trial was designed, there was no proven method for identifying patients for whom hemodynamic factors were of primary importance in the pathogenesis of recurrent stroke. Since that time, advances in medical imaging have made it possible to identify patients who are at high risk of recurrent stroke due to hemodynamic factors. COSS was designed to determine if EC-IC bypass could reduce subsequent ipsilateral ischemic stroke in a select group of patients with symptomatic carotid artery occlusion who were at high risk due to poor effective collateral circulation (high OEF). Based on the results of this study and the original EC-IC Bypass Trial, EC-IC should not be employed as a treatment to prevent stroke recurrence in patients with presumed atherosclerotic carotid occlusion, even when imaging demonstrates poor cerebral perfusion.

Fluoxetine Improves Motor Function in Patients with Severe Motor Deficit When Given Early After Ischemic Stroke

François Chollet, MD, Centre Hospitalier Universitaire de Toulouse, Toulouse, France, presented data from the Multicenter Randomized Double-Blind Placebo-Controlled Trial with Fluoxetine on Motor Rehabilitation After Acute Ischemic Stroke (FLAME; NCT00657163) trial, showing that in patients with severe motor deficit resulting from ischemic stroke, early use of fluoxetine in addition to physiotherapy enhances motor recovery after 3 months.

Animal studies indicate that serotonergic neurons can modulate motor output [Jacobs BL and Fornal CA. *Curr Opin Neurobiol* 1997], exert a neuroprotective effect in the postischemic brain [Lim CM et al. *J Neurosci Res* 2009], and promote hippocampal neurogenesis after stroke [Li WL et al. *J Neurosci Res* 2009]. Similar results have been reported in a few small clinical trials [Pariente J et al. *Ann Neurol* 2001; Dam M et al. *Stroke* 1996; Zittel S et al. *Neurorehabil Neural Repair* 2008; Gerdelat-Mas A et al. *Neuroimage* 2005].

FLAME was a double-blind, placebo-controlled trial of 118 patients with hemiparesia or hemiplegia that resulted from ischemic stroke and a Fugl-Meyer motor scale score (FMMS; a validated scale exclusively testing motricity in an analytical and global manner) ≤55 from nine stroke centers in France. Subjects were randomly assigned to once-daily treatment with fluoxetine 20 mg (n=59) or placebo (n=59), starting 5 to 10 days after stroke onset and continuing for 3 months. All subjects also received physiotherapy and standard care. The primary study endpoint was change in FMMS score between baseline and Day 90. Secondary outcomes included score changes in the National Institutes of Health Stroke Scale (NIHSS), the modified Rankin Scale (mRS), and the Montgomery-Åsberg Depression Rating Scale (MADRS) between baseline and Day 90.

Subjects in the fluoxetine group were slightly older than those in the placebo group (mean age 66.4 years vs 62.9 years) and more likely to have had a prior stroke (16.9% vs 6.8% of placebo subjects). Baseline mean FMMS score was 13.4 (±8.8) and 17.1 (±11.7) in the placebo and fluoxetine groups, respectively, a significant difference that was adjusted for in the analysis.

FMMS score progression at Day 90 was significantly (p=0.003) greater in the fluoxetine group (+34.0; 95% CI, 29.7 to 38.4) than in the placebo group (+24.3; 95% CI, 19.9 to 28.7), with the majority of benefit being seen for the upper limb part of the scale (+22.9 for fluoxetine; +13.1 for placebo; p=0.002; Table 1). Overall, there was no difference in NIHSS or MADRS score between the two groups; however, when only the motor portion of the NIHSS was considered, there was a significant (p=0.012) improvement, favoring fluoxetine. The number of independent patients (mRS score of 1–2) was significantly higher in the fluoxetine group at Day 90 than in the placebo group (26.3% [n=15] vs 8.9% [n=5]; p=0.015; Table1). Fluoxetine was well tolerated; a slight, positive effect on mood was detected, as indicated by a reduction in mean adjusted MADRS score (-0.1 [SD= –2.1 to 1.9]).

Table 1. Primary Outcome: Change in FMMS Score Baseline to Day 90.

	Placebo* n=56	Fluoxetine* n=57	p value
FMMS	+24.3 [19.9-28.7]	+34.0 [29.7-38.4]	0.003
FMMS upper limb	+13.1 [8.9-17.4]	+22.9 [18.6-27.1]	0.002
FMMS lower limb	+9.5 [7.8-11.2]	+12.8 [11.1-14.5]	0.010

*Adjusted mean [95% CI]; FMMS=Fugl-Meyer motor scale.

Prof. Chollet noted that although the FLAME trial was limited by its small size, the short-term nature of the trial and the fact that it was conducted in a group of patients who were specifically selected for having a severe motor deficit render the study treatment a new and promising therapeutic approach. The treatment target is neural plasticity, for which the only existing validated treatment is arterial deocclusion with IV thrombolytic agents. Fluoxetine is well tolerated and can potentially be given to a large cohort of patients at a reasonable cost and without the need for advanced treatment facilities.