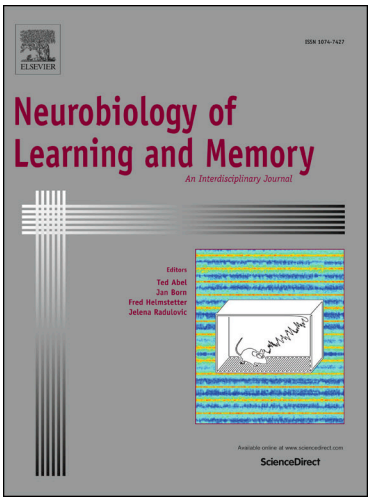


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# 17 beta- estradiol synthesis modulates cerebellar dependent motor memory formation in adult male rats

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## Abstract

Neurosteroid 17 beta-estradiol (E2) is a steroid synthesized *de novo* in the nervous system that might influence neuronal activity and behavior. Nevertheless, the impact of E2 on the functioning of those neural systems in which it is slightly synthesized is less questioned.
The vestibulo-ocular reflex (VOR) adaptation, may provide an ideal arena for investigating this issue. Indeed, E2 modulates cerebellar parallel fiber-Purkinje cell synaptic plasticity that underlies encoding of VOR adaptation. Moreover, aromatase expression in the cerebellum of adult rodents is maintained at very low levels and localized to Purkinje cells. The significance of age-related maintenance of low levels of aromatase expression in the cerebellum on behavior, however, has yet to be explored. Our aim in this study was to determine whether E2 synthesis exerts an effective and persistent modulation of VOR adaptation in adult male rats.
To answer this question, we investigated the acute effect of blocking E2 synthesis on gain increases and decreases in VOR adaptation using an oral dose (2.5 mg/kg) of the aromatase inhibitor Letrozole in peri-pubertal and post-pubertal male rats.
We found that Letrozole acutely impaired gain increases and decreases in VOR adaptation without altering basal ocular-motor performance and that these effects were similar in peri-pubertal and post-pubertal rats.
Thus, in adult male rats neurosteroid E2 effectively modulates VOR adaptation in both of the periods studied.
These findings imply that the adult cerebellum uses E2 synthesis for modulating motor memory formation and suggest that low and extremely localized E2 production may play a role in adaptive phenomena.

**Keywords**: Neurosteroids, Plasticity, Vestibulo-ocular reflex adaptation, Cerebellum, Purkinje Cell, Behavior

## 1. Introduction

The steroid 17 beta-estradiol regulates structural and functional adjustments in neuronal circuits, including changes in spine density, synaptic connectivity, synaptogenesis and synaptic activity (McEwen and Alves, 1999; Kim et al., 2002; Leranth et al., 2003; Hara et al., 2015; Tuscher et al., 2016) that underlie learning and memory formation (Fu and Zuo, 2011)

Thus, it is not surprising that 17 beta-estradiol is also involved in the modulation of various forms of behavior (Andreescu et al., 2007; Taziaux et al., 2007; Luine, 2014).

Although the effects of 17 beta-estradiol have been historically associated with the long term action of circulating hormone on genomic mechanisms that require several days to occur (Good et al., 1999; Cooke and Woolley, 2005), it also has been found that this steroid acutely modulates neuronal activity and behavior within a few minutes after its