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Letter to the Editor

Letter regarding "Cognitive outcomes in meningioma patients undergoing surgery: individual changes over time and predictors of late cognitive functioning"

Dr Rijnen and colleagues identified preoperative determinants of 12-month postoperative cognitive performance in 82 adults who underwent meningioma surgery. Preoperative determinants were assessed with a computerized neuropsychological battery on the day before surgery and during follow-up.[1] It raises two methodological questions about (1) how the use of medication has been taken into account and (2) the validity of the measurements on the day before surgery.

With regard to medication use, the approved study protocol's summary states the following inclusion criterion: "adult patients (. . .) with no (. . .) medication use that interferes with cognitive function."[2] However, the published article included users of medication that affects cognitive function.[1] A wide range of drug classes were lumped into one category labeled "psychotropic medications." These included corticosteroids, "stimulants," anticonvulsants, and a wide range of other medications. A thorough understanding of the onset and offset of effects of medication use in observational studies in relation to their underlying pharmacological effects is important.[3] This paper did not clearly distinguish between medication classes, or define specific time windows of exposure. A clarification would hopefully explain why Table 2 showed that on the day prior to resection, 43% of 261 patients were non-users of psychotropic drugs (including corticosteroids).[1] Since dexamethasone is usually initiated on the day before meningioma surgery (ie, T0), I would have expected this proportion to be zero.

Diagnoses of a proportion of symptomatic meningiomas are triggered by seizures. Patients admitted for meningioma surgery may have continuously used anticonvulsants from their first seizure onward, during and after surgery. A couple of months after resection, anticonvulsants may or may not have been tapered off. Both epilepsy and the use of anticonvulsants affect neurocognitive function.[4] Amnesia or impaired cognitive function are common side effects of levetiracetam, valproic acid, phenytoin, gabapentin, topiramate, and pregabalin. Cognitive side effects of clobazam have been poorly researched among adults. But adverse effects on memory are well established for adult patients using other benzodiazepines for epilepsy, such as midazolam or diazepam.[4] Why were these drugs lumped into one category together with substances that do not have well-established effects on cognition (such as "stimulants"[4,5]), or potentially in the opposite direction? While the published study protocol's summary suggested to exclude patients using medication that interferes with cognition,[2] this was not further reported or explained.[1] Were any other (statistical) methods used to explore or deal with this potential source of distortion of cognitive assessments at baseline and during follow-up?

The second methodological question relates to the timing of the baseline assessment of cognitive function, ie, on the day before surgery. How would a patient´s psychological stress on the day before meningioma resection (T0[1]) have affected test outcomes? Some patients might still be in shock after diagnosis[6] or just started to understand the short-term risks of a meningioma resection in relation to the potential long-term benefits. At this stage, histopathological results were unknown to all patients.[1] May stress have been treated with anxiolytics which could have affected cognitive function?[5] What is the validity and usefulness of the current T0 measurement of cognitive function, not more than 24 hours before surgery? Was a restriction to the analysis of only postsurgical assessments of cognitive function considered?

Conflict of interest statement. I co-supervise 2 PhD students who are employed by F. Hoffmann–La Roche (Basel, Switzerland and Welwyn Garden City, UK). The topics of their PhDs are not related to this letter and I have not received any fees or reimbursements for this.

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