

Received: 11.12.2015
Accepted: 28.06.2016

A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search
G – Funds Collection

DOI:10.5604/17307503.1213003

THE PROCEDURE OF INTRAOPERATIVE NEUROPSYCHOLOGICAL ASSESSMENT IN THE EXCISION OF CEREBRAL TUMOURS LOCATED IN ELOQUENT AREAS

Elżbieta Agata Ormezowska^(A,B,C,D,E,F),
Dariusz Jan Jaskólski^(A,B,C,D,E,F)

The Clinic for Neurosurgery and Oncology of the Nervous System, The Medical University in Łódź, Łódź, Poland

Background:

This paper discusses in detail the procedure of neuropsychological assessment before, during and after awaked craniotomies carried out for the excision of neoplasms located in the eloquent areas of the brain.

Material/ Methods:

In the years 2000-2015 we performed awake craniotomies in 123 patients. The authors present their personal experience in the applicability of the diagnostic tools used for the intra-operative monitoring of selected cognitive and executive functions. The tests assess various aspects of speech, verbal memory, precise movements and streognosis. The inclusion and exclusion criteria for the awake craniotomy were listed along with the tricks of the trade – the possibilities of maintaining the number of intra-operative tests and the practical ways of assessing patients' cognitive processes.

Results:

It was found that in 85 (69%) of the patients through the use of direct electrical stimulation (DES), we identified the eloquent areas (both verbal and motor) and subsequently monitored the patient's condition on the resection of the tumour. Among these cases there were 28 (23%) without a postoperative deficit and 32 (26%) in whom deficits were transient, subsiding within 1 to 3 weeks. Neurological deficits persisting for over 4 weeks were observed in 10 (8%) of these patients. In the group of 38 patients with negative stimulation, there were no new postoperative neurological or neuropsychological deficits. Our experience confirms that awaked craniotomy facilitates the safe resection of tumours located in the eloquent brain allowing one to maximise the excision and minimise the risk of a postoperative deficit.

Conclusions:

Key words: neuropsychological assessment, cerebral tumour, operative treatment, awaked craniotomy

SUMMARY

INTRODUCTION

Awaked craniotomy, i.e., a craniotomy during which it is possible to communicate with a patient, is used in the surgical excision of cerebral tumours located in the eloquent areas of the brain. This technique seems to be essential for the operability of certain neoplasms. Procedures pioneered by Penfield and Roberts and then followed by Ojemann [1979] facilitated research on the cortical organisation of verbal functions. The advent of non-invasive imaging techniques, namely fMRI, enabling the identification of the eloquent areas, suggested that traditional anatomical knowledge on their location was far from precise: for example, the position of structures essential for verbal communication turned out to display substantial inter-individual variability. Nonetheless, limitations of fMRI arising from its sensitivity and specificity are significant enough to render this technique insufficient as a single measure for planning a surgical procedure [Petrovich et al. 2005; Tuominen 2013]. Therefore, intra-operative mapping of the functional cortex prior to the excision improves the outcome both in terms of the extent of tumour resection and preserving the function [De Benedictis 2010; Duffau 2013; Tonn 2007; Ciechomska et al. 2005; Bilotta et al. 2014]. It is possible to map and monitor simple motor and sensory functions as well as complex ones, such as speech and memory. However, whereas the basic sensory and motor functions can be successfully mapped and monitored in an anesthetised patient by means of intra-operative neuro-electrophysiological techniques such as SSEP and MEP (somatosensory and motor evoked potentials), this is not the case in the complex functions. The intra-operative assessment of speech or memory requires careful observation of the alert patient performing various tasks in order to reach the goal of a safe maximal resection of the neoplasm. This paper presents our experience on the practical aspect of psychological methodology in pre-, intra- and postoperative assessment of 123 patients operated on for the years 2000-2015.

MATERIAL AND METHOD

In the years 2000-2015 we performed awake craniotomy in 123 patients – 64 men and 59 women. The mean age was 46, the average period of education was 7 years. The majority were patients who lateralized to the right – 112 (91%); the strength of lateralization was from +24 to +15. Histopathological examination showed glioblastoma in 49 cases, fibrillary astrocytoma in 42, oligodendroglioma in 12 and secondaries in 20 cases. The tumours were most frequently located in the frontal (49 cases) or temporal (42 cases) lobes. The others were situated in the frontotemporal region (15), the frontoparietal (14) and the temporooccipital (3).

The diagnostic tools were used for the intra-operative monitoring of selected cognitive and executive functions. The tests assess various aspects of speech, verbal memory, precise movements and streognosis.

Assessment: preoperative procedures

The specificity of the neuropsychological assessment during an awake craniotomy imposes the application of a particular diagnostic methodology. An impairment of the assessed function brought about by stimulation of a certain cortical region, allows us to classify this zone as a structure essential for the tested functionality. For this reason the diagnostic means chosen must meet a number of criteria. The primary one is the possibility of the comprehensive and precise assessment of patient performance. Another one, though equally important, comes from the necessity for the practical implementation of the existing neuropsychological tests into operating-theatre conditions (immobilised patient, restricted time, non-standard environment, necessity for prompt decisions-making). Finally, the employed tests have to be reliable since their results are crucial for defining the area of resection.

The first stage of the procedure is a preoperative assessment carried out in order to ensure the feasibility of the awake craniotomy. The goal is to define the areas of patient functioning which could be effectively monitored during surgery as well as to determine their ability to cooperate, particularly in terms of susceptibility to fatigue and understanding and following instructions.

The preoperative assessment can be achieved by means of the following diagnostic measures:

- Laterality inventory – to determine the direction and force of laterality [Lezak 1995];
- Mental Control Test (counting backwards from 20 to 1, repeating the alphabet, counting “every three “ from 1 to 40 [Lezak 1995];
- Rey 15 Words Auditory Verbal Learning Test [Lezak 1995];
- Rey-Osterrieth Complex Figure Test [Lezak 1995];
- Halstead-Wepmann Aphasia Screening Test-FAST [Lezak 1995]; Tests for motor perseveration (repeating graphic elements and geometric figures) [Lezak 1995];
- Verbal Fluency Tests [Pąchalska, Kaczmarek i Kropotov 2014];
- Mini-Mental State Examination [Folstein 2010];
- Stereognosis Tests (experimental);
- Naming and pointing to pictures (experimental);
- Wechsler Adult Intelligence Scale (WAIS-R) [Brzeziński i Hornowska 1993].

Assessment: intra-operative procedures

Intra-operative assessment employs the same test which were used preoperatively. The duration necessary to wake up the patient ranges from 15 to 30 minutes. In this period of time one attempts to establish verbal communication with the patient and to determine the feasibility of cooperation. Simultaneously, one ought to assess the patient’s neurological condition to recognise any possible motor impairment of the limbs and/or facial nerve palsy.

The score of Mental Control Tests is an admitted indicator confirming that communication with the patient was established. In order to proceed to the prin-

cial tests this score should be not less than 1-2 points compared to the preoperative result. This is crucial since based on our experience, if the score is worse than that the risk of inaccurate results of the stimulation increases substantially. Whilst mapping and then the excision of a defined brain area, one ought to assess current, i.e. that resulting from the on-going surgical activity, state of the patient's cognitive and executive functions. This monitoring includes:

- verbal functions, particularly naming and pointing
- fine movements and stereognosis
- verbal memory, both short- and long-term

The emotional state of the patient and his/her current ability for cooperation is also watched.

Any alteration in the scope of the assessed function can alert the surgeon to the fact that the eloquent area has been disturbed and that the approach should be subject to change. Verbal functions are monitored by testing a patient's ability to name objects. The method which was worked out by us combines experimental features with standardised tests. We use 70 pictures on cards 6x8 cm, presented one by one. The depicted objects come from The Boston Naming Test, The Everyday Objects Recognition Test, The Drawing Test "Images And Patterns". The names of the presented objects have either a medium or high frequency range for the Polish language. After a preliminary set of 76 objects had been tested on 38 healthy individuals recruited from amongst the personnel, six pictures were rejected as improperly recognised and for being equivocal. In order to facilitate the differentiation of qualitative naming disorders brought about by the stimulation or the surgeon's performance, we employed a procedure introduced by Ojemann [1989]. We placed a sign: "there is..." above each picture, so that the patient should every time read the sign and name the object. Should the patient have trouble in naming certain objects during the preoperative examination, at surgery we would use only those pictures that did not cause problems. In many instances one employs an analysis of aspects of the patient's verbal function other than naming. The choice of the tests depends on the location of the pathology and the condition of the patient. For example, a test during which the patient points to objects after hearing their names, may be an invaluable addendum in the assessment of naming in the case of difficulties in the verbal expression as well as on the excision of tumours located in the temporal lobe. Under such circumstances, pointing to objects seen by the patient facilitates a surveillance of speech comprehension. This test is carried out with the same pictures which are used for the naming test, however this time they are presented simultaneously. The task for the patient is to point out the one whose name was just given. Depending on the requirements suggested by the surgeon and the potentials of the patient, one can gradually step-up the complexity of the test, by presenting an increasing number of pictures, usually from two up to six at one time. An extra advantage is that this form of the test creates an opportunity to monitor the motor function of the hand with which the patient points at the picture. In yet another variant of this test, one uses pictures with captions. Moreover,

speech fluency tests may be employed to assess fluctuations in the verbal functions in patients undergoing an excision of tumours located in the frontal lobe of the dominant hemisphere. In those with pre-existing dysphasia one can rely on monitoring the remnants of the verbal functions. This can be achieved by asking the patient to produce so-called automatic word strings, such as the names of the days of the week or months, or by counting. Apart from the verbal, there are a number of other functions that may be tested in the patient being operated on, e.g., the ability to perform requested fine movements, stereognosis and memory. In order to assess fine movements, we employ various drawing tests, The Halstead-Wepman Aphasia Screening Test, as well as tasks consisting of writing certain words and phrases as well as drawing repetitive patterns. Examining stereognosis relies on testing the patient's ability to recognise objects by touch. For this purpose we use plastic tokens of two sizes and shaped into geometric figures. Furthermore, we perform graphaesthesia (the patient identifies figures being written on the palm) and kinaesthesia tests (the patient reports the position of the fingers). Short-term memory tests are carried out by us as a clinical experiment. We present a string of pictures to the patient and regularly (e.g. at every other picture) ask what was the object in the picture shown before. We use data from the preoperative examination to assess long-term memory.

RESULTS

Intra-operative stimulation

Eloquent areas were identified by means of DES in 85 patients (69%): in 55 cases these were verbal areas, in 11-motor and in 26, both verbal and motor. In all these cases speech and motor function were monitored on the excision of the tumour. Comparing the pre- and postoperative condition in this group, there was no change in 28 cases (33%), a transient – lasting up to 3 weeks weakness in the limbs or/and speech disorders was observed in 32 (38%) patients. In 15 (18%) cases the deficit was present for up to 4 weeks and in 10 (12%) for longer than this. The most common reaction for DES in an eloquent area was a temporary activation disorder – a type of *absence*-like state with the concomitant lack of any reaction to stimuli, later on described by the patient as a feeling of empty headedness. The feeling subsided after stimulation ceasing. This reaction was observed more or less frequently in almost half of the patients (42 cases) in whom we managed to identify verbal areas. In almost all patients who underwent the excision of a tumour located in the vicinity of the verbal areas (68 cases), we observed perseverations which persisted relatively long after withdrawing the stimulation. The most frequent speech disorder present at stimulation was dysnomia with prolongation of the reaction time required for the correct unassisted actualisation of the word. This comprised 65% of all the cases with intra-operative speech disorders). Less frequently we noted dysnomias with word paraphasias (20%). In these cases the patients usually managed to give a correct answer

after prompting either phonematic (more frequently) or semantic (more rarely). The least common speech problem was articulation disorders, which appeared in 15% of the patients.

In 38 patients both DES and resection did not affect the function. No eloquent areas were identified and there was no postoperative deficit.

DISCUSSION

Electrical stimulation of the cortex can either excite or depress neuronal activity, not only in the stimulated area but also in distant regions of the brain via the fibres passing through the stimulated zone. In practice, stimulation usually impairs the function as a result of a temporary depolarisation blocking activity by a certain group of neurons [Łuria 1976]. Spatial distribution of this phenomenon is difficult, if not impossible to foresee [Ojemann 1996]. Experiments dealing with the stimulation of verbal centres [Buren 1978] have shown that the size of the affected zone varies and enlarges along with a number of stimuli applied in the same area. Nonetheless, there seems to be no constant correlation between the two parameters, and this observation remains in-keeping with our experience. The effects of the stimulation are also affected by technical factors, such as: magnitude of the stimulus, the choice of the target in which it is applied (random or not) and the number of stimuli. Another crucial issue is that of the functional specificity of a stimulated area. E.g. the stimuli may be subject either to afferent or efferent transmission (i.e. they could be conveyed either from projecting areas up to structures of higher hierarchy or another way round) [Łuria 1976a]. All those factors affect directly the result of the stimulation, determining the expected reaction of the patient and influencing the magnitude of the stimuli necessary to evoke it. Language centres are located in the secondary and tertiary cortex, in association areas. Their efficiency depends upon synchronisation of several neighbouring structures of different modalities, as well as the association fibres with which these structures are interconnected. It is much easier to cause malfunction of complex activities such as speech, than this is the case with simple functions based in primary – projecting cortical structures [Łuria 1976a; Pačhalska, Kaczmarek i Kropotov 2014]. This was confirmed in our practice. Furthermore, since the persistence of pathological symptoms resulting from stimulation depends on cytoarchitectonics as well as on the specific function of the tested zone, the effect of the stimulation on simple motor reactions does not last longer than the stimulation itself, whereas disorders of the complex function, such as speech, subside after a much longer time. Temporary interruptions of the activation, presenting as *absence*-like states with no reaction to any stimuli and subsequently reported on by the patient as “feeling empty headed” usually disappeared right after stopping the stimulation. They were observed in almost half of the patients (42 cases) in whom we managed to identify cortical eloquent areas. In contrast, perseverations were much more persistent, lasting relatively long after the ceasing of the stimulation. They were present in almost all the patients

(68 cases) who had resection of a tumour located near speech areas. Their probable cause may be the temporal and spatial summation of the stimuli in association structures. The perseverations constitute a major difficulty in the excision of large subcortical tumours.

Determining if changes in behaviour ensuing local inactivation of the cortex mirror true language disorders of the anomia-type, or rather other problems of perception, executive functions or articulation muscles, may be important for the future condition of the patient. The crucial element is the absence of either a motor or sensory response evoked simultaneously with the language disorders. The patient is able to read a sign above the picture "this is...", but either cannot say the name of the object, or gives a wrong name. The most common language disorder brought about by the stimulation is omitting or an inability to say the appropriate name of the recognised object. The pathomechanism of the problems with finding the right word may be elucidated by using certain cues given to the patient. A phonematic cue (the first syllable) provokes an erroneous search for a word pattern; it indicates that the durability of the auditory pattern of the word was disrupted. This disorder is often encountered beyond the classic auditory area in the paraprojective zone of the dominant hemisphere, e.g., at the resection in subcortical structures. Its putative mechanism implies a temporary disruption to the activation and feedback transmission in the cortico-thalamic tracts [Duffau 2002].

On the other hand, in a patient in whom the phonematic cue was unproductive, an effective prompt, e.g., in the form of asking about the use of the object, indicates that the naming problems with omitting words may result from a disruption of other mechanisms of language processing. Such a situation may probably take place in the case of disruption of the arcuate fascicle. Apart from the fact that such an analysis is important for the sake of research, it may also be relevant in choosing the right speech therapy, should there be a postoperative dysfunction. It is believed that the true speech area that which on being stimulated produces disorders of the language mechanisms, presenting themselves in mistakes in naming, counting and perseverations. The patient reports an "inability to speak." For this reason one has to be aware that although a sudden speech arrest occurring at stimulation is of a practical importance, it does not entitle us to call the stimulated zone a language area. The testing of a working hypothesis involves the analysis of pathognomonic signs at the time of a preliminary cortical mapping and taking a second look at ambiguous signs. On excision such an assessment is much more difficult.^[18] Interference with subcortical structures comprises many factors which may have an effect on both the symptoms presented by the patient and explaining their nature. For instance, a lack of patient reaction, making us repeat the order, may involve either pulling or compressing, resulting in an irritation of verbal structures, or a damage done to the thalamo-cortical tracts, which are known to be crucial for maintaining selective attention.

In fact, a gradual decline in the performance of all tested functions and a prompt improvement after surgery – a scenario often seen at long operations – may be connected to a transient inactivation of the thalamo-cortical tracts. This condition

was seen in 28 (33%) patients with positive stimulation. Problems with interpreting correctly the changes in the patient's behaviour may be provoked also by other disrupting factors, such as: anaesthesia, temporary and spatial summation of the stimuli (stimulation and resection), patient weariness, cerebral oedema and the excision in itself.

CONCLUSIONS

Individual surgical strategy benefitting from the results of intra-operative stimulation (DES), decreases the risk of postoperative deficits and helps patients with intraaxial neoplasms to maintain a good quality of life. Examining the organisation of the motor as well as the afferent and sensory systems, creates an opportunity for an intra-operative assessment of functions such as speech, memory and fine movements. Our experience confirms the efficacy of the methodology, which made possible the application of neuropsychological assessment for the intra-operative mapping of neuroanatomical structures and the testing of the relevant cognitive and executive functions.

REFERENCES

- Bilotta F; Stazi E; Titi L; Lalli D; Delfini R; Santoro A; Rosa G. Diagnostic work up for language testing in patients undergoing awake craniotomy for brain lesions in language areas. *British Journal Of Neurosurgery*. 2014; 28 (3) : 363-7.
- Brzeziński J., Hornowska E.(red.) (1993). *Skala Inteligencji Wechslera WAIS –R*
- Buren J.M. et al. (1978), Mechanism and localisation of speech parietotemporal cortex, *Neurosurgery*, 2, 233-239.
- Chacko AG, Thomas SG; Babu KS i wsp. Awake craniotomy and electrophysiological mapping for eloquent area tumours. *Clinical Neurology And Neurosurgery*. 2013; 115 (3): 1872-6968.
- Ciechomska E.A., Komuński P., Tybor K., Zawirski M. Śródoperacyjne badanie wybranych funkcji poznawczych i wykonawczych u pacjentów z guzem mózgu. *Neurologia i Neurochirurgia Polska*. 2005; 39, 3: 196–201.
- De Benedictis A; Moritz-Gasser S; Duffau H. Awake mapping optimizes the extent of resection for low-grade gliomas in eloquent areas. *Neurosurgery*. 2010; 66(6): 1524-4040.
- Duffau H. Intraoperative mapping of the subcortical language pathways using direct stimulation. *Brain*. 2002; 125, 199-214.
- Duffau H. New concept in Surgery for diffuse low-grade gliomas; Towards functional neurooncology. *EANS Annual Meeting 2013*. Tel Aviv, Israel, 11-14 Nov., 2013.
- Folstein M.F., Folstein S.E., Fanjiang G. Krótka Skala Oceny Stanu Umysłowego (MMSE). 2010. Adaptacja J. Stańczak PTP.
- Lezak M.D. *Neuropsychological assessment*. 1995. Oxford University Press, N York
- Łuria A.R.(1976) *Problemy neuropsychologii i neurolingwistyki*. PWN Warszawa.
- Łuria A.R. (1976a) *Podstawy neuropsychologii*. PZWL Warszawa.
- Ojemann G.A. Individual variability in cortical localization of language. *J.Neurosurg*. 1979; 50:164-169.
- Ojemann G.A. Ojemann, J., Lettich, E. & Berger, M. et al. Cortical language localization in left, dominant hemisphere, *J. Neurosurg*. 1989; 71: 316-326.
- Ojemann G.A., Miller J.W., Silbergeld D.L. Preserved function in brain invaded by tumor. *Neurosurgery*. 1996; 39 (2); 253-258.
- Pąchalska M., Kaczmarek B.L.J., Kropotov J.D. *Neuropsychologia kliniczna: od teorii do praktyki*. Warszawa: Wydawnictwo Nauowe PWN, 2014

- Petrovich N, Andrei B.A., Holodny I., Viviane M.D., et al. Discordance between functional magnetic resonance imaging during silent speech tasks and intraoperative speech arrest. *J Neurosurg.* 2005; 103:267–274.
- Tonn J. C. Awake craniotomy for monitoring of language function, benefits and limits. *Acta Neurochir.* 2007; 149: 1197-1198.
- Tuominen J., Yrjänä S., Ukkonen A. et al. Awake craniotomy may further improve neurological outcome of intraoperative MRI-guided brain tumor surgery. *Acta Neurochir.* 2013; 155: 1805–1812.

Address for correspondence:

Elżbieta Agata Ormezowska,
The Clinic for Neurosurgery and Oncology of the Nervous System,
The Medical University in Łódź
ul. Kopcińskiego 22
90-153 Łódź
elzbieta.ormezowska@umed.lodz.pl