NEUROPSYCHOLOGICAL GROUNDS IN THE AWAKE BRAIN SURGERY

V. C. Buraga1, Dana Mihaela Turluc1,3*, S. Turluc4,
A. I. Cucu1, Claudia Florida Costea2

University of Medicine and Pharmacy “Grigore T. Popa”-Iasi
Faculty of Medicine
1. Department of Neurosurgery Unit II
2. Department of Ophthalmology
3. Department of Surgery
4. Department of Medical Specialties (II)

* Corresponding author. E-mail: turluc_dana@yahoo.com

NEUROPSYCHOLOGICAL GROUNDS IN THE AWAKE BRAIN SURGERY (Abstract): Traditionally, the awake cerebral neurosurgical interventions are carried out when the primary motor areas and the areas involved in language are concerned. This procedure is also known as mapping (Intraoperative Brain Mapping). The intraoperative neuropsychological protocol supposes the setting of a list of steps and tasks that the patient must perform during the surgery, taking into account the lesion localization (both the cortical and the subcortical structures), the cognitive functions involved and the individual particularities of each patient. As a result of the high validity of certain tests, we propose a common minimal set of tests, which can allow a minimal standardization and replicability. Keywords: BRAIN AWAKE SURGERY, BRAIN MAPPING, INTRAOPERATIVE NEUROPSYCHOLOGICAL PROTOCOL.

Relatively recent archaeological findings show that cranium trepanation is not a new procedure, as we could believe. She has been successfully carried out long ago the appearance of the general anesthesia. A number of skulls discovered in Peru shows a healing percentage of 55% of 214 patients (1). From several points of view, the modern era of awake craniotomy starts more than 50 years ago, when Wilder Penfield and Andre Pasquet (1) published their reference work regarding the surgical and anesthetic aspects of the surgical interventions after the local and intermittent administration of sedatives and analgesic drugs. However, as chronological attestation, Penfield seems to be preceded in the cortical stimulation by Robert Bartholow (1) early from 1874. This one describes the case of a 30-year-old patient, Mary Rafferty, who addresses to him for a consultation, with a cranial orifice of 51 mm, most probably acquired after a scalp carcinoma. Inspired by the testing on animals of David Farrier, Bartholow (1) applies a low-intensity electric current in different areas of the exposed brain of his patient. These stimulations lead to the appearance of certain motor reactions. Several concepts highlighted by Penfield and Pasquet are still relevant.

The cognitive neurosciences benefit nowadays from a better knowledge of the neuronal grounds of the cognitive processes
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and their clinical applications, mostly in the neurosurgical practice. Over the last decades, remarkable progress has been made in the non-invasive cortical mapping (magnetoencephalography, functional MRI), but also at the level of the invasive mapping (awake intraoperative cortical stimulation) (2). The main reason in using awake craniotomy is the cortical mapping, the observation of cortical stimulation effects on the cerebral functions and at the same time the reduction of lesions in the adjacent eloquent tissue during tumor resection. Traditionally, the awake cerebral neurosurgical interventions are carried out when the primary motor areas and the areas involved in language are concerned, but are not limited to them.

After the analysis of a numbers of articles, we were not very surprised to find out that the non-verbal functions mapping received less attention, even though the functional deficits, other than aphasia, can have an equally strong impact on patient’s activities and on his quality of life. Visual-spatial and cognitive deficits are more frequently reported after the detailed and extended neuropsychological assessments. In several countries, a diagnostic of hemianopsia or unilateral spatial neglect leads to the interdiction to drive (3).

**Verbal and nonverbal functions’ mapping in the dominant and nondominant hemisphere - electrical brain mapping findings**

**Language mapping**

The perisylvian areas of the dominant left hemisphere are classically described as being involved in language (4). Consequently, specific language tasks have been enforced during surgeries for the tumors located in these areas, in order to avoid permanent postoperative deficits of the written or oral language. For instance, the spontaneous speaking, counting, objects and actions naming, recognizing famous personalities, reading and written have been used for the mapping of the superior and posterior areas of the temporal lobe, inferior parietal lobe and lateral part of the frontal lobe.

Because of the intraoperative tasks, the electric mapping made possible the establishment of anatomic and functional correlations which led to an updated vision of language connections in general. Therefore, a new paradigm was proposed, based on a parallel and interactive distribution model of the network at a higher scale. This model includes an anterior path which connects the orbitofrontal, prefrontal and dorsolateral prefrontal areas with the temporo-occipito-parietal regions, by means of the inferior fronto-occipital fasciculus. This anterior path is involved in the semantic processing and the direct electrical stimulation during the denomination tests determines semantic paraphasias. Moreover, the posterior path interesting the superior longitudinal fasciculus, which connects the inferior frontal gyrus and the ventral premotor cortex with the superior temporal cortex and passes through the inferior parietal lobe, is involved in the articulatory components of language. The direct electrical stimulation of these structures causes phonemic paraphasias and dysarthria. Recent articles presenting the morbidity profile describe a percentage of 13% of the patients with dysphasia after an aggressive resection of parietal lobe gliomas (5).

Other cortico-subcortical regions of the left hemisphere are also involved in speech articulation and namely, the left additional motor area (dominant hemisphere), the anterior part of the insula and the lentiform
nucleus causing dysarthria upon electrical stimulation. These circuits converge towards a final common path in sensorial-motor primary cortex causing a dysarthria or anarthria when stimulated during speech (6). Moreover, this extended network is modulated by cortico-striate circuits, provoking language control troubles or self-regulation upon electrical stimulation. More than that, the posterior part of the inferior longitudinal fasciculus plays a crucial role in the visual recognition in the image denomination tasks, but also in lexical items tasks. A subordinate network serving to the written language was also described, comprising the additional motor area, the Exner area and the superior and inferior parietal lobe, but also the superior longitudinal fasciculus.

Language mapping in patients speaking several languages or the mapping of sentence translation has been carried out in bilingual and polyglot patients. Therefore, a sub circuit involved in language, dedicated to the change/switching has also been remarked. The control of choosing the spoken language can temporarily be affected mainly during the stimulation of the left caudate nucleus (7) (which provokes perseverations), showing at the same time its role in the executive functions, such as selection, inhibition, planning and attention processing.

Finally, the right hemisphere, described as having a “mirror” configuration is involved in prosody, the semantic processing of words and of the speech, the processing of the context and of language pragmatic abilities, beside its involvement in executive functions, mainly the attention and the working memory.

Nonlanguage mapping

With regard to the sensorial-motor functions, the classical intraoperative neurophysiological monitoring using evoked potentials or motor stimulation during the general anesthesia, allows the mapping through muscle contractions during the procedure and prevents therefore hemiplegia. But movement is not action. By opposition, the direct electrical stimulation in patients in vigil/awake phase allows the objectivisation of certain high level perseverations in the visual-spatial processing due to the mapping, not only of the motor function, but also of the somato-sensorial and visual function and even of the spatial cognition. The execution of movements in the contralateral hemi body, when the resection comes very close to the pyramidal and thalamocortical paths, brings valuable information in preserving the fine motor activity, essential for a normal life standard.

In the same train of thought, a complete hemianopsia can have a major negative impact on patient’s life quality, affecting his daily activities, mainly because the development of this type of deficiency leads in most cases to the interdiction to drive. Visual pathways mapping is possible by using the direct electrical stimulation of the awake patient in case of tumors from temporal-occipital junction, through the appearance upon stimulation of the positive visual responses (phosphines or illusions such as metamorphopsia) and negative, such as visual field defects or blurred vision (8). Therefore, hemianopsia or the visual field deficits should be avoided.

Moreover, the cortical areas (mainly the right supramarginal gyrus or the superior temporal cortex) as subcortical paths (the right superior longitudinal fasciculus) serving to the spatial cognition, can be identified and preserved during the resection of
the parieto-occipital junction, asking the patient to carry out tests such as the line bisection task (the patient must draw a sign at the middle of a line and one presents to the patient a range of several lines placed in different positions as compared to the margins of the paper or of the computer screen). The cerebral structures highlighting the vestibular functions, mainly the superior temporal gyrus and the parietal-insular cortex, connected by the superior longitudinal fasciculus of the “non-dominant” hemisphere for language, can also be objectivized and spared during the intervention for the temporal-parietal lesions, using the direct electrical stimulation in the awake condition, having as result the reproducible vertigo.

Other superior cognitive functions received less attention, but they can however be tested during the awake mapping procedure (for instance, calculation tests during the left parietal resections, mainly in the left angular gyrus). The stimulations during the memorization, retention/storage or delayed memory were also used for the mapping of the mnemic function, by means of the awake craniotomy procedure, involving the premotor areas in the dominant hemisphere, the left anterior temporal lobe or the fornix. The frontal visual field, which provokes saccades and is related to the attention and to the working memory, was also investigated. The use of a non-verbal semantic association test during the intraoperative stimulation highlighted the neural basis, accentuating the multimodal semantic processing (verbal and non-verbal).

The trans-modal (visual-verbal) association tasks were carried out by the patients during the resections of tumors located between the left dorsolateral prefrontal cortex and the temporal posterior cortex, which is connected through the inferior occipito-frontal inferior fasciculus. Emotional aspects of feeling recognition at the level of the superior part of the face, at the level of the eyes (“mirror of the soul”) were also described in patients with posterior perisylvian tumors. Finally, the use of a song interpretation task in patients that were vocal singers was reported in five cases, describing dissociations between speech and melodicism outside the primary sensorial-motor area.

**The need to develop a personalized protocol**

We must be aware of the fact that the eloquence of the functional areas cannot be accurately anticipated only based on anatomic structures. The anatomic knowledge is necessary but not sufficient to operate with a high degree of certainty mostly in the “functional neurooncology”. Therefore, neurosurgeons must benefit from the advantages of the direct electrical stimulation technique in order to develop customized protocols for each patient, rather according to the functional borders than to the tumor borders in gliomas resection. In order to support these ideas, a major anatomical and functional individual variability was proved, by using the functional neuroimagergy in healthy volunteers, but also by using the direct electrical stimulation in patients with epilepsy. In a recent report, Ius et al. 2011 (9), proposed an atlas of the functional resections in patients who developed a low-grade glioma, mainly represented by the main association paths which should not be resected if one wants to avoid permanent deficits. Moreover, the authors found eloquent areas which can be compensated, mainly at cortical level. The
authors concluded that the identification of a given functional area cannot be accurately carried out before the intervention because of the plasticity, conferring a crucial role to the electric mapping for the “online” anatomical and functional correlations and the preservation of the eloquent areas during the awake brain surgery.

Furthermore, the intraoperative mapping through direct electrical stimulation is not only an instrument, but it is also considered an access door to the functional network which allows us a better understanding of the neural basis, by means of the cerebral processes. The neurophysiologists brought into discussion ethical aspects of this invasive technique, in which we must not forget that the main objective is patient’s benefit through the maximal resection and the preservation of the important functions. As a consequence, it is important to find equilibrium in the number of tests strictly necessary in order to preserve patient’s life quality and not enforce too many tests which can be time consuming over the intervention, inefficient and possibly harmful.

A multidisciplinary approach involving neurosurgeons, neurologists, neuropsychologists and speech therapists is crucial in order to build an adequate intraoperative protocol and practically adapted to each individual patient, with the selection, to the possible extent, of sensitive tests capable of assessing more than one cerebral function. For instance, the classical picture naming task allows an integrated, complex testing which involves visual recognition, semantic processing, lexical access/vocabulary, phonological decoding and verbal production at the same time. An accurate analysis, in real time of the possible functional deficiencies produced by direct electrical stimulation or the resection itself should be carried out by a specialist during the tumor resection.

The selection of the intraoperative tasks must be based both on the features of the patient and of the lesion. The neuropsychologist must first of all determine the hemisphere dominance. The identification of the manual dominance is not sufficient, as cases of postoperative crossed aphasia were reported. Therefore, the most important factor in assessing the cerebral dominance is the existence of certain preoperative language transformations, even subtle ones, highlighted by a detailed neuropsychological examination.

Furthermore, patient life features (job, hobby, habits) must play an important role in selecting the intraoperative tasks. As compared to a standard protocol, one must use specific tests in order to assess the individual needs of each patient. For instance, a calculation test can be necessary for a mathematics teacher, mostly when the lesion is located in the left parietal lobe; a reasoning task is important for a lawyer; a spatial cognition task is crucial for a military strategist or for a cartographer, while a synthesis and analysis and mental rotation task is absolutely necessary for a draftsman or an architect.

Lesion features (localization, volume) must also be taken into account. A lesion does not affect one specific anatomic structure only, but it can involve the entire cerebral functional network.

Preoperative psychological counseling and assessment

It is recommended to explain to the patient the intraoperative procedure and to present him to the members of the surgical team, but also to perform a neuropsychological counseling and assessment.
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Neuropsychological assessment at least one day before the surgical intervention. The neuropsychological assessment aims at determining the base line of neurocognitive functions, carrying out the tests included in the intraoperative protocol, for familiarization purposes and for removing the items causing difficulties to the patient, so as not to obtain false negative intraoperative responses. The involuntary movements, but also the inhibition of the voluntary ones can create to the patient a discomfort, anxiety accompanied by vegetative manifestations and even the alteration of the vital signs (10, 11). All these manifestations without an acceptance and a good compliance of the patient, based on the information and gaining the trust of the patient can threaten the proper development of the neurosurgical procedure. Therefore, besides the neuropsychological assessment sessions, the patient is informed with regard to the neurosurgical technique and procedure to which he will be subject and one shall explain to him the importance of his cooperation – he shall be made aware of the need to have an active – participative behavior during the surgery. Moreover, he shall be informed that during the stimulation can appear movements or reactions that the patient did not want to perform or, to the contrary, that he wants to perform, but he is not able to do so. He must be assured that these incidents are transient and are caused by the direct cortical stimulation and will not have long-term consequences. As we already mentioned, it is important that the intraoperative neuropsychological protocol be customized, adapted according to the interested cerebral area, to the eventual existing deficits, so as to obtain an optimal cooperation of the patient and to take into account the individual features of the patient.

The neuropsychological assessment

It is recommended to perform an objective and reproducible neurocognitive assessment, in the preoperative and postoperative stages, not only for assessing the neurosurgical side effects on the cognitive functions, but also for adapting the eventual functional rehabilitation in accordance with the results of the neurocognitive assessment (12).

The neuropsychological protocol in the cortical mapping imposes the determination of the base line, by the assessment of the following functions: temporal and spatial orientation, orientation to self and others; verbal and visual memory, working and delayed memory; attention; language: fluency, comprehension and repetition, vocabulary, written form, calculation; visuospatial analysis and synthesis, mental rotation; testing the rough motor function and the fine movements; tactile, visual, auditory and proprioceptive sensitivity; executive functions, affective mood. Two neuropsychological assessment sessions are needed: preoperative and postoperative.

The intraoperative protocol

In light of the recent data, certain authors propose the drafting of a common minimal protocol, which can test not only the language, but also other cognitive functions, which can be enforced in preoperative, intraoperative and postoperative stages in the awake craniotomies (7). The objective would be to facilitate the replicability between different neuro-oncology centers.

Therefore, in order to meet a minimum standard on pre- and postoperative language testing, the protocol should include: a subjective questionnaire which can inventories
patient’s plaints, handedness assessment, verbal fluency assessment / verbal spontane-
ity, a picture naming task with the calculation of the reaction time, a semantic fluency
test, a timed semantic association task and also a timed vocabulary task. Of course, it is
possible that the testing battery be extended in accordance with the variables related to
the individual habits of the patient. The list of specific tasks can comprise the symbolic
side of language - metaphors, repetition, vocabulary and written form.

The proposed protocol for testing the pre- and postoperative non-verbal functions
can include: a subjective questionnaire which may inventorize patient’s complaints also,
the assessment of the information processing speed, the working memory, the executive functions (flexibility, inhibition),
ideomotor and reflexive praxis and visuospatial cognition. And here appears
the freedom of adding other specific tasks which will assess different aspects of social
cognition or feelings, for instance.

Even though this set of tests is a proposal only, must be noted the fact that they have already been validated by favorable functional results, reported in hundreds of cases of extended resection of gliomas, carried out according to the functional limits. Besides

language, it has been proven that intraoperative mapping also allowed the preservation
of the complex neurocognitive functions, such as the working memory, the spatial
cognition, calculation, linguistic switching in bilingual patients, trans-modal reasoning
and executive functions.

CONCLUSIONS

The selection of the tests which shall constitute the intraoperative neuropsychological protocol must take into account both lesion localization and the functional areas involved, but also the subcortical association paths and the individual habits of the patient (job, hobby and customs). By the detailed assessment of the general condition of the patient, of the global cognitive functions and of the verbal skills, the psychologist has an important contribution in selecting the patients for the cortical mapping procedure, but also in its intraoperative development. The intraoperative neuropsychological protocol should contain a minimal common set of tests which would also allow a certain degree of standardization and statistical analysis, but which can be adapted to each patient with additional tests specific to the individual habits of each patient.

REFERENCES

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**NEWS**

**PUBO-FEMURAL DISTANCE: A MORE ACCESSIBLE TECHNIQUE FOR EARLY DIAGNOSE OF DEVELOPMENTAL HIP DYSPLASIA IN NEWBORN**

Ultrasound imaging is, and has been for some time now, the gold standard for early diagnose of developmental hip dysplasia. Although there are several techniques, they usually require an experienced pediatric orthopedic surgeon or radiologist to interpret the results. The pubo-femoral distance represents the distance between the lateral aspect of the pubic bone over the acetabular incisure and the medial surface of the cartilaginous epiphysis of the femoral head, both from a neutral position and with approximately 90 degrees hip flexion, without rotation, adduction or abduction. The coronal view necessary for obtaining a correct measurement is far more easily obtained that the incidence that the other methods require, making it a more accessible technique for the less experienced practitioners, but with similar results. This method could make possible a screening program for detecting developmental hip dysplasia, without the extensive training (Teixeira SR, Dalto VF, Maranho DA et al. Comparison between Graf method and pubo-femoral distance in neutral and flexion positions to diagnose developmental dysplasias of the hip. *Eur. J. Rad.* 84 (2015) 301–306).

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