

Articles relevant to the Focus on vascular neurology

Research supports establishment of specialized TIA clinics

A quarter of strokes are preceded by a transient ischemic attack (TIA). The attacks last only minutes and recovery is quick and complete, so TIAs can easily be ignored by sufferers or missed by physicians. Even if patients do attend hospital after a TIA, immediate assessment with brain and vascular imaging and rapid initiation of preventive treatment is not the norm. To improve care for patients with TIA, Lavallée *et al.* set up the 'SOS-TIA' clinic to provide 24 h access to assessment and treatment facilities for doctors working in the administrative region of Paris.

During the period 2003–2005, the clinic admitted 1,085 patients with suspected TIA. Just over half of patients were seen within 24 h of the symptomatic episode. Neurological, arterial and cardiac imaging was performed within 4 h of admission. TIA was confirmed in 643 patients and strongly suspected in 144, and 58 patients had minor ischemic strokes. Patients began a stroke prevention program, with additional treatment as necessary, including oral anticoagulants for atrial fibrillation ($n=30$), initiation or modification of blood-pressure-lowering or blood-lipid-lowering therapy ($n=225$ and $n=315$, respectively), and urgent carotid revascularization ($n=43$). Almost three-quarters of all patients seen were sent home on the same day as admission. This prompt evaluation and treatment reduced the risk of subsequent stroke within 90 days of a TIA to a rate of only 1.24%, as compared with 5.96% as predicted by the ABCD² scores.

The authors conclude that immediate assessment and treatment in specialist clinics with 24 h access could prevent a substantial number of subsequent strokes in patients presenting with TIA.

Original article Lavallée PC *et al.* (2007) A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): feasibility and effects. *Lancet Neurol* 6: 953–960

Capsaicin facilitates pain-specific local anesthesia

Local anesthetics such as lidocaine block pain effectively, but they also impair motor and autonomic functions by indiscriminately blocking sodium channels in all neurons. Binshtok *et al.*

theorized that it could be possible to exploit the transient receptor potential vanilloid type 1 (TRPV1) channel, which is sensitive to noxious heat and capsaicin, to selectively target primary sensory nociceptor neurons and thereby produce a pain-specific local anesthetic.

Electrophysiological studies in cultured adult rat dorsal root ganglion neurons demonstrated that application of extracellular QX-314—a positively charged, membrane-impermeable lidocaine derivative—had no effect on sodium channel currents when applied alone, but that when co-applied with capsaicin it produced $98 \pm 0.4\%$ inhibition of excitability, an effect limited to neurons expressing TRPV1. *In vivo*, intraplantar injection of QX-314 followed by capsaicin anesthetized adult rats to mechanical and thermal noxious stimuli for around 3 h. Injection adjacent to the sciatic nerve with QX-314 followed 10 min later by capsaicin produced a local anesthesia to noxious heat and mechanical stimuli applied to the lower limbs, without the motor deficit produced by similar injection with lidocaine alone. The QX-314 + capsaicin-injected animals showed no response to a mechanical stimulus of 57 g, whereas the threshold before sciatic injection was 15.2 ± 3.4 g ($P < 0.01$); similarly, thermal response latency increased from 14.9 ± 0.4 s before injection, to 22.3 ± 2.3 s after injection ($P < 0.05$).

The results of this study suggest that delivery of a lidocaine derivative together with a TRPV1 receptor agonist selectively inhibits nociceptors to produce a long-lasting decrease in pain without the loss of motor or autonomic responses.

Original article Binshtok AM *et al.* (2007) Inhibition of nociceptors by TRPV1-mediated entry of impermeant sodium channel blockers. *Nature* 449: 607–610

QoL is lower in female survivors of stroke even after adjustment for prognostic factors

Female survivors of stroke have been shown to have a worse outcome and poorer quality of life (QoL) than male survivors, even after adjustment for prognostic factors. Gray *et al.* used data from the Tinzaparin in Acute Ischaemic Stroke Trial (TAIST), which enrolled 1,484 patients within 48 h of stroke onset, to further determine the relationship between sex and QoL following stroke.

QoL was measured in 1,268 patients (45% female) at 180 days after treatment randomization, using the Short Form-36 health survey. The mean age of female patients was significantly greater than that of male patients (73.4 years vs 68.4 years; $P < 0.0001$). In addition, female patients were more likely to have atrial fibrillation, to have a lower premorbid functional status (as measured by the modified Rankin Scale [mRS]), and to be in a nursing home, than were male patients.

Overall, QoL scores for female patients were markedly lower than those for male patients; female patients scored particularly poorly on the domains relating to physical functioning, vitality and mental health. Even following adjustment for age, baseline systolic blood pressure, Scandinavian Stroke Scale score, history of myocardial infarction, stroke type, premorbid mRS score, premorbid residency (home/nursing home), and treatment group, female patients had considerably lower scores for physical functioning and mental health than did male patients. Notably, lower scores on the physical functioning and mental health QoL domains were associated with poor functional outcome at 6 months, as assessed by the mRS ($P < 0.0001$ for both).

Original article Gray LJ *et al.* (2007) Sex differences in quality of life in stroke survivors: data from the Tinzaparin in Acute Ischaemic Stroke Trial (TAIST). *Stroke* 38: 2960–2964

Blood plasma biomarkers could predict Alzheimer's disease

Early and definitive diagnosis of Alzheimer's disease (AD) could lead to better and more-targeted treatment for patients. Ray *et al.* have recently identified a group of plasma signaling proteins that reflect changes in the brain during the early stages of AD pathology. Levels of the 18 proteins in blood plasma can be used to identify patients with AD, or to predict the onset of AD in presymptomatic patients, with close to 90% accuracy.

First, the authors measured the relative abundance of 120 signaling proteins in an initial set of samples from 43 patients with AD and 40 controls without dementia, and through statistical analysis found significantly different expression patterns of 19 proteins (q -value $< 3.4\%$), from which a set of 18 predictors of AD was

identified. When the predictors were then tested in independent samples from patients with AD ($n = 42$) and other types of dementia ($n = 11$) and controls without dementia ($n = 39$), patients were classified with 89% accuracy ($P < 0.001$). Furthermore, in 47 patients with mild cognitive impairment, progression to AD was predicted with 81% accuracy ($P < 0.001$) up to 6 years before clinical diagnosis. Functional profiling of the 18 predictor proteins pointed to involvement in systemic dysregulation of intracellular pathways of immune response, hematopoiesis and apoptosis.

Further tests are needed before this approach can be used in patients, but the identification of blood plasma biomarkers early in the course of AD could open the door to more-effective interventions.

Original article Ray S *et al.* (2007) Classification and prediction of clinical Alzheimer's diagnosis based on plasma signaling proteins. *Nat Med* 13: 1359–1362

Early exposure to mercury-containing vaccines has no consistent effect on neuropsychology

Concerns have been expressed about the potentially negative neuropsychological effects of the mercury-containing preservative thiomersal (thimerosal) in pediatric vaccines; however, a recent cohort study found no evidence to indicate a causal relationship between deficits in neuropsychological functioning at 7–10 years and early exposure to thiomersal-containing vaccines.

The study used standardized tests to assess 42 neuropsychological outcomes in 1,047 children aged 7–10 years; autism-spectrum disorders were not assessed. Each child's exposure to mercury from thiomersal was determined from computerized immunization records, medical records, parent immunization records and parent interviews. The median cumulative exposure to mercury from thiomersal from birth to 7 months was $112.5 \mu\text{g}$ (range 0– $187.5 \mu\text{g}$); 16 children had no thiomersal exposure during this period. After adjustment for potential confounding factors, few significant associations were found between test performance and exposure to thiomersal. Those associations that were detected were small, almost equally divided