COMMENTARY - NEUROLOGY

2011 was another fruitful year for the field of stroke research. Two very important landmark papers are worth mentioning.

The most important of these was the FLAME study published in Lancet Neurology in Feb 2011. In this study the French have for the first time provided evidence that SSRIs like flouxetine may have some role in improving motor function after stroke. Before this study came there was little evidence to suggest the use of flouxetine in stroke patients for motor recovery. Fugl-Meyer motor scale (FMMS) scores of 55 or less was used as the inclusion criteria for assessment of motor recovery. 59 patients were enrolled in the placebo group and 59 in the drug group. All underwent the same physiotherapy program. FMMS improvement at 90 days post stroke was significantly greater in the flouxetine group than placebo.

Another important study that drew everyone's attention was the SAMMPRIS published in NEJM in July 2010. Most important was the fact that it turned out to be a negative study. More over it reinforces the value of intensive medical management which per se was able to reduce the risk of stroke more than intracranial stenting. Bringing an end to the practice of intracranial stenting for symptomatic ICAD this trial has reopened the front for aggressive medical management for symptomatic intracranial stenosis.

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STENTING VERSUS AGGRESSIVE MEDICAL THERAPY FOR INTRACRANIAL ARTERIAL STENOSIS

BACKGROUND: Atherosclerotic intracranial arterial stenosis is an important cause of stroke that is increasingly being treated with percutaneous transluminal angioplasty and stenting (PTAS) to prevent recurrent stroke. However, PTAS has not been compared with medical management in a randomized trial. **METHODS:** We randomly assigned patients who had a recent transient ischemic attack or stroke attributed to stenosis of 70 to 99% of the diameter of a major intracranial artery to aggressive medical management alone or aggressive medical management plus PTAS with the use of the Wingspan stent system. The primary end point was stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during the follow-up period or stroke in the territory of the qualifying artery beyond 30 days. **RESULTS:** Enrollment was stopped after 451 patients underwent randomization, because the 30-day rate of stroke or death was 14.7% in the PTAS group (nonfatal stroke, 12.5%; fatal stroke, 2.2%) and 5.8% in the medical-management group (nonfatal stroke, 5.3%; non-stroke-related death, 0.4%) (P=0.002). Beyond 30 days, stroke in the same territory occurred in 13 patients in each group. Currently, the mean duration of follow-up, which is ongoing, is 11.9 months. The probability of the occurrence of a primary end-point event over time differed significantly between the two treatment groups (P=0.009), with 1-year rates of the primary end point of 20.0% in the PTAS group and 12.2% in the medical-management group. **CONCLUSIONS:** In patients with intracranial arterial stenosis, aggressive medical management was superior to PTAS with the use of the Wingspan stent system, both because the risk of early stroke after PTAS was high and because the risk of stroke with aggressive medical therapy alone was lower than expected. (Funded by the National Institute of Neurological Disorders and Stroke and others; SAMMPRIS ClinicalTrials.gov number, NCT00576693.).

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FLUOXETINE FOR MOTOR RECOVERY AFTER ACUTE ISCHAEMIC STROKE (FLAME): A RANDOMISED PLACEBO-CONTROLLED TRIAL

BACKGROUND: Hemiplegia and hemiparesis are the most common deficits caused by stroke. A few small clinical trials suggest that fluoxetineenhances motor recovery but its clinical efficacy is unknown. We therefore aimed to investigate whether fluoxetine would enhance motor recovery if given soon after an ischaemic stroke to patients who have motor deficits. **Methods:** In this double-blind, placebo-controlled trial, patients from nine stroke centres in France who had ischaemic stroke and hemiplegia or hemiparesis, had Fugl-Meyer motor scale (FMMS) scores of 55 or less, and were aged between 18

years and 85 years were eligible for inclusion. Patients were randomly assigned, using a computer random-number generator, in a 1:1 ratio to fluoxetine (20 mg once per day, orally) or placebo for 3 months starting 5-10 days after the onset of stroke. All patients had physiotherapy. The primary outcome measure was the change on the FMMS between day 0 and day 90 after the start of the study drug. Participants, carers, and physicians assessing the outcome were masked to group assignment. Analysis was of all patients for whom data were available (full analysis set). This trial is registered with ClinicalTrials.gov, number NCT00657163. **Findings:** 118 patients were randomly assigned to fluoxetine (n=59) or placebo (n=59), and 113 were included in the analysis (57 in thefluoxetine group and 56 in the placebo group). Two patients died before day 90 and three withdrew from the study. FMMS improvement at day 90 was significantly greater in the fluoxetine group (adjusted mean 34·0 points [95% CI 29·7-38·4]) than in the placebo group (24·3 points [19·9-28·7]; p=0·003). The main adverse events in the fluoxetine and placebo groups were hyponatraemia (two [4%] vs two [4%]), transient digestive disorders including nausea, diarrhoea, and abdominal pain (14 [25%] vs six [11%]), hepatic enzyme disorders (five [9%] vs ten [18%]), psychiatric disorders (three [5%] vs four [7%]), insomnia (19 [33%] vs 20 [36%]), and partial seizure (one [<1%] vs 0). **Interpretation:** In patients with ischaemic stroke and moderate to severe motor deficit, the early prescription of fluoxetine with physiotherapy enhanced motor recovery after 3 months. Modulation of spontaneous brain plasticity by drugs is a promising pathway for treatment of patients with ischaemic stroke and moderate to severe motor deficit. **Funding:** Public French National Programme for Clinical Research