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γ-氨基丁酸通过其A型受体参与小鼠母胎血管的形成研究

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Title: Gamma-aminobutyric acid participates in mouse feto-maternal vasculogenesis through GABA type A receptor

作者: 赵海; 马婧; 卢俊杰; 谭冬梅; 张倩; 罗文萍; 谭毅
重庆医科大学实验动物中心

Author(s): Zhao Hai; Ma Jing; Lu Junjie; Tan Dongmei; Zhang Qian; Luo Wenping; Tan Yi
Laboratory Animal Center, Chongqing Medical University, Chongqing, 400016, China

关键词: γ-氨基丁酸; 蜕膜化; 迷路区; 胎盘

Keywords: γ-aminobutyric acid; decidualization; labyrinth; placenta

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摘要: 目的 探讨不同浓度的γ-氨基丁酸 (γ-aminobutyric acid, GABA) A型受体激动剂/抑制剂对小鼠胎盘形成的影响。 方法 免疫组化检测孕鼠中晚期胎盘中GABA的A型受体（$GABA_AR$）π亚基（GABRP）的表达规律。将昆明孕鼠分为8组，每组3只，处理组从妊娠第7～13天分别腹腔注射0.009 5、 0.095 mg/kg及0.95 mg/kg A型受体激动剂和0.018 4、0.184 mg/kg 及1.84 mg/kg的A型受体抑制剂溶液，对照组注射生理盐水，空白组不作任何处理。第14天时称量各组胎盘和胚胎，HE染色观察胎盘形态学变化，检测增殖细胞核抗原(proliferating cell nuclear antigen, PCNA)及血管内皮生长因子（vascular endothelial growth factor, VEGF）表达情况。 结果 GABRP强表达于孕鼠第10～17天的母胎蜕膜区；与对照组比较，0.95 mg/kg $GABA_AR$激动剂组蜕膜区血管数量和胎盘迷路区胎儿有核红细胞的数量显著增加（$P<0.05$），同时迷路区PCNA和VEGF的表达显著增加（$P<0.05$）；1.84 mg/kg $GABA_AR$抑制剂组胎盘和胚胎的质量显著降低（$P<0.05$），同时迷路区PCNA和VEGF表达均降低。 结论 GABA可能通过与其A型受体结合参与调节小鼠胎盘增殖和血管的生成过程。

Abstract: Objective To study the potential roles of γ-aminobutyric acid(GABA) type A receptor ($GABA_AR$) agonist and antagonist in mouse placentation.

Methods Immunohistochemistry was applied to detect the expression of the π subunit of $GABA_AR$ (GABRP) in the placentas of mid and late phase during mouse

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pregnancy. Kunming pregnant mice were divided into 8 groups (n=3) randomly, including 3 treatment groups with daily intraperitoneal injection of $GABA_AR$ agonist of 0.009 5, 0.095, and 0.95 mg/kg separately from D7 to D13, 3 treatment groups with daily intraperitoneal injection of $GABA_AR$ antagonist of 0.018 4, 0.184, and 1.84 mg/kg separately from D7 to D13, a control group with injection of saline solution, and a blank group without any treatment. The weights of embryos and placentas were measured and the structure of placenta was observed by HE staining on D14. Besides, the state of proliferation and vasculogenesis in the placenta were evaluated by the expression levels of proliferating cell nuclear antigen (PCNA) and vascular endothelial growth factor (VEGF) using immunohistochemical assay. Results GABRP was mainly expressed in the decidua basalis of the uterus from D10 to D17 in pregnant rats. The numbers of blood vessels in the placental decidual zone and nucleated red cells in the labyrinth were significantly increased in the 0.95 mg/kg $GABA_AR$ agonist group (P<0.05), while the expression of PCNA and VEGF was also significantly increased in the placenta labyrinth (P<0.05). Surprisingly, the weights of placenta and embryo were significantly decreased in the 1.84 mg/kg $GABA_AR$ antagonist group as compared to the control group (P<0.05), while the expression of PCNA and VEGF was reduced in the placenta labyrinth. Conclusion GABA may participate in mouse placentation and vasculogenesis *via* $GABA_AR$.

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