Dienst Neurochirurgie UZ Leuven

AANVRAAG BEURS MEDISCHE STICHTING M. HORLAIT-DAPSENS

Tom THEYS

Leuven, Juni 2012

Title of the project: *"Sensorimotor Processing in Neurosurgical patients"*

Table of Contents

Scientific background and previous research

Humans and other primates possess an exquisite capacity to grasp and manipulate objects. The seemingly effortless interaction with objects in everyday life is subserved by a number of cortical areas of the visual and the motor system. In order to succesfully grasp an object, the complex pattern of visual information impinging on the retina has to be transformed into a motor plan that can control muscle contractions. The neural basis of visuomotor transformations necessary for directing actions towards objects, however, has remained largely unknown.

When we look at the world around us, we perform an analysis of the environment and its objects. Object information can be processed for the purpose of object recognition as well as for action. In our brain, this information follows two parallel pathways directed towards the temporal (ventral visual pathway) or the parietal lobe (dorsal visual pathway) for object recognition and actions, respectively (Ungerleider and Mishkin, 1982; Goodale and Milner, 1992). The visual system extracts relevant information with respect to the three-dimensional (3D) structure of objects from binocular horizontal disparity, which results from the slightly different positions of the images on the two retinas. Disparity selectivity is ubiquitous in the visual system, found in early visual areas in the dorsal visual stream and in the ventral stream. While disparity information encoded in the ventral stream is used for object recognition, the dorsal stream presumably processes disparity for actions (related to object manipulation) (Neri, 2005; Goodale, 2010). The posterior parietal cortex and the premotor cortex play an important role in the processing and integration of visual information in order to control and direct voluntary movements. Successful grasping depends on extracting the 3D properties of an object to select the proper hand configurations (Castiello and Begliomini, 2008). A thorough understanding of the object representation in posterior parietal and premotor areas is crucial for the rapidly-developing field of brain-machine interfaces and biologically-inspired robotics: identifying the specific object features that the primate visual system extracts for guiding the hand during grasping may help to build flexible and autonomous robots capable of dexterous object manipulation.

In previous experiments we have shown that neurons in the posterior parietal cortex (Anterior Intraparietal Area, area AIP) and the premotor cortex respond selectively to disparity-defined three-dimensional shapes (Srivastava et al., 2009). Moreover, we showed that the same regions involved in processing three-dimensional shapes are also involved in visually-guided grasping (Theys et al., 2012). These studies strongly suggest that the dorsal visual stream computes a distinct object representation that is action-oriented (fast, coarse, metric, and boundary-based) but not readily available for perception. Area AIP – situated at the end of the dorsal visual stream – contains motor-dominant neurons, visuomotor and visual-dominant neurons. Most of these visual-dominant AIP neurons exhibit object selectivity, which is congruent with the preferred grip type (whole hand grip versus precision grip during grasping certain particular objects). Neurons in premotor cortex – which is reciprocally connected with AIP – display very similar response properties. Reversible inactivation of one of these areas results in a deficit in the preshaping of the hand during grasping (Gallese et al., 1994; Fogassi et al., 2001). In humans, lesions of the anterior intraparietal sulcus (IPS) produce a similar grasping deficit (Castiello, 2005).

The neural basis of visuomotor transformations for grasping actions towards objects remains largely unknown. Indeed, little is known about how and which incoming visual information is translated into a "motor code" so that a precise grasping can occur, in accordance with the specific properties of the object. If this "code" can be unraveled, or "decoded", it could be used in brain machine interface technology, where information from the posterior parietal cortex and premotor cortex could provide control signals to operate specific devices according to certain grasp configurations. Cognitive control signals for neuroprosthesis derived from the parietal reach region and dorsal premotor cortex have been decoded for reaching tasks, but not for grasping (Andersen et al., 2010).

The objectives of the current project consist of obtaining "invasive" neurophysiological data from the neurosurgical patient population. We hereby aim to describe and study specific neurophysiological mechanism in certain cortical areas of the brain (Part 1) and also at the level of the spinal cord (Part 2).

Part 1: Brain

Part 1A: Imaging and micro-electrode recordings in awake craniotomy patients

In this part of our study, we want to verify the results obtained in animal models of grasping in human patients using single-unit and Local Field Potential (LFP) recordings in premotor cortex during awake surgery. Patients with low grade gliomas (LGG) in or near highly eloquent brain regions like Broca, Wernicke and primary motor cortex, often can be operated on using cortical and subcortical mapping in awake craniotomies ((Duffau, 2007)). After mapping of the critical areas, resection boundaries are delineated before maximalized resection is performed, respecting crucial eloquent zones in the fully awake patients without any interference of anesthetics. Neuronal activity may still be present in LGG (Schiffbauer et al., 2001), but recordings of single-cell activity have not been performed. We will record in the premotor cortex of human patients during awake surgery in parts that will be resected because of a low-grade glioma.

If we can record normal neural activity in the marginal zone around the tumor – which in all likelihood is still functional – while the patient is performing grasping movements, we can obtain a truly unique data set that can be readily compared with the monkey data and likewise implemented in a brain-inspired model of grasping. Additionally, because these patients will be scanned preoperatively these recordings can provide critical evidence with respect to the relationship between the fMRI signal and single-cell activity. Permission from the ethical committee has been granted.

Candidate patients will be scanned (fMRI) preoperatively during passive viewing of images of objects and scrambled control stimuli, naming of objects, passive viewing of videos of actions (grasping with the hand, foot and mouth) and control stimuli (phase scrambled videos of the same actions). The brain region that is likely to be resected (hence from which we can record during surgery) will be mapped onto the fMRI activations.

We will record single-unit activity, multi-unit activity and local field potentials using two multielectrode arrays (32 electrodes per array) implanted in those parts of the mapped LGG which will be resected after testing. First, we will assess to what extent normal spontaneous activity is present in LGG. If we can record normal single-unit activity we will subsequently investigate stimulus-driven activity in premotor cortex. Testing can be performed both during and between the periods the patient performs the relevant intra-operative tasks, i.e. confrontation naming of objects, and the passive viewing of videos of grasping actions (the same stimuli as used in the fMRI experiment). The neural activity (spikes and LFPs) will be related to the fMRI activations obtained. We will also record during reaching and grasping actions performed by the patient to assess the presence of mirror-neuron activity in human premotor cortex (Gallese et al., 1996; Kraskov et al., 2009).

The same paradigm can be used in patients with epilepsy operated on in awake conditions, for example in cases of frontal lobe cortical dysplasia.

Part 1*B*: Intracranial EEG (iEEG/ ECOG) recordings in epilepsy patients

A similar paradigm as in the awake patient can be used in epilepsy patients who undergo placement of subdural grids and electrodes. The advantage in this patient population is the possibility to perform more complex and precise testing since testing can be performed after placement of the grid (bedside). The disadvantage is the lower spatial resolution of the ECOG signal compared to intracortical micro-electrode recordings. In this patient group we want to analyze the activity during presentation of 3D-stimuli. In this way we want to unravel the neural network involved in 3D shape processing and compare this to previous fMRI results published by our group (Georgieva et al., 2009). The experimental paradigm used in patients with subdural grids has to be adapted on the location of the grids and can also consist of grasping tasks or visual tasks depending on the brain area studied.

Moreover, in these patients we can stimulate via the grid contacts and look at behavioural effects such as perceptual changes or motor effects.

Part 1*C*: Psychophysics in neurosurgical patients

3D shape perception after temporal lobectomy

As previously mentioned the temporal lobe presumably plays an important role in 3D shape perception and categorization. We are currently examining epilepsy patients undergoing temporal lobectomy and we test their ability to discriminate three-dimensional shapes. Precise psychophysical testing is performed. Subjects are asked to discriminate between convex and concave 3D shapes (random dot stereograms). Task difficulty is manipulated by varying the signal strength of the stimuli which can be done by decreasing stereocoherence (percentage of dots defining the 3D shape of the objects). Patients are tested before and after surgery to see if resection of the anterolateral part of the temporal neocortex has any effect on depth perception.

Hand preshaping in patients with premotor lesions

This strategy of testing before and after surgery can also be used for patients undergoing resections in the premotor cortex. So far, no real lesion studies have been done in patients with premotor lesions. In this group of patients a reach-to-grasp task can be performed with an analysis of the dynamics of hand preshaping. The kinematics of the hand consisting of hand aperture and velocity, type of grip, finger position and dexterity can be analysed using The Optotrak Certus® (this motion capturing system tracks the different joints of the fingers using multiple markers on the hand). In this way the grasping deficit, probably a dynamic process, can be analyzed over time during rehabilitation.

Part 2: Spinal cord

Recording Spinal Cord Evoked potentials (SCEPs) in patients with dorsal column stimulation

In collaboration with prof. dr. B. Nuttin we are currently working on analyzing spinal cord evoked potentials in patients undergoing epidural electrode placement for treatment of refractory pain, In this patient group we have so far succeeded in recording the spinal cord evoked potential (SCEP) from the eight contact points of the epidural electrode. The aim of this part is to investigate the relationship between different patterns of electrode stimulation and peripheral sensory stimulation and the spinal cord-evoked potentials. In this way we could maybe optimize electrode placement in the future.

We also want to look at the influence of certain aspects of sensory-motor processing on the spinal cord by investigating the influence of action observation (mirror neuron activity) and mental action simulation (mental imagery) on the so-called "gating process" in the spinal cord, more particular its influence on the spinal cord evoked potential.

Summary

Most of what we know of human nervous system functioning is based on lesion studies and on indirect techniques such as BOLD activity in fMRI. As neurosurgeons, we have the unique opportunity to record the neural activity directly from certain brain regions.

We want to take this opportunity to perform direct electrophysiology experiments in the human nervous system, in collaboration with the lab of neurophysiology (Prof. P. Janssen), to elucidate certain brain mechanisms especially those related to three-dimensional shape perception and grasping. In collaboration with Prof. B. Nuttin we also want to explore neural signals from the spinal cord. We are currently already working on these projects.

Projected stay in a foreign center

As previously mentioned, the proposed project is already partly running at the Department of Neurosurgery, Leuven and we intend to continue the current project in the upcoming years. I defended my PhD in May 2012 and will go abroad for a fellowship from August 2012 until July 2013. I will be working in the 'Institut des Neurosciences' in Grenoble where they have extensive expertise with intracranial

References

Andersen RA, Hwang EJ, Mulliken GH (2010) Cognitive neural prosthetics. Annu Rev Psychol 61:169-3.

Castiello U (2005) The neuroscience of grasping. Nat Rev Neurosci 6:726-736.

Castiello U, Begliomini C (2008) The cortical control of visually guided grasping. Neuroscientist 14:157-170.

Duffau H (2007) Contribution of cortical and subcortical electrostimulation in brain glioma surgery: methodological and functional considerations. Neurophysiol Clin 37:373-382.

Fogassi L, Gallese V, Buccino G, Craighero L, Fadiga L, Rizzolatti G (2001) Cortical mechanism for the visual guidance of hand grasping movements in the monkey: A reversible inactivation study. Brain 124:571-586.

Gallese V, Murata A, Kaseda M, Niki N, Sakata H (1994) Deficit of hand preshaping after muscimol injection in monkey parietal cortex. Neuroreport 5:1525-1529.

Georgieva S, Peeters R, Kolster H, Todd JT, Orban GA (2009) The processing of three-dimensional shape from disparity in the human brain. J Neurosci 29:727-742.

Goodale MA (2010) Transforming vision into action. Vision Res.

Goodale MA, Milner AD (1992) Separate visual pathways for perception and action. Trends Neurosci 15:20-25.

Neri P (2005) A stereoscopic look at visual cortex. J Neurophysiol 93:1823-1826.

Srivastava S, Orban GA, De Maziere PA, Janssen P (2009) A distinct representation of three-dimensional shape in macaque anterior intraparietal area: fast, metric, and coarse. J Neurosci 29:10613-10626.

Theys T, Srivastava S, van Loon J, Goffin J, Janssen P (2012) Selectivity for three-dimensional contours and surfaces in the anterior intraparietal area. J Neurophysiol 107:995-1008.

Ungerleider LG, Mishkin M (1982) Two cortical visual systems. In: Ingle DJ, Goodale MA, Mansfield RJW, eds. Analysis of visual behavior. pp 549-586. Cambridge, MA: MIT.