FENS Forum 2010 - Amsterdam

- Posters: to be on display from 8:00 to 13:15 in the morning and from 13:30 to 18:45 in the afternoon. Poster sessions run from 09:30 to 13:15 in the morning and from 13:30 to 17:30 in the afternoon. A one hour time block is dedicated to discussion with the authors (authors should be in attendance at their posters as from the time indicated.)
- For other sessions, time indicates the beginning and end of the sessions.

First author Pilar-Cuellar, Fuencisla (poster)

Poster board C115 - Sun 04/07/2010, 12:15 - Hall 1
Session 017 - Mental disorders 1
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Title Subchronic treatment with the selective serotonin re-uptake inhibitor fluoxetine and the 5-HT2A/2C antagonist ketansesrine induces an increase in BDNF and beta-catenin in hippocampus

Text

A neurotrophic hypothesis has been recently proposed to explain the molecular effects of antidepressant drugs. Chronic antidepressant treatment with selective serotonin re-uptake inhibitors (SSRIs) induces an increase in the expression of some neurotrophic factors such as brain derived neurotrophic factor (BDNF). An increase of the proliferation marker beta-catenin has also been associated to antidepressant treatment. Both BDNF and beta-catenin have been correlated to a higher cell proliferation in the dentate gyrus (DG) of the hippocampus. It has been proposed that the coadministration of SSRIs and 5-HT2A antagonists could enhance antidepressant responses leading to an early-onset of action.

In this work we have studied the effects of a subchronic treatment (7 days) with fluoxetine (5 mg/kg/day; i.p.) and fluoxetine+ketanserine (association group, 0.1 mg/kg/day; i.p.) on mRNA expression of BDNF and TrkB (in situ hybridization), cell proliferation in the DG of the hippocampus (BrdU incorporation), beta-catenin levels in hippocampus (Western blot) and 5-HT2A receptor functionality ([35S]GTPgammaS labeling). Forced swimming test (FST) was also carried out to confirm the antidepressant response.

In contrast with the results of the fluoxetine group, BDNF expression increased significantly in the association group in the CA3 (130±16%; $p<0.05$) and DG (146±22%; $p<0.05$) of the hippocampus, without modification in TrkB expression. There were no significant changes in 5-HT2A receptor functionality. As well, BrdU labeling was not significantly modified, although there was a tendency to the increase in the association group. A clear increase in beta-catenin expression was observed in the association group in total homogenate (120±7%; $p<0.05$) and membrane (134±9%; $p<0.001$) fractions of the hippocampus, in contrast to the lack of changes in the fluoxetine-treated animals. The coadministration of fluoxetine+ketanserine also produced a reduction in the immobility time in the FST when compared to the vehicle group ($p<0.05$).

These results suggest that 5-HT2A antagonism could contribute to an increase in neural plasticity prior to SSRI-induced proliferative changes in hippocampus, as a mechanism for a short-acting response.

Theme C - Disorders of the nervous system
Mental disorders - Affective disorders

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