

Final report summary:

Does fluoxetine improve recovery after stroke?

A Multicentre randomised trial to establish the effect (s) of routine administration of Fluoxetine in patients with a recent stroke: start-up phase

PROJECT CODE: TSA 2011/01
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Why did we fund this research?

Over 80% of stroke survivors will be left with arm or leg weakness as a result of their stroke, significantly affecting their quality of life and independence¹.

Fluoxetine, more commonly known as 'Prozac', is an effective and safe drug which has been successfully used for many years to relieve depression.

Previous studies also suggest that fluoxetine may have effects on the brain that help patients make a better recovery from the physical effects of their stroke^{2,3}. Unfortunately, the differences in the methods used between these studies means that there is not enough evidence to justify giving fluoxetine routinely to people affected by stroke. Large clinical trials are needed to show whether the drug benefits stroke patients, and also what the risks of taking fluoxetine may be.

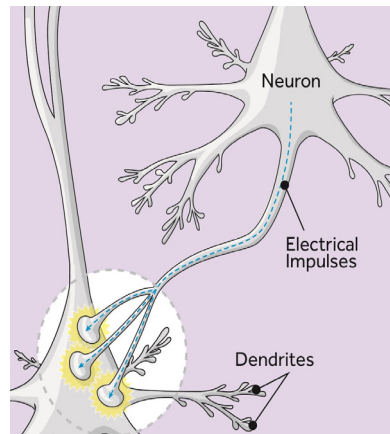
Importantly, fluoxetine may be able to treat the 15% of stroke patients who have a brain bleed (haemorrhagic stroke), in addition to the 85% of stroke patients whose stroke is caused by a blocked blood vessel in the brain (ischaemic stroke)^{3,4}. As there is currently no effective treatment for haemorrhagic stroke, fluoxetine treatment for stroke may prove to be a vital development.

The main aim of FOCUS was to conduct a randomised controlled trial (RCT) which could reliably show whether patients who received treatment with fluoxetine, from the early days after their stroke, would make a better physical recovery than those patients who did not. An additional aim of the trial was to see if fluoxetine could improve additional problems caused by stroke including problems with using language and thinking.

A start-up trial was necessary to determine how feasible the full trial would be, and this is the stage of the study that the Stroke Association funded.

The aim of the start-up trial was to recruit 200 patients in order to learn lessons for how full recruitment could be achieved. It would provide important information on how reliably those patients would take the fluoxetine pills prescribed to them, and how feasible it would be to follow them up to check how they were doing, and what the longer term effects of taking fluoxetine might be.

The FOCUS trial also formed part of a collaboration with sister trials in Australia and New Zealand, called AFFINITY (Assessment of fluoxetine in stroke recovery) and in Sweden, called EFFECTS (Efficacy of Fluoxetine – a randomisEd Controlled Trial in Stroke). The hope was that if all three trials recruited according to plan, the results could be combined to provide even more robust evidence for whether fluoxetine can help recovery after stroke.



Fluoxetine may help by growing new brain cells, called 'neurons', or protecting existing brain cells from the damage caused by stroke.

What did the researchers do?

Patients who had an ischaemic or haemorrhagic stroke within the previous couple of weeks, and had residual problems such as a weak arm, weak leg or language problems were recruited to the start-up trial. FOCUS recruited beyond its target of 200 patients, and by the end of the start-up trial (March 2015) had recruited 1014 stroke patients (the target for the full FOCUS trial is 3,000 patients). Half of these patients were given a course of daily fluoxetine pills for six months, starting between two and 15 days after their stroke. The other half of patients received a 'dummy' (placebo) pill instead. Neither the doctor giving the pills or the patient knew which type of pill the patient had received.

Each patient and their GP were followed up at six and 12 months after the patient's stroke, in order to assess the effects of the treatment.

Follow up was primarily achieved through a postal questionnaire, with a phone call made to those who did not respond. The main outcome of the study was recorded as the change in Modified Rankin Scale (mRS) which is a seven point scale of the degree of disability or dependence in the daily activities of people who have suffered a stroke. It has become the most widely used clinical outcome measure for stroke clinical trials.

What did the research find?

The trial methods used in the FOCUS start-up trial were found to be acceptable to all involved, including patients and their carers. By the end of the Stroke Association funded start-up phase, 52 recruiting sites had been activated throughout the UK.

More than 70% of the patients completed the six month course of the pills they had been given (either fluoxetine or a dummy drug). The follow-up assessments at six and 12 months after the patient's stroke were found to be feasible to be given by postal questionnaire.

There were no concerns about the safety of the treatment during the start-up trial, which was closely monitored by an independent data monitoring committee. Nor were there concerns about how the trial is being run, which is being overseen by a trial steering committee which includes patients and carers.

Due to the success of the FOCUS start-up trial, the National Institute of Health Research (NIHR) Health Technology Assessment (HTA) programme began funding the full FOCUS trial from October 2014 until October 2019. The FOCUS trial is due to report its main results in 2018.

In addition, the AFFINITY trial in Australia and New Zealand and the EFFECTS trial in Sweden are also now recruiting participants to clinical trials in fluoxetine for stroke, and are collaborating with the FOCUS group. A protocol for these studies was published in the open-access journal, *Trials* in March 2015⁵. Once the trials are completed a 'meta-analysis' of the results from all three could give the most precise estimate of whether, and by how much, fluoxetine helps stroke recovery.

Although these trials will show whether fluoxetine for stroke works or not, none of them investigate the way in which fluoxetine might work. A separate, Stroke Association funded study (TSA 2014-04) has now been set up in the UK to test whether fluoxetine works by promoting the growth of new brain cells and the re-wiring of the brain (known as neuro-plasticity). This study is recruiting a smaller group of the patients already recruited to the FOCUS trial, with final results expected in 2018.

What does this mean for stroke survivors?

For many with arm and hand weakness after stroke, repeated task-specific exercises could lead to improved independence in activities of daily living, when compared with current usual care.

A larger, definitive trial is required to answer this question. If successful, the findings could then be incorporated into clinical guidelines to help recovering stroke survivors across the UK and beyond.

References

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The Stroke Association is the leading stroke charity in the UK. We believe in the power of research to save lives, prevent stroke and ensure that people make the best recovery they can after a stroke.

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