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研究課題名（和文） ニューロステロイドによる脳の性分化メカニズム

研究課題名（英文） Mechanisms of brain sex differentiation induced by neurosteroids

研究代表者

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研究成果の概要：

脳の性分化機構は未解明の重要課題である。本研究は、脳の自立的性分化機構の解明を目的として、脳の構造と行動に最も典型的な性差を示す鳥類のウズラを用い、脳が合成するニューロステロイドに着目して、ニューロステロイドによる脳の性分化誘導作用を解析した。その結果、脳の性分化に重要となる感受性期の間脳では、転写調節因子である Ad4BP/SF-1 がニューロステロイド合成酵素の発現に性差を導くことでニューロステロイド合成に性差が生じて脳の性分化が誘導されることが見いだされた。

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キーワード：(1) 脳の性分化 (2) 性的二型核 (3) ニューロステロイド (4) アポトーシス抑制因子 (5) Ad4BP/SF-1 (6) 鳥類

1. 研究開始当初の背景

脳の性分化機構は未解明の重要課題である。従来、脳の性分化には生殖腺が合成する性腺ステロイドホルモンが重要な役割を担うと考えられていたが、最近になり、性腺ステロイドホルモンに依存しない脳の自立的性分化機構が鳥類などの研究により示唆されるようになった。

2. 研究の目的

本研究は、脳の構造に最も典型的な性差を示す鳥類のウズラを用い、脳が合成するニューロステロイドに着目して、ニューロステロイドによる脳の自立的性分化機構の解明を目的として実施した。

3. 研究の方法

ニューロステロイドによる脳の自立的性分化機構を明らかにするために、ニューロステロイドによる脳の性分化誘導作用、脳の性分化を誘導するニューロステロイドの作用機構、ニューロステロイド合成の性差を誘導する分子機構を解析した。

4. 研究成果

ニューロステロイドによる脳の性分化誘導作用を明らかにするために、まずニューロステロイド合成の性差を解析した結果、脳の性分化に重要となる感受性期の間脳ではニューロステロイド合成酵素であるP450_{arom}とP450₇の発現に明確な性差があり、エストラジオールと7 α -ヒドロキシプレグネノロンの合成は雄が雌に較べて高いことがわかった。感受性期の雄の間脳においてこれらのニューロステロイド合成を阻害したところ、性的二型核である内側視索前核の発達が抑制されて間脳が雄型から雌型になった。

脳の性分化を誘導するニューロステロイドの作用機構を解析したところ、ニューロステロイドがアポトーシス抑制因子 PEP-19 の発現を誘導して間脳の内側視索前核の性差が形成されることが示された。

ニューロステロイド合成の性差を誘導する分子機構を解析したところ、感受性期の間脳ではAd4BP/SF-1がP450_{arom}とP450₇の発現の性差を導いてエストラジオールと7 α -ヒドロキシプレグネノロンの合成に性差が生じることが示された。

5. 主な発表論文等

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