Postoperative cognitive dysfunction related to Alzheimer disease?

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Postoperative cognitive dysfunction (POCD) following cardiac surgery affects a substantial proportion of patients (up to 80%) and consistently increases morbidity, mortality, and health care expenditures. Unfortunately, very little is known about POCD pathophysiology and diagnosis is challenging. Duan and colleagues1 from China shed some potentially useful light on this dark subject.

Duan and colleagues1 examined the potential link of glial cell line-derived neurotrophic factor (GDNF) and development of POCD in 80 patients undergoing elective valve replacement secondary to rheumatic heart disease. The GDNF protein is of particular interest because it is known to promote neuronal health and low GDNF levels are found in patients with Alzheimer’s disease.2 GDNF also has neuronal regenerative properties and has demonstrated potential as a therapeutic treatment for certain neurologic diseases.3

The prospective, observational study presented by Duan and colleagues1 examined patients undergoing hypothermic (28°C-32°C) cardiopulmonary bypass. Trained physicians conducted a battery of 5 neurocognitive tests twice (1 day before and 7 days after surgery) and compared the results with those of 20 healthy volunteers tested in the same manner. GDNF immunoassays were performed from blood samples obtained at 4 time points (immediately before surgery and 1, 2, and 7 days after surgery).

The 80 patients were assessed for POCD using the Z-score, a previously defined (although somewhat nebulous) technique that assesses for a decrease in test performance from baseline while accounting for the expected improvement in score from serial testing in the same individual.1 The score is normalized by comparison with volunteer controls, which in this case, creates a problematic assumption that the same degree of test–retest change occurs in healthy volunteers as occurs in patients following a major surgical insult. Nevertheless, the blood levels of GDNF were lower in the POCD group (38 patients) compared with the non-POCD group (42 patients) at all time points. The change in GDNF levels on day 2 and day 7 after surgery were particularly predictive of the development of POCD. Although there are significant limitations to this clinical investigation (limited detail about baseline clinical risk factors, differences between group education level, and lack of cerebrospinal fluid assessment), the results seem to implicate GDNF in POCD following cardiac surgery. The ability to use postoperative blood levels of GDNF to predict POCD (vs time-consuming neurocognitive testing) would be a useful tool.

This study1 raises many interesting questions for future research, particularly considering emerging data surrounding therapeutic interventions in Alzheimer’s disease.1,3,5 Do low levels of GDNF continue to predict prolonged POCD beyond the immediate recovery period from surgery? Do GDNF levels increase back to baseline in patients whose POCD resolves? Is decreased GDNF in POCD a marker of the disease or the causative factor behind symptoms? Can POCD be prevented by increasing GDNF levels with currently available drugs such as amantidine5 or by exercise-induced increases in neurotrophic factors7? The answers to some of these questions may lead to important discoveries in understanding, and hopefully treatment of, the challenge of POCD.

References


