Perinatal Dietary Protein Deficiency Alters Neurodevelopment and Reproductive health of F0 and F1-Generations of Sprague-Dawley Rat Models

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Introduction

The development of human conceptus absolutely depends on adequate and balanced supplies of nutrients, therefore an important element of neurodevelopment is improved nutritional status in women of child bearing age. (Guoyao et al., 2012; Colombo et al., 2018). Nutrients are dietary signals detected by cellular sensor systems that can influence phenotypic changes which may alter activities and homeostatic control process (Calder et al., 2013). Mental and reproductive health are one of the leading causes of disability worldwide (Atefe et al., 2019). This study sought to investigate the mechanistic consequence of modeled dietary protein deficiency (5% and 10%PD) in reproductive and neurodevelopmental process of F0 and F1-generations. Access to quality food is deteriorating and hence, maternal and neonatal health. While research is still limited, nutrition is expected to play a key role in potential neurodevelopmental plasticity.

Methodology

Diet and Animal treatment: F₀ Vaginal cytology was evaluated 3 weeks prebreed, time-mated reproductive male, the confirmed pregnant rats were separated to produce F₁ generation.

Fig 1: Schematic Diagram of Feeding design

Neurobehavioral Test:

- Surface Righting Reflex(SRR):** Evaluated on PN day 2-6 to measure the motor function and coordination. Christian et al., 2017
- Y-maze:** as described by Wright et al. (2006), The number and the sequence of arms entered were also recorded.
- Moriz Water Maze Test:** The time spent to reach the platform (escape

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latency) was measured. (Wang et al., 2015)

Brain Neurotransmitter Quantification: Using HPLC, serotonin and dopamine contents was determined by comparing the peak(Ebuehi et al., 2016).

Brain Antioxidant Status: determined by measuring activity of SOD and Catalase and quantity of nitric oxide and lipid peroxidation (Ebuehi et al., 2016).

Table 1: F₁-Reproductive Function Test

	21%PD	CONTROL	10%PD	5%PD
Fertility Index	100	99 ± 1.4	64 ± 1.8a**	51 ± 1.4a**
Birthweight	5.08 ± 0.5	4.8 ± 0.3	3.5 ± 0.8	3 ± 0.7a**
Survival Rate	95 ± 0.02	96 ± 0.02	68 ± 0.03	56 ± 0.01
Pubertal Age (PND)	36	40	48	56

a < significantly difference from 21%, and control Protein Diet group > Asterisks indicate the level of significance (*P<0.05; **P< 0.01), *** P<0.0001 . PND: Postnatal Day.

Fig4:Escape Latency; Statistically significant difference among the groups are identified as; * 21% vs 10% , 5% PD and Control, # Control vs 21%, 10%, and 5% at P< 0.05..

Table 2: F₀ Brain Oxidative Stress

GROUPS	TOTAL PROTEIN (mg/ml)	CATALASE (U/L/min)	GSH (μmol/L)	SOD (U/L/min)	MDA (μmol/L)	NITRIC OXIDE (mg/ml)
CONTROL	31.43 ± 6.1	20.72 ±4	45 ± 3.8	0.0249	0.29 ± 0.09	6.989 ± 1.2
21%PD	41.35± 8	15.92 ±3.99	53.14 ± 4	0.0438	1.02± 0.9	7.147 ± 0.4
10%PD	34.16± 1.41	21.29 ±1.96	45.89 ± 0.98	0.1989	2.5 ± 0.7a**	1.585 ± 0.7 a**b**
5%PD	20.23± 2.98a*	34.89 ±5a**b*c*	37.74 ± 4.7a*	0.00334a**	24.55±4.6a**b**	1.6 ± 1.1 a**b**

a < significantly difference from 21% Protein Diet group >
c < significantly difference from 10% Protein Diet group >

Fig 5: Oestrus Cyclicity; Development of oestrus cycle irregularity within three weeks of vaginal cytology. 5% PD showed a significantly increased time in the diestrus phase and decreased time in estrus phase compared to other diet groups, at P<0.05.

Fig2: Mean reflex response score:*; significantly reduced response time in 5% protein deficient group, at P< 0.05. compared to other groups. PD; Protein

Fig 3:%Spontaneous Alternations: φ; Statistically significant difference between individual group and the hypothetical value of 50% at P< 0.05.

Discussion

Protein Restriction altered the reproductive function of F₀ and F₁ protein deficient models, displayed as lowered fertility index (5%PD;35%±2.5 10%PD; 66%±2.2 compared to 21%PD;88.4%±0.8, and control 85.8%±1.3), delayed onset of puberty, irregular cyclicity and changes in endocrine events as a result of the suboptimal perinatal exposure. Increased oxidative damage and altered neuro-transmission in the brain of F₁ generation(Brain serotonin and dopamine levels respectively; 5%:2.7±0.3;36.25±0.57., 10%;2.9±0.3 ;17.75±0.94., 21%;7.8±0.9; 7.95±1.1., control;7±0.2;11.55±0.7), underlie the perturbed neurobehavioral display and cognitive deficit in the nutritionally challenged groups.

Conclusion

There was a perturbed neurobehavioral display and altered reproductive and cognitive function of F₀ and F₁ models of the nutritionally challenged groups. Therefore, Every woman especially of reproductive age and neonates should be placed at priority in caregiving and nutrient supply, because the downstream effects of the consequences not only end with them, but with subsequent generations, which could translate to transgenerational psychosis and turbulence. Every child has a right to optimal cognitive, social, and emotional behavioral development.

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