Antidepressants enhance neuronal plasticity in the visual system

April 17 2008

In the April 18 issue of *Science*, scientists from the Scuola Normale Superiore in Pisa, Italy and the Neuroscience Centre at the University of Helsinki, Finland, provide new information about the mechanism of action of antidepressant drugs. In addition, the study suggests that antidepressants could also be used for the treatment of amblyopia. However, to produce a functional effect, antidepressant treatment also seems to require environmental stimuli, such as rehabilitation or therapy.

According to Professor Eero Castrén at the University of Helsinki, the original objective of the study was to learn more about why the antidepressant effect of fluoxetine (also known as Prozac) and other selective serotonin reuptake inhibitors develops so slowly, many weeks after starting treatment.

Castrén's research group has approached this question by examining the growth factor, brain-derived neurotrophic factor (BDNF), which influences plasticity of the nervous system or in other words, the ability of brain cells to change their structure or function in response to stimuli. Antidepressants seem to act through BDNF, thus enhancing the plasticity of the nervous system, at least in certain brain areas. However, it has been unclear how antidepressant-induced increases in BDNF could relieve depression.

Neuronal plasticity of the developing visual cortex has been well characterised. Therefore, this classical model of the visual cortex was utilised to examine the effect of fluoxetine on neuronal plasticity,

although there was previously no evidence that antidepressants would act on the visual system. During early childhood, if one eye remains weaker than the other eye, the neuronal connections of the stronger eye take over the visual cortex while the connections of the weaker eye retract. During a critical period of early childhood, neuronal connections are in a highly plastic state, and the vision of the weaker eye can be strengthened by covering the better eye, thus reinforcing the connections of the weaker eye to the visual cortex. In adolescence however, after the critical period has closed, plasticity is reduced and covering the better eye no longer strengthens the connections of the weaker eye which remains poor in vision throughout adulthood.

The experiments, mainly conducted by the research group of Professor Lamberto Maffei in Pisa, showed that treatment with the antidepressant, fluoxetine reopened the critical period of plasticity in the visual cortex of adult rats. In experiments where one eye of a young rat was covered during the critical period and reopened only in adulthood, vision improved in the weaker eye to finally equal that of the healthy eye when fluoxetine treatment was combined with covering the healthy eye. This fluoxetine-induced enhancement of plasticity was associated with increased BDNF and reduced cortical inhibition in the visual cortex, which advanced reorganisation of the neuronal connections.

Since fluoxetine, when combined with covering the better eye, improved vision in the weaker eye of adult rats, it is possible that antidepressants could be similarly used in amblyopic humans. The results suggest that the improved plasticity induced by antidepressants leads to a functional neuronal reorganisation in the cerebral cortex. The ability of an antidepressant to facilitate the reorganisation of neuronal connections in a brain area not associated with mood, suggests that similar treatment strategies might also be useful in the treatment of other brain disorders.

It is important to note that fluoxetine improved vision in the weaker eye

only if the better eye was covered. This suggests that while antidepressants provide the possibility of rearranging cortical connections, environmental stimuli are required to guide the rearrangement to produce the desired effect.

It is possible that defective neuronal connections in cortical areas related to mood regulation might predispose people to depression. The enhanced plasticity provided by the antidepressant might allow reorganisation of cortical connections and function. However, Castrén emphasises that antidepressants do not repair the network on their own, but that functional recovery also requires environmental guidance, such as social interaction, rehabilitation or therapy.

Source: University of Helsinki