EXPOSED TO PERFLUOROOCTANE SULFONATE DURING EMBRYONIC PERIOD RESULT IN IMPAIRED DEVELOPMENT OF THE NERVOUS SYSTEM

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Introduction

Perfluorooctane sulfonate (PFOS) is a class of environmental pollutant with versatile toxicities[1]. In May 2009, the Stockholm Convention listed PFOS as a persistent organic pollutant. PFOS can accumulate in breast milk and be passed to the fetus[2], thereby increasing the risk of damage to the offspring. As a neurotoxic environmental contaminant, PFOS has made a great impact on brain tissue. Neurotoxicity studies have shown that PFOS can elevate the glutamate level in the nervous system, and destroy the central nervous system (CNS)[3]. PFOS can pass through the blood-brain barrier, becoming enriched in brain tissue, and impacting on the nervous system. Exposure to PFOS at early age can induce adult behavioral defects in mice, affect the cholinergic system, confirming that PFOS has potential toxic effects on the development of the nervous system[4]. However, the developmental neurotoxicity study of PFOS is still lacking. Cross-foster model was established in this study, to investigate the developmental neurotoxicity of PFOS, and to identify the sensitive period of exposure.

Materials and methods

Pregnant rats were exposed to PFOS by drinking water which contained 0, 5, 15mg/L PFOS throughout gestation and lactation period. On the day of birth, litters born to treated and control dams were cross-foster, set as unexposed control (CC), pups exposed only prenatally (TC5, TC15), only postnatally (CT5, CT15) or both prenatally and postnatally (TT5, TT15). During the exposure, body weights of litters were measured every week, and the length of eye opening was recorded. Morris water maze (MWM) was used to study the learning and memory abilities of pups[5]. The escape latency was recorded to investigate in rats learn ability at postnatal day 35-41 (PND35-41). A probe trial was performed at the next day after finishing the hidden platform acquisition task (at PND42) to investigate in rats memory ability of the original platform. Data were analyzed via SPSS 16.0 software and expressed as mean ± SE (standard error). One-way ANOVA and two-repeated measure ANOVA were used to determine the differences between the control and treatment groups.

Results and discussion

The results showed that PFOS caused growth retardation, prolongation of eye opening, and reducing in birth weight of pups compared with the control group. Pups weight of PFOS exposure groups is significantly lower than the control group from PND7 (Table 1). Body weights of pups with prenatal exposure were lower than that with postnatal exposure under the same concentrations of PFOS exposure, indicating that the prenatal exposure to PFOS can affect the growth and development. Eye opening of the TT15, TC5, CT15 and TC15 groups were significantly delayed compared with the control group. In 5mg/L exposure group, eye opening was significantly prolonged in TC5 group, but not in CT5 group, indicating that the embryonic pups are more sensitive to PFOS (Fig. 1).

Table 1 Mean (±SE) pups weight in postnatal days.

Groups	Postnatal days					
	PND1	PND7	PND14	PND21	PND28	PND35
CC[a]	5.32±0.14	15.39±0.67	31.93±0.70	48.40±0.88	70.41±1.40	103.44±2.65
TT5[a]	5.26±0.08	13.66±0.81**	22.51±0.93**	34.20±1.50**	52.98±2.39**	93.06±6.18**
TT15[a]	5.29±0.09	12.54±0.30**	27.46±0.79**	39.98±1.20**	58.36±1.54**	85.46±2.49**
CT5[b]	5.84±0.24	14.67±0.59	26.73±0.64**	38.90±1.09**	56.25±1.65**	72.61±1.42**

TC5[b]	5.02±0.06	12.03±0.12**	24.16±0.58**	37.20±0.65**	56.84±1.25**	75.98±2.08**
CT15[c]	5.50±0.14	10.87±0.21**	23.92±0.96**	32.42±1.03**	47.09±1.64**	65.99±1.89**
TC15[c]	4.71±0.07**	13.30±0.42**	27.97±0.69*	42.77±1.01**	66.35±1.15	88.06±1.39**

* Statistically significant ($p < 0.05$), ** Statistically significant ($p < 0.01$).
[a] n= 14 rats in CC, TT5, TT15 groups respectively.
[b] n= 17 rats in CT5, TC5 groups respectively.
[c] n= 20 rats in CT15, TC15 groups respectively.

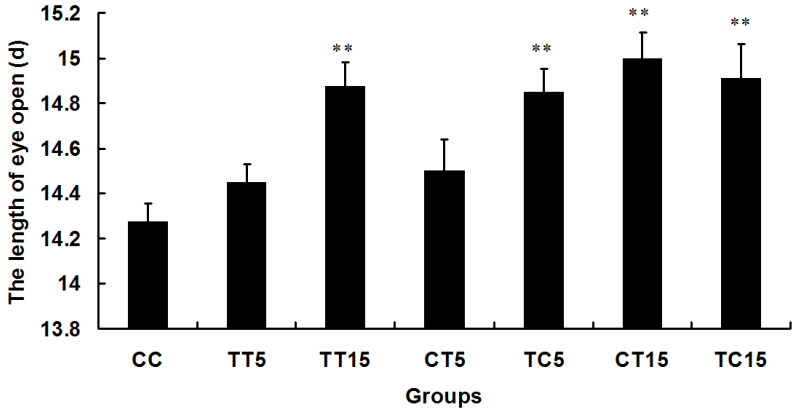

Fig. 1 The length of eye opening in exposure groups. * Statistically significant ($p < 0.05$), ** Statistically significant ($p < 0.01$). n=40 rats in CC, TT5, TT15, TC5, CT15 groups respectively, n=14, 23 in CT5, TC15 groups respectively.

Hidden platform test can reflect the learning ability of the offspring. MWM results showed that the escape latency of TT15 and TC15 exposure groups was significantly longer than the control group from PND37. In addition, escape latency of pups with prenatal exposure to PFOS was longer than those with postnatal exposure at the same PFOS exposure levels (Fig. 2), which suggested that stronger neurotoxic effects occurred on the developing nervous system when pups were exposed to PFOS at embryonic period. These results showed that PFOS exposure resulted in the decline of offspring learning abilities, especially the prenatal exposure. Probe trial experiment to reflect the memory ability of the offspring of the original platform. Probe trial experiment indicated that the time spent in the target quadrant of pups from TT15 group was significantly shorter than those from control group, which suggested that pups from TT15 group have poor memory ability than those from control group (Fig. 3). PFOS caused the decline of offspring memory abilities may be the result of co-exposure of prenatal and postnatal. As senior functional activity of the CNS, the molecular cytology basis of learning and memory ability is synaptic plasticity, and the decline of learning and memory ability maybe one performance of the synaptic plasticity injury. Prenatal exposure of PFOS may inhibit the growth of synapses, thus elevating the glutamate level in the nervous system, destroying the CNS, and influencing behavioural response. Cross-foster model has been built to evaluate the possible mechanisms of the developmental neurotoxicity of PFOS. Exposure to PFOS during the critical period of development of the brain may have neurotoxic effects on the CNS by mediating the molecules of calcium signaling pathway[6], which may be one of important ways PFOS led to the decline of learning and memory ability.

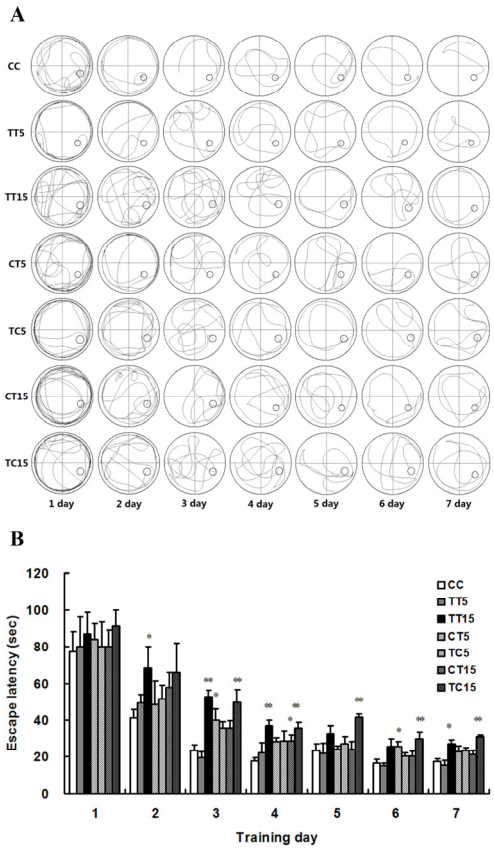

Fig. 2 Escape latency of MWM after PFOS exposure. A, typical swim trajectories of rats in exposure groups in searching for the hidden platform. B, average escape latencies, mean±SE. * Statistically significant ($p < 0.05$), ** Statistically significant ($p < 0.01$). n = 8 rats in CC group, n = 6 rats in TT5 group, n = 10 rats in TT15, TC5, CT15, TC15 groups respectively, and n = 9 rats in CT5 group.

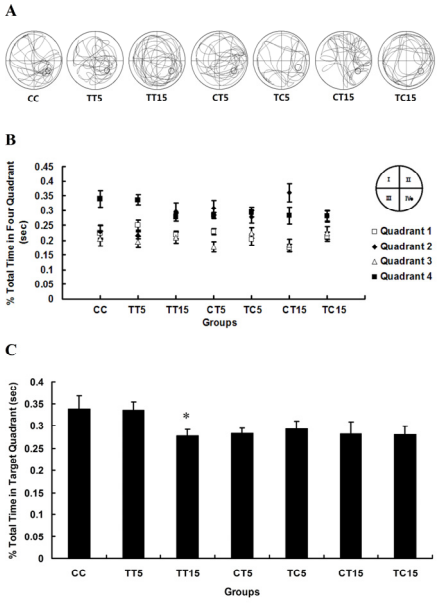

Fig. 3 Percentage of swimming time in different directions at 8th training day. A, representative original swimming traces. B, the percentage of time spent in four quadrants in various groups, mean±SE. Quadrants 4 represents the target quadrant. C, the percentage of time spent in the target quadrant in different groups. n = 8 rats in CC group, n = 6 rats in TT5 group, n = 10 rats in TT15, TC5, CT15, TC15 groups respectively, and n = 9 rats in CT5 group.

PFOS caused the developmental delay of offspring, as well as decline of learning and memory abilities, and prenatal period might be the critical stage to PFOS exposure. In summary, these findings contribute to clarify the neurotoxic mechanism of PFOS, and provide further scientific basis for learning and memory ability, which needs to be further explored.

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