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Can Selective Serotonin Reuptake Inhibitors (SSRI) improve motor recovery after stroke? What is the role of Neuroplasticity?

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What is neuronal plasticity?

Neuronal plasticity or Neuroplasticity refers to the ability of the brain to change as a result of one's experience. It is basically a flexible property of the neurons or neuronal networks to change their physiological and morphological characteristics and adapt to new situations arising from environmental situations like trauma or stroke.

Why is this concept important? What was tested in the FLAME study?

The lifetime prevalence of stroke in Pakistan as quoted by a recent community based study is 19% which is dramatically high. Approximately two thirds of these stroke survivors have residual neurological deficits. At the present time, only tissue plasminogen activator (tPA) is approved for use in the management of acute ischaemic stroke in an attempt to reduce the severity of brain damage. However, the use of tPA is limited due to several factors, including the narrow time window over which it must be used, delays in diagnosis, misdiagnosis, cost constraints or fear of adverse side effects. Therefore more attention needs to be focused on alternative strategies to reduce the long-term disability and functional impairment after stroke, probably by enhancing brain plasticity.

The aim of a new study called "FLAME" (Acronym for - Fluoxetine for Motor Recovery After Acute Ischaemic Stroke) was to investigate if fluoxetine was capable of enhancing motor recovery, when given soon after an ischaemic stroke to patients who have moderate to severe motor deficits.

This is because earlier clinical trials have suggested that fluoxetine (a drug used in the treatment of depression, obsessive-compulsive disorders) enhances motor recovery by increasing serotonergic transmission, formation of new synaptic contacts and cortical over-stimulation but its clinical efficacy was still unknown.

Who were the participants? What was the Intervention?

Patients with acute ischaemic stroke causing hemiplegia or hemiparesis were prospectively enrolled from 9 stroke units in France. They were mostly between 60-66 years of age. Most of them had cortical (anterior circulation) infarcts and moderate to severe disability as measured by MRS. Both the intervention arm (fluoxetine 20mg PO daily for 3 months) and the placebo arm were well matched for their risk factor profile, demographics and stroke severity.However, patients with severe post-stroke disability and clinically diagnosed depression were excluded.

All patients received standard physiotherapy.

What were the findings?

A total of 118 patients were randomly assigned to fluoxetine (n=59) or placebo (n=59), and 113 were included in the analysis (57 in the fluoxetine group and 56 in the placebo group). Two patients died even before day 90 and three withdrew themselves from the study.The results showed that the Fugl-Meyer motor scale (FMMS) improvement at day 90 was significantly greater in the fluoxetine group than in the placebo group (an improvement of 36 vs 24 points).

The mRS scores showed more independent patients (scores 0-2) in the fluoxetine group than in the placebo group at day 90.Occurrence of depression during the 3 months was significantly lower in the fluoxetine group than in the placebo group.

What were the conclusions?

The study revealed that in patients with ischaemic stroke and motor deficits, the early prescription of fluoxetine along with physiotherapy helped in enhancing the motor recovery over a period of 3 months. The authors also concluded that early use of Fluoxetine also prevents against post-stroke depression, which is another important cause of functional debility after stroke. This is the first largest randomized placebo controlled trial to show that treatment with an SSRI is associated with improved motor recovery after an acute ischaemic stroke. This study provides new information regarding the role of fluoxetine in plasticity, neurogenesis, and neuronal differentiation. It has identified the superiority of fluoxetine over placebo in improving functional recovery in stroke patients , independent of its effects on depression.

How can this study effect our clinical practice?

Stroke survivors and their families often find it

difficult to manage this long-term condition given the abrupt transition from being "healthy" to having disability. The situation is further exacerbated by the lack of community-based programmes and rehabilitation services that may help survivors reduce the risk of recurrent events and improve quality of life. At present, most patients with ischaemic stroke are not given antidepressant drugs unless they show appreciable symptoms of depression. This study has provided useful evidence regarding the role of fluoxetine in neuroplasticity, particularly when it is started in the acute phase of stroke, thereby helping motor recovery.

Acknowledgement and Disclosure Statement

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Recommended Reading

1. Chollet F, Tardy J, Albucher JF, Thalamas C, Berard E, Lamy C, et al. Fluoxetine for motor recovery after acute ischemic stroke (FLAME): A randomised placebo-controlled trial. Lancet Neurol 2011; 10: 123-30.