and memory, and also modulates synaptic plasticity (Graves et al., 2016). Similarly NGF is also reported to mediate neuroprotection and cell survival (Oliveira et al., 2013). These neurotrophins (BDNF and NGF) bind to tropomyosin related kinase receptors (TrkB and TrkA respectively). Binding of neurotrophins to their receptors leads to autophosphorylation resulting in the activation of the transcription factor CREB (cAMP response-element binding protein). CREB regulates the expression of genes responsible for survival, growth, synaptic plasticity,

Abbreviations: ALA, Alpha linolenic acid; AA, Arachidonic acid; BDNF, Brain derived neurotrophic factor; CREB, cAMP regulatory element binding protein; DHA, Docosahexanoic acid; LA, Linoleic acid; MUFA, Monounsaturated fatty acids; NGF, Nerve growth factor; NA, Nervonic acid; PUFA, Polyunsaturated fatty acids; RME, Reference memory error; RWME, Reference and working memory error; TrkB, Tropomyosin receptor kinase; WME, Working memory error

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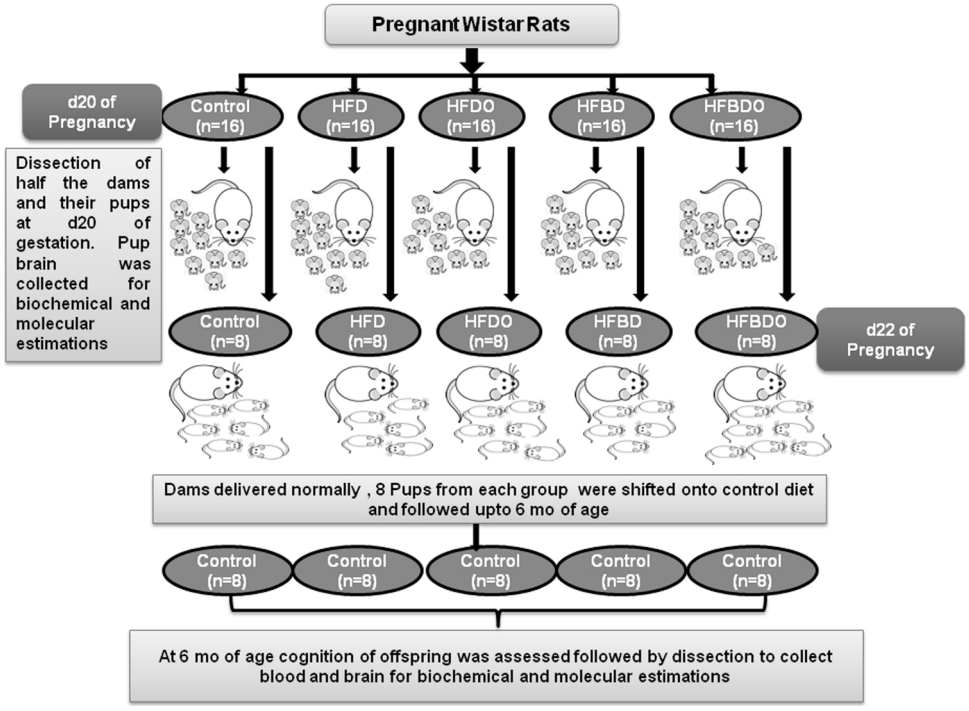

Fig. 1. Study Design.
Dietary Groups: Control (C); High Fat Diet (HFD); High Fat Diet Supplemented with Omega-3 Fatty Acids (HFDO); High Fat Diet Deficient in Vitamin B_{12} (HFBD); High Fat Diet Deficient in Vitamin B_{12} Supplemented with Omega-3 Fatty Acids (HFBDO).

Table 1
Pup Brain Fatty Acid Levels (g/100 g fatty acids) at d20 of Gestation.

Fatty acids (g/100 g fatty acids)	Control (n = 8)	HFD (n = 8)	HFBD (n = 8)
Linoleic Acid [18:2(n-6)]	1.40 ± 0.61	1.24 ± 0.93	1.02 ± 0.52
Alpha Linolenic Acid [18:3(n-3)]	0.44 ± 0.36	0.16 ± 0.05	0.18 ± 0.09
Arachidonic Acid [20:4(n-6)]	9.55 ± 1.17	10.15 ± 1.6	10.84 ± 4.04
Nervonic Acid [24:1(n-9)]	1.74 ± 1.17	2.09 ± 1.48	2.19 ± 0.82
Docosahexaenoic Acid [22:6(n-3)]	5.45 ± 1.44	5.51 ± 1.47	4.3 ± 1.03
Omega-3 Fatty Acids	6.44 ± 1.53	6.18 ± 1.62	5.96 ± 2.25
Omega-6 Fatty Acids	11.64 ± 1.21	11.78 ± 2.49	12.41 ± 4.29
Monounsaturated Fatty Acids (MUFA)	14.01 ± 4.77	14.53 ± 4.72	12.71 ± 5.51
Saturated Fatty Acids (SFA)	52.57 ± 10.22	51.61 ± 12.02	42.1 ± 12.35*

Values are expressed as Mean ± SD. p: Level of Significance; *p < 0.05 compared to control. Omega-3 (Alpha linolenic acid + Eicosapentaenoic acid + Docosahexaenoic acid), Omega-6 (Linoleic acid + Gamma linolenic acid + Di-homo-gamma-linoleic acid + Arachidonic acid + Docosapentaenoic acid); SFA (Myristic acid + Palmitic acid + Stearic acid); MUFA (Myristoleic acid + Palmitoleic acid + Oleic acid + Nervonic acid).
Dietary Groups: Control (C); High Fat Diet (HFD); High Fat Diet Supplemented with Omega-3 Fatty Acids (HFDO); High Fat Diet Deficient in Vitamin B_{12} (HFBD); High Fat Diet Deficient in Vitamin B_{12} Supplemented with Omega-3 Fatty Acids (HFBDO).

Table 2
Pup Brain Fatty Acid Levels (g/100 g fatty acids) at d20 of Gestation.

Fatty acids (g/100 g fatty acids)	Control (n = 8)	HFD (n = 8)	HFDO (n = 8)
Linoleic Acid [18:2(n-6)]	1.40 ± 0.61	1.24 ± 0.93	0.91 ± 0.54
Alpha Linolenic Acid [18:3(n-3)]	0.44 ± 0.36	0.16 ± 0.05	0.14 ± 0.08
Arachidonic Acid [20:4(n-6)]	9.55 ± 1.17	10.15 ± 1.6	8.74 ± 5.1
Nervonic Acid [24:1(n-9)]	1.74 ± 1.17	2.09 ± 1.48	0.79 ± 0.25
Docosahexaenoic Acid [22:6(n-3)]	5.45 ± 1.44	5.51 ± 1.47	6.76 ± 1.84
Omega-3 Fatty Acids	6.44 ± 1.53	6.18 ± 1.62	8.67 ± 2.19#
Omega-6 Fatty Acids	11.64 ± 1.21	11.78 ± 2.49	11.93 ± 3.82
Monounsaturated Fatty Acids (MUFA)	14.01 ± 4.77	14.53 ± 4.72	11.49 ± 3.3
Saturated Fatty Acids (SFA)	52.57 ± 10.22	51.61 ± 12.02	48.42 ± 12.04

Values are expressed as Mean ± SD. p: Level of Significance.Omega-3 (Alpha linolenic acid + Eicosapentaenoic acid + Docosahexaenoic acid), Omega-6 (Linoleic acid + Gamma linolenic acid + Di-homo-gamma-linoleic acid + Arachidonic acid + Docosapentaenoic acid); SFA (Myristic acid + Palmitic acid + Stearic acid); MUFA (Myristoleic acid + Palmitoleic acid + Oleic acid + Nervonic acid).
Dietary Groups: Control (C); High Fat Diet (HFD); High Fat Diet Supplemented with Omega-3 Fatty Acids (HFDO); High Fat Diet Deficient in Vitamin B_{12} (HFBD); High Fat Diet Deficient in Vitamin B_{12} Supplemented with Omega-3 Fatty Acids (HFBDO).

differentiation, dendritic spine formation, and long-term memory (Bathina and Das, 2015; Moosavi et al., 2015; Autry and Monteggia, 2012).

Currently, in India as a consequence of rapid nutrition transition there is an increase in the intake of dietary fat (Deepa et al., 2017; Mani and Kurpad, 2016), suboptimal consumption of vitamin B_{12} (Yajnik et al., 2008) and omega- 3 fatty acids. Till date animal studies reporting the effect of a maternal high fat diet on the spatial memory and learning are inconsistent with some showing beneficial effect (Bilbo and Tsang, 2010), others have shown the adverse effects of maternal high lard fat diet on the spatial memory in the offspring (Page et al., 2014; Tozuka et al., 2010) and still others have shown no effect (White et al., 2009). Reports also indicate that lard affects the function of the hippocampus (Niculescu and Lupu, 2009). In contrast a recent review reports the association of dietary dairy product cheese, yogurt consumption in humans with beneficial effects on cognition (Hess et al., 2016). Studies