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Cognitive potentials in the basal ganglia—frontocortical circuits. An intracerebral recording study

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Abstract We studied cognitive functions related to processing sensory and motor activities in the basal ganglia (BG), specifically in the putamen and in cortical structures forming the BG-frontocortical circuits. Intracerebral recordings were made from 160 brain sites in 32 epilepsy surgery candidates. We studied P3-like potentials in five different tests evoked by auditory and visual stimuli, and two sustained potentials that are related to cognitive activities linked with movement preparation: BP (Bereitschaftspotential) and CNV (contingent negative variation). We compared the presence of a potential with a phase reversal or an amplitude gradient to the absence of a generator. All of the studied cognitive potentials were generated in the BG; the occurrence in frontal cortical areas was more selective. The frequency of all but one potential was significantly higher in the BG than in the prefrontal and in the cingulate cortices. The P3-like potentials elicited in the oddball paradigm were also more frequent in the BG than in the motor/premotor cortex, while the occurrence of potentials elicited in motor tasks (BP, CNV, and P3-like potentials in the CNV paradigm) in the motor cortex did not significantly differ from the occurrence in the BG. The processing of motor tasks fits with the model by Alexander et al. of segregated information processing in the motor loop. A variable and task-dependent internal organisation is more probable in cognitive sensory information processing. Cognitive potentials were recorded from all over the putamen. The BG may play an integrative role in cognitive information processing.

Keywords Basal ganglia · Bereitschaftspotential · Contingent negative variation · Putamen · P3

Introduction

Interest in brain function localisation is continually increasing. One quite new advance is the recent progress in the detection of brain functions through metabolic studies using positron emission tomography and functional magnetic resonance imaging (fMRI). Despite their spectacular results, these techniques should be interpreted in conjunction with electrophysiological methods. Electrophysiology reveals other physiological mechanisms, providing information complementary to metabolic studies. This is principally due to the better time resolution. Only electrophysiological techniques can currently provide us with information about the time sequence of cerebral activation with respect to movement and to cognitive processes. Electrophysiological research is primarily targeted towards the study of the cortex. Recording through electrodes placed on the scalp can bring only an indirect indication of the function of the cortex, and even less indication about the function of the subcortical structure. The use of mathematical models can provide hypotheses about the location of generators, but it can hardly provide proof for such postulates. In some cases, intracranial electrodes are implanted in human subjects for medical reasons, enabling recordings from the brain tissue. Direct recording from cerebral structures remains an important and yet irreplaceable source of information.

We studied potentials related to a variety of cognitive activities (attentional, decisional, motor preparation, sensory processing, etc.) in brain structures that participate in cortico-basal ganglia-thalamo-cortical loops; and we chose relatively simple and well-known protocols that have been consecutively tested. The occurrence of several cognitive potentials has partially been published in previous studies (Rektor et al. 1994, 1998, 2001a, b, c, 2003; Lamarche et

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al. 1995; Brázdil et al. 1999, 2001; Bareš 2001; Bareš and Rektor 2001; Rektor 2002).

We tested:

- a) The appearance of slow potential shifts expressing cognitive activities related to the preparation and execution of the movement in the cued movement in the contingent negative variation (CNV), and of the self-paced movement in the Bereitschaftspotential (BP) paradigms. BP includes some actions that could be considered as cognitive: the timing, the decision to perform the movement, the preparation for and the initiation of the motion (Libet 1985; Rektor et al. 2001c). The CNV is believed to be linked to different mental states and activities, including the level of vigilance, arousal, stress, attention, expectation, the will to elaborate the response, decisional performance, time estimation, and preparation of a motor response (Brunia and Damen 1988; Verleger et al. 1999; Cui et al. 2000). More details of BP and CNV have been reported in previous papers.
- b) Cognitive processing of visual and auditory signals in a simple oddball paradigm, and in a more complex task in the CNV paradigm (P3-like potentials).

In all, we studied the elicited appearance or the absence of ERP at approximately 250–500 ms latency in five different tests using two sensory modalities. Four protocols were performed: an auditory oddball (aP3) and a visual oddball (vP3); and CNV protocols, in which the potentials evoked by auditory warning (aCNV) and visual imperative (vCNV) stimuli were evaluated. In all oddball protocols, the patients were asked to silently count the target stimuli. In the protocols aP3, vP3, and vCNV, the tested person also responded by flexing his/her thumb or hand. In the aCNV paradigm, and in a further auditory oddball paradigm (aP3c), no motor response was required.

An ERP in the 300-ms range may represent various functions—the closure of sensory analysis, the update of working memory, the attentional and decisional processes and, in a motor task, the facilitation of motor pathways (Brunia and Damen 1988). The intracerebrally recorded oddball ERP are probably elicited by a cognitive process that shares critical common features with the P300 wave recorded on the scalp. The mechanisms underlying the ERP elicited in the CNV paradigm by S1 and S2 stimuli share features with the mechanisms underlying the P300 elicited by a variety of protocols; however, they cannot be fully identified with them. The ERP following the warning stimulus evokes a process of orientation and alertness, and it is not followed by an overt action, while the P3-like potential following the imperative stimulus is related primarily to identifying the stimulus as an imperative, and might be influenced by the motor task that follows. More details about the P3-like protocols have already been discussed elsewhere.

In regards to the relation of the potential to the motor activity, we obtained three types of data:

- Potentials related directly to the movement activity in terms of the timing, the decision to perform the movement, planning, programming, preparing, initiating and executing a movement. BP are generated by processes specifically involved in the preparation for or intention to perform a movement (Libet 1985; Rektor et al. 2001b). The processes associated with attention, cognition and expectancy could not solely account for BP. The movement was self-initiated in the BP protocol, and cued in the CNV protocol. The CNV reflects the will to elaborate the response, decisional performance, time estimation, and preparation of signalled movements (Brunia and Damen 1988; Verleger et al. 1999; Cui et al. 2000).
- ERPs that were not directly related to the motor functions. In the auditory oddball protocol (aP3c) and the auditory ERP after the warning stimulus (aCNV), there was no motor activity.
- ERPs not directly related to the movement, nevertheless elicited in a paradigm that included a motor task (vCNV, aP3, vP3). The ERPs covered identical cognitive activities (closure of sensory analysis, the update of working memory, the orientation, expectation, and decisional processes, etc.) as above when performed in the absence of an overt movement; however, in this case the behavioural context was motor. There was a substantial difference in the behavioural meaning of the motor task between the oddball-elicited ERP and ERP elicited in the CNV paradigm. While in the first case the movement was just an auxiliary task additional to the mental counting, in the latter case the movement was the only goal of the task.

The study was originally designed for three purposes. The first goal was to investigate the intracerebral sources of several types of cognitive and/or movement-related potentials and several types of protocols that were designed and tested for this purpose. The second aim was to map task-related networks and to localise the task specific and task unspecific areas by mutually comparing various protocols. This idea was based on the fact that we could obtain various ERPs from one site, i.e. recorded through one well-defined electrode contact, and that we could obtain such data from many sites across the brain. While the first goal was reached, and several papers identifying the origin of several potentials have been published, the second goal has not yet been achieved, as the data are rather inconsistent. The third goal was to study the relationship between the cortex and the basal ganglia (BG). We have already reported that the occurrence of all recorded P3-like potentials was higher in the BG than in the motor/premotor cortices (Rektor et al. 2003). In the present study, we review our data from the point of view of the cortico-basal ganglia-thalamo-cortical circuits.

Our previous results indicated that the BG, specifically the striatum (from which we obtained the bulk of our recordings), not only receive external information, but participate in the cognitive processing of such information.

The BG may play an integrative role in cognitive information processing, in motor as well as in non-motor tasks. This role seems to be non-specific in terms of stimulus modality and of the cognitive context of the task. The BG are in a position to influence the cognitive activity of the forebrain (Graybiel 1997).

This study addresses the following question: are the cognitive activities, on the one hand movement-related and on the other hand movement-unrelated, processed in segregated cortico-basal ganglia-thalamocortical circuits?

Subjects and methods

The study protocol was approved by the local ethics committee. All patients freely gave their informed consent to participate in the program. Using intracerebrally inserted electrodes (in one patient, also subdural strip electrodes), ERP recordings were obtained from 32 patients suffering from intractable epilepsy, examined in the diagnostic phase of preparation for epilepsy surgery. The patients were candidates for epilepsy surgery who had remained unresponsive to conventional forms of therapy, and who were recommended by a special commission for stereotactic exploration. There were 24 men and eight women; the mean age was 27.1 years (range: 14–38 years). A neuropsychological examination excluded cognitive disturbances and dementia in each patient. All the patients had normal motor performance, normal hearing, and normal or corrected-to-normal vision.

Depth electrodes were implanted before surgical treatment to localise the seizure origin. Each patient received 4–9 orthogonal platinum electrodes in the temporal and/or frontal lobes using the methodology of Talairach et al. (1967), and/or diagonal electrodes inserted stereotactically into the amygdalo-hippocampal complex. The diagonal electrodes were always targeted only into the mesiotemporal structures via a frontal approach, passing through the BG. Standard platinum MicroDeep semiflexible electrodes (DIXI Instruments, Briançon, France) with diameters of 0.8 mm, lengths of 2 mm, and intercontact intervals of 1.5 mm were used for invasive EEG recordings. Contacts at the electrodes (5–15) were always numbered from the medial to the lateral side. We recorded from 58 electrodes in all. The recordings were obtained from a total of 530 sites in the brain. After the exclusion of contacts with far field potentials, artefacts, etc., we obtained recordings with potential generators or those with a clear absence of a generator in 160 sites.

The exact positions of the electrodes and their contacts within the brain were verified using post-placement brain magnetic resonance imaging (MRI) with electrodes in situ. The inversion recovery sequences were particularly useful in determining the location of the depth electrode contacts in the BG. We were able to distinguish the location of a contact in the BG from the location in the white matter; however, we could ascertain its exact position inside a BG structure only approximately (Fig. 1).

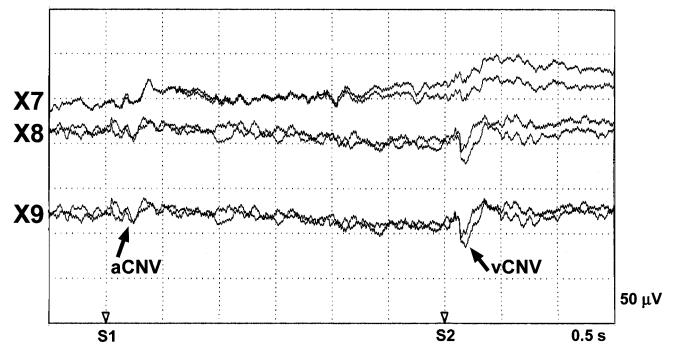


Fig. 1 The phase reversal of CNV and the steep amplitude gradient of vCNV between the 7th and 8th contact of the electrode X (basal ganglia-pallidum) suggest a local source of the investigated potentials in the BG

Recordings from intracerebral electrode contacts were done in a referential montage (with the contact serving as the active pole, and connected earlobes used as the reference). The signal was filtered in the range between 0.1 (LFF) and 100 Hz (HFF), and the time base was 1,000 (auditory) or 2,000 (visual) ms for the oddball P3 recordings; for the CNV recordings, the signal was filtered in the range between 0.01 (LFF) and 100 Hz (HFF), and the time base was 5,000 ms. All ERP recordings were done using either the 8-channel Nihon Kohden Neuropack 4200 EP/EMG device (Nihon Kohden Electronics, Osaka, Japan) or the 64-channel Brain Quick EEG system (Micromed, Mestre, Italy) with ScopeWin (Jurák Electronics, Brno, Czech Republic) tailored software. Subjects were seated comfortably in a semi-reclined chair in a moderately lighted room during the recordings. The SEEG and video recordings were made during the tests. Recordings from lesional structures and epileptogenic zones and recordings with epileptic discharges were not included in the analysis. Electro-oculograms (EOG), recorded from an electrode placed laterally to the lateral canthus, were monitored simultaneously, using the same filtering and sensitivity as for an EEG recording. Any other outgoing artefacts (saturating DC shift of the trace, erratic movement of the patient, blinking, etc.) were rejected on-line when possible and during the off-line analysis. For the surface EMG, the band pass filter was 200 Hz–3 kHz.

At least two recording sessions using each paradigm were made to ensure reproducibility. All recordings were stored in the equipment memory for further off-line and statistical analysis.

Before the start of each recording session, the subjects were carefully instructed about the tasks, and any uncertainties were clarified. Thirty to sixty artefact-free trials in the BP and CNV paradigms, and 40 sweeps for each type of stimulus (target and frequent) in the oddball paradigm were independently averaged. The ERP recordings were made consecutively using the following paradigms:

a. Auditory P3 paradigms

1. Oddball paradigm (aP3c). The classic auditory ERP oddball paradigm was used. Tones were delivered

through earphones, at a 2-Hz frequency: frequent (“masking”) tones were delivered at 1,000 Hz and 70 dB, for a 0.1-s duration; rare (“target”) tones were delivered at 2,000 Hz and 70 dB, for a 0.1-s duration. The tones were randomly generated at a 5:1 ratio. The subjects were instructed to recognise the target tones, and to silently count them; they were asked for the total number of target tones at the end of each recording session. The subjects were also instructed not to perform any motor activity during the test.

2. Modified motor & oddball paradigm (aP3). A modified auditory ERP oddball paradigm, involving a motor task and an increased cognitive load, was used. The tones were delivered through earphones, at a 2-Hz frequency: frequent (“masking”) tones were delivered at 1,000 Hz and 70 dB, for a 0.1-s duration; rare (“target”) tones were delivered at 2,000 Hz and 70 dB, for a 0.1-s duration. The tones were randomly generated at a 5:1 ratio. The subjects were instructed to recognise the target tones, to silently count them, and to tell the examiner the total number of target tones at the end of the session. The subjects were also instructed to respond to each target tone by using their thumb to press the button of a response switch held in the dominant hand. The EEG epochs following both the masking and target stimuli were displayed, averaged, and stored separately. Thirty target and 150 frequent stimuli were averaged in each recording session.
- b. Visual P3 paradigm (vP3). Subjects were seated with a monitor screen positioned 1 m in front of their eyes, and were requested to continuously focus their eyes on a small fixed point in the centre of the screen, and to minimise blinking during the examination. The standard visual oddball paradigm was performed, with a stimulus exposure duration of 200 ms. Two types of emotionally neutral stimuli—target and frequent—were presented in the centre of the screen in random order. The experimental stimuli consisted of yellow uppercase Xs (target) and Os (frequent) on a white background. The ratio of target to frequent stimuli was 1:5. The stimuli were displayed on a black screen subtended at a visual angle of 3°. The interstimulus interval varied between 2 and 5 s. Subjects were instructed to respond to the target stimulus as quickly and as accurately as possible by pressing a response switch button in the dominant hand, and simultaneously to silently count the target stimuli. The distribution of P3 potentials in various cortical areas in this study has already been published (Brázdil et al. 1999, 2001).
 - c. Bereitschaftspotential (BP) paradigms. Slightly modified versions of classical BP testing protocol were used (Kornhuber and Deecke 1965; Rektor et al. 1994). Subjects were instructed to perform brisk-onset simple movements, specifically, a hand or foot flexion, without any external stimulus (i.e. in the self-paced mode). The subjects were also instructed to keep their eyes open, and to fix the gaze on a given point, in order to prevent the interference of eye movements with brain potentials. Slow potentials appearing before a simple repetitive distal limb movement, were recorded. In one series, a more complex movement (turning pages in a book) was used Rektor et al. 2001b. The intracerebral potentials occurred with both positive and negative polarities. This was due to variances in the positions of the electrode contact and of the dipole generator. Absolute amplitudes were measured from the baseline, which was defined as the electrical activity that occurred 3,000–3,500 ms before the movement. The distance from the electrode to the generator heavily influences the amplitude of intracerebrally recorded potentials, and thus the differences of amplitude can only be compared intraindividually. A clearly larger amplitude in one structure than in its neighbouring structures, particularly an amplitude involving a steep voltage gradient and polarity inversion over a short distance, implied a local BP generator. A steep voltage gradient probably indicated that the electrode was in the immediate vicinity of the generator. A polarity inversion probably indicated that the depth electrode was recording from directly inside the generating tissue. The potentials that had amplitudes that remained unchanged over several consecutive contacts were considered as far-field potentials.
 - d. CNV paradigms (CNV, aCNV and vCNV). Each patient underwent CNV testing with pseudo-random inter-trial intervals. A slightly adapted version of Walter’s classical protocol (Walter et al. 1964; Lamarche et al. 1995) was used. The CNV recordings were performed in an audio-visual paradigm (S1-S2 task) with the 3-s interstimulus interval. As a warning stimulus (S1), a single acoustic tone was randomly presented through headphones (80 dB intensity, 0.1 Hz stimulus rate, 0.1 ms duration). The imperative stimulus (S2) was a visual stimulus, a single 0.1-Hz flash delivered through goggles; this stimulus regularly followed 3 s after the S1. This audio-visual paradigm (A-V) was used in conjunction with a motor task (flexion of the hand). Usually the movement of the flexor carpi ulnaris muscle contralateral to the implanted electrode was recorded by a pair of cup electrodes placed on the skin overlying that muscle. The subjects reclined in a comfortable armchair; they were adequately informed about the task they were to perform before the beginning of the recordings. They were instructed to perform a brisk flexion of the hand immediately following the imperative stimulus. They were also instructed to keep their eyes open, and to avoid any voluntary movement during the task. Before the recording session, each subject was given a short practice period until the examiner was satisfied that the subject was able to consistently produce brisk movements preceding and following complete relaxation.

All data were acquired and averaged by the Nihon Kohden Neuropack 8 set. The analysis window was 5 s; the sampling frequency was 2,000 Hz. The recordings started 0.5 s before the S1 stimulus. Each CNV session took about 20–25 min. The recordings were unipolar. Linked earlobe electrodes were used as a reference.

The results concerning the CNV distribution in this study have also already been published (Bareš 2001; Bareš and Rektor 2001). For the evoked potential analysis, a time interval of 100 ms before and 900 ms after each type of stimulus was analysed (zoom analysis) off-line pursuing the reproducible components.

Analysis of recorded potentials

The main ERP components in the 250–600 ms latency range following target stimuli or S1/S2 stimuli were identified by visual inspection and quantified by latency and amplitude measures. The peak latencies were measured from the stimulus onset. We evaluated the first distinctive potential to occur in the 250–600 ms time window that displayed an amplitude gradient in several adjacent contacts. Only the P3-like potential “phase reversal” and “steep voltage change” were considered as generators, because of their significance as the accepted signs of proximity to generating structures (Vaughan et al. 1986). A clearly larger amplitude in one structure than in neighbouring structures, particularly a steep voltage gradient and polarity inversion over a short distance, implied a local generation of P3-like potentials (Halgren et al. 1998). The statistical analysis of recorded potentials was done by comparing the presence of ERP with an amplitude gradient with the absence of a potential or with a far field potential. If the ERP in a brain region were recorded from several consecutive contacts of an electrode, the contact with the highest ERP amplitude was used for the statistical analysis.

The amplitudes of averaged peaks were also measured; however, further analysis was not performed, as their values within the different cortical sites varied widely. The amplitude of intracerebrally recorded potentials is heavily influenced by the distance from the electrode to the generator; thus, the differences can be compared only

intraindividually. The intracerebral potentials occurred with both positive and negative polarities. This is due to the variable position of the electrode contact and of the dipole generator. In fact, with depth electrode recording, even a CNV can be positive.

Statistical analysis was performed using the STATISTICA program (StatSoft). For the latency analysis, ANOVA and a post-hoc Tukey test were used, with a $p < 0.05$ level of significance. A non-parametric Friedmann ANOVA was used to gauge the frequency of the recorded potentials.

Results

A clear amplitude gradient or a phase reversal of the evoked potential components (“P3-like”) and of slow potential shifts was repeatedly found in the explored structures of the BG and the cortex (Fig. 1). Potentials with no amplitude gradient on consecutive contacts were also observed. Due to the absence of amplitude gradient, the origin of these potentials was unknown, and therefore they were not considered in the final assessment. Results are given in Tables 1 and 2 and in Fig. 2.

Table 2 Comparison of the frequency of the P3-like potentials and of slow potentials in the cortical sites and in the basal ganglia

	BG versus motor	BG versus prefrontal	BG versus cingulate
VP3	2.93	0.99	1.07
AP3	5.51	5.13	3.82
AP3c	5.27	5.01	3.97
VCNV	0.83	2.54	3.07
ACNV	0.71	2.66	1.17
CNV	0.20	3.35	2.17
BP	0.51	2.40	2.99

Statistically significant differences between the basal ganglia and cortical sites are indicated in grey

Table 1 Frequency (absolute and relative) of P3-like potentials and slow potentials in explored cortical sites and basal ganglia

gen/meas total number of generators/measurements in the designated explored site using the indicated paradigm, *Std. Dev* standard deviation

	Motor and premotor		Prefrontal		Cingulate		BG	
	Gen/meas	%	Gen/meas	%	Gen/meas	%	Gen/meas	%
VP3	4/26	15.3	14/31	45.1	15/34	44.1	8/13	61.5
AP3	3/14	21.4	2/10	20.0	8/15	53.3	13/13	100.0
AP3c	4/14	28.2	3/11	27.3	8/15	53.3	15/15	100.0
VCNV	13/18	72.2	6/15	40.0	5/16	31.2	11/13	84.6
ACNV	16/18	88.9	6/17	35.3	10/19	52.6	12/15	80.0
CNV	13/17	76.5	3/17	17.6	7/19	36.8	11/15	73.3
BP	11/14	78.6	6/19	31.6	5/21	23.8	12/17	70.5
Mean	-	54.50	-	30.99	-	42.16	-	81.41
Std. Dev	-	28.94	-	9.36	-	11.00	-	13.55

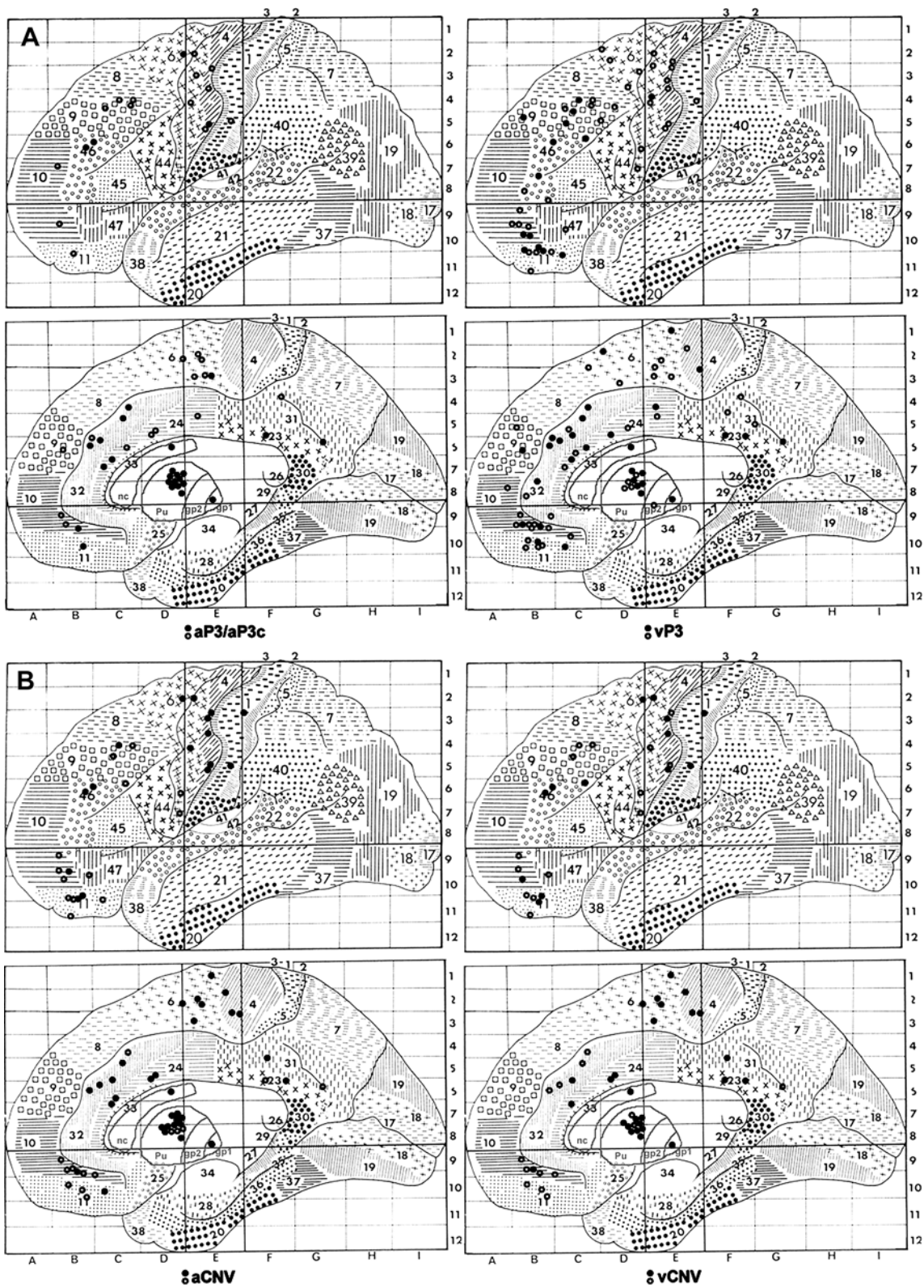


Fig. 2a–c The distribution of generators of the P3-like potentials (a, b), of the Bereitschaftspotentials and of the Contingent Negative Variation (c), in the cortex and in the basal ganglia. *Solid circles* indicate the presence of the P3 generators in the investigated sites,

and *empty circles* indicate the absence. *Upper part*: medial aspect. Approximate Brodmann areas are also indicated as mapped in Talairach and Tournoux (1988)

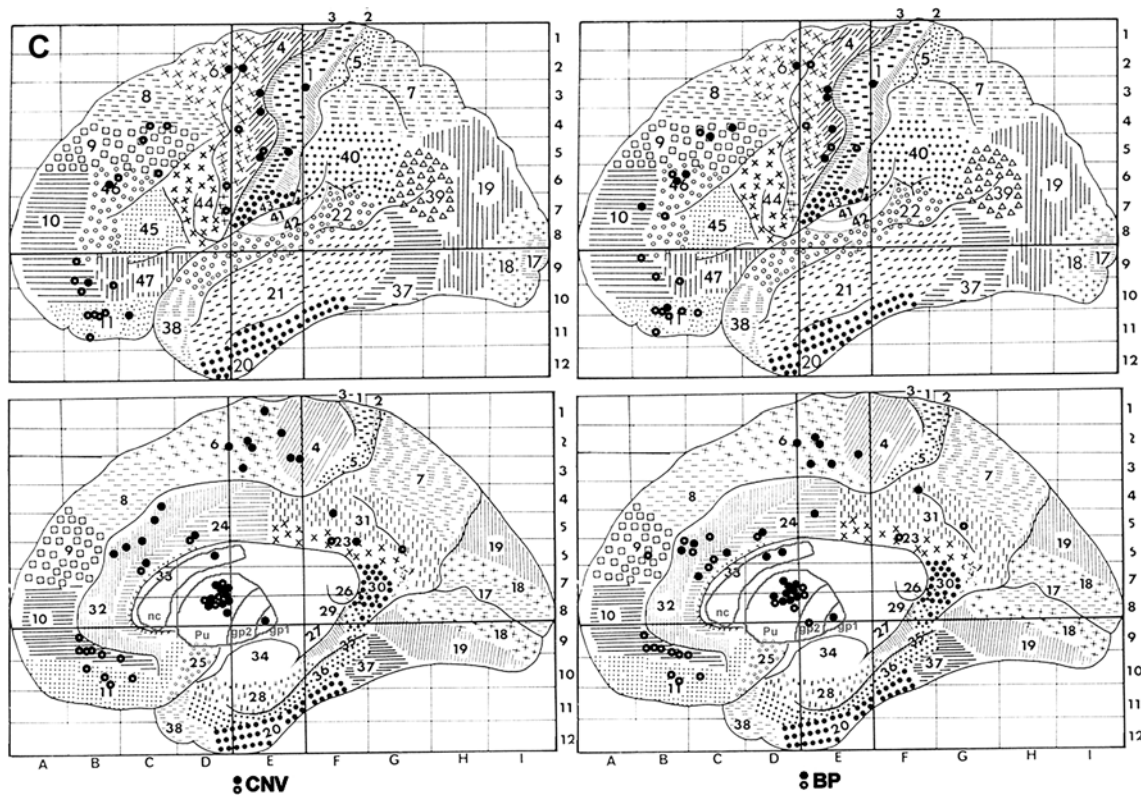


Fig. 2a-c (continued)

Comparison of the frequency occurrence of ERP, CNV, and BP in different paradigms between individual cortical sites and BG sites (Tables 1 and 2)

The test of relative frequency occurrence based on the testing of binomic distribution was used for the statistical analysis. The critical value of the test characteristics for $p=0.05$ is 1.96.

Basal ganglia versus motor/premotor cortex

The frequency of vP3, aP3, and aP3c was statistically significantly higher in the BG in the explored premotor sites ($p<0.05$). The difference of the frequency occurrence of the vCNV, aCNV, CNV and BP between the BG and premotor cortex was non-significant.

Basal ganglia versus prefrontal cortex

The frequency of aP3 and aP3c, vCNV, aCNV, CNV and BP was statistically significantly higher in the BG than in the dorsolateral prefrontal/lateral orbitofrontal cortex ($p<0.05$). vP3 displayed non-significant results.

Basal ganglia versus cingulate cortex

The frequency of aP3 and aP3c, vCNV, aCNV, CNV and BP was statistically significantly higher in the BG than in the cingulate/medial orbitofrontal cortex ($p<0.05$). vP3 displayed non-significant results.

Comparison between basal ganglia and individual cortical sites (all used paradigms)

The frequency occurrence of all P3-like potentials (vP3, aP3, aP3c, aCNV, vCNV) and slow potentials (CNV, BP) in the BG was statistically higher than the frequency occurrence of all these potentials in the entire explored cortex (t -test, $p<0.05$).

Comparison of the P3-like potential latencies in cortical sites and in the basal ganglia

A multivariate ANOVA with a Duncan post-hoc test was used for the statistical analysis of the latency. The difference between all the latencies of all of the P3-like potentials in the BG and the latencies in the cortex was insignificant. When the latencies in individual paradigms were mutually compared, a statistically significant difference between the mean latencies of vP3 and the other paradigms used was observed. Additionally, vCNV and aCNV displayed longer mean latencies than aP3 and aP3c.

No significant difference was found between the mean latencies of aP3 and aP3c, and vCNV and aCNV, respectively (Duncan post-hoc, $p > 0.05$). When the latencies in individual paradigms in the BG were compared with the latencies in the cortex, the latencies were shorter in the BG for all paradigms except that of vP3. Statistically significant differences between the mean latencies of vP3 and vCNV in the cortex and in the BG were observed ($F_{(4,177)} = 2.8234$, $p < 0.05$, Figs. 1, 3).

The location of recorded potentials in the basal ganglia

The potentials were distributed in all of the explored BG areas. A functional topography of cognitive potentials in the BG was not displayed. We recorded cognitive potentials from all over the putamen, caudate, and pallidum. Various potentials on the same lead or nearby contacts were recorded (Figs. 4 and 5).

Discussion

We are aware of several limitations of this study. The protocol was not designed to study the cortico-subcortico-circuitries. The data in this paper is combined and reviewed from an unusual point of view. The data are ranged according to the generally accepted (Alexander's) model of cortico-subcortico-cortical loops, but despite the significant results, we cannot fully exclude the possibility that the presented data do not reflect the BG/cortex relationship at all. It is improbable but possible that the studied activities are processed in the cortex and in the BG independent of each other and do not reflect the activity in the circuits. However, the contemporary knowledge of the circuitries does not support such an option.

This study was focussed on sources of brain electrical potentials elicited by cognitive activities in structures participating in the BG-thalamo-frontocortical loops. The scope of our study was determined by the location of the

sites implanted for recording for clinical purposes. The locations of the contacts in the BG were mostly restricted to the putamen. We were able to record from principal frontal cortical areas that appeared to be the target of topographically organised output from the BG (Middleton and Strick 2000). Given our interest in cognitive functions, both related and unrelated to motor activity, we studied the cognitive potentials in the cortical areas directly involved in movement preparation and execution (the motor, the lateral premotor, and the mesial premotor, including the SMA), as well as in the areas that appear to be mostly involved in behavioural, emotional, and other cognitive activities [the dorsolateral prefrontal cortex (DLPFC), the cingulate, and the orbitofrontal cortex (OF)]. Most cingulate contacts were located in the anterior cingulate—areas 24 and 32.

The evidence for a local generator of intracerebral ERP is a polarity reversal or a steep current gradient across a short distance of brain tissue (Fig. 1). A polarity reversal is recorded from the generating tissue; with a steep current gradient, the generator is located in the vicinity of the electrode. The characteristics of the electrodes used in this study, e.g. up to 15 consecutive contacts, the small volume of the lead, and the short intercontact distance (1.5 mm) enabled the relatively precise localisation of the signal source within the explored cerebral structure. With intracranial recordings, not all of the relevant brain regions may be sufficiently sampled because of poor spatial resolution. The intracerebral recording alone may not explore the distributed neural system in its whole complexity. Multiple techniques, including those with poorer temporal resolution but with better spatial resolution (fMRI, PET), will be required in order to completely understand the role of the BG-frontocortical circuits in cognitive processes. Nevertheless, the limited spatial resolution may be partially overcome by a larger number of recordings. This study presents the results of a relatively large number of recordings obtained from various cortical and subcortical sites (Figs. 2 and 4). We were able to record from 160 sites in the brain.

There are several theories about the role of the BG in processing the cognitive functions. It has been suggested that this system provides for planning movement (Marsden 1980), in preparing the movement (Romo et al. 1992; Rektor 2000), in selecting motor programs, and in enabling movement to be automatic (Brochier et al. 1991). It has also been suggested that it is a cognitive pattern generator (Graybiel 1997), and involved in the attention process (Stein and Volpe 1983). Kropotov and Ponomarev (1991) suggested that P300-like activity in the BG could be considered as a reflection of the program selection; a mechanism related to response to stimulus. According to Kimura (1986, 1990) the putamen is involved in the initiation of movement by the selection of a particular learned movement associated with contextual sensory cues. Our results confirm the cognitive processing of sensory information in the striatum, and possibly also in the pallidum. The sensory cues are processed in the BG with, as well as without, a motor task.

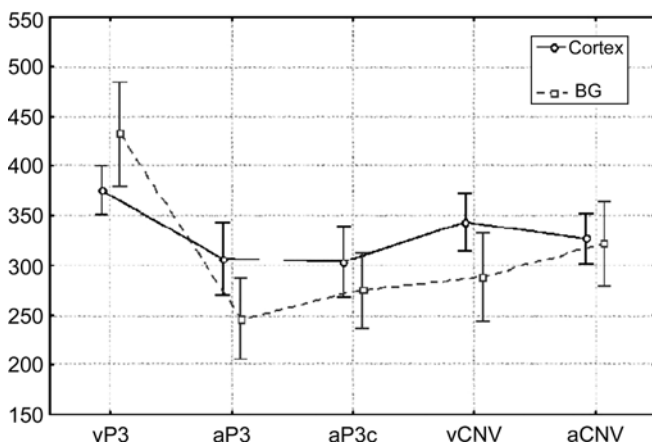
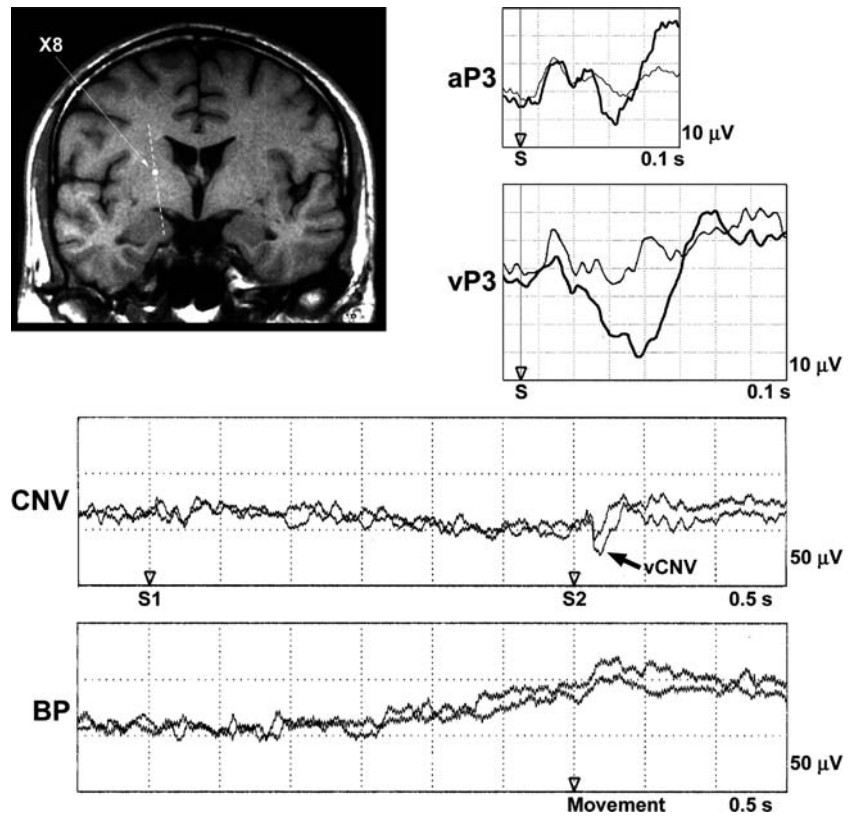


Fig. 3 Mean latencies of P3-like potentials in all explored cortical sites (premotor, cingulate and orbitofrontal cortex) and the basal ganglia. Current effect: $F_{(4,177)} = 2.823$, $p = 0.026$. Vertical bars denote 0.95 confidence intervals

Fig. 4 P3-like evoked potentials (aP3, vP3, vCNV) and slow potentials (CNV and Bereitschaftspotential) recorded from the contact X8 in the right-sided pallidum. The diagonal electrode X was implanted into the mesiotemporal region passing through the BG



It is generally accepted that the BG-thalamocortical loops contribute to a wide variety of cognitive and emotional functions besides motor activity. The internal organisation of each circuit follows a similar scheme: the striatum receive input from wide cortical regions, then the circuits traverse the BG and the thalamus through direct and indirect pathways, and projects back upon the frontal cortex. The circuits promote the execution of cortical programs and exercise a control function in suppressing unwanted elements. According to Alexander et al. (1986) the motor and premotor cortex are parts of the “motor” circuit, and the lateral orbitofrontal cortex with DLPFC are parts of the “prefrontal” circuit, while the medial orbitofrontal cortex with the anterior cingulate forms the “limbic” circuit. The non-motor frontal areas are related to higher executive functions, including working memory, planning, attention, etc. These circuits would explain the BG involvement in a broad range of behaviour (Middleton and Strick 2000). It is matter of discussion whether the circuits are anatomically and functionally fully segregated and act in a parallel manner, or whether they are mutually interconnected and form open systems (Joel 2001). Recently, Joel (2001) suggested three circuits: motor, associative and limbic. In terms of cognitive activities, each circuits plays a different role. The BG-thalamo-motor circuits (including the motor striatum, the motor cortex and the SMA) contributes to motor control. The associative circuit is involved in cognitive activities. It comprises the associative striatum and prefrontal cortex, including the DLPFC. The BG-thalamo-limbic circuit

(including the limbic striatum, and the orbitofrontal and anterior cingulate cortex) contributes to emotion.

Parent and Cicchetti (1998) have criticised the current models as simplistic. They described the BG as part of a highly complex and widely distributed network, in which sequences of activation and inhibition are coded in both time and space, enabling the fine modulation of motor behaviour.

We compared the occurrence of ERPs, CNV, and BP in the motor, prefrontal and limbic cortical sites with the occurrence in the BG sites. The frequency of all but one potential (vP3) was significantly higher in the BG than in the DLPFC/lateral OF or in the cingulate/medial OF cortices (Fig. 2). In the motor/premotor cortex, the frequency of all of the P3-like potentials elicited in the oddball paradigm was lower than in the BG; nevertheless, the occurrence of BP, CNV, and P3-like potentials elicited in the CNV paradigm did not significantly differ. This is in accordance with the description of the cortical location of BP and CNV restricted to central cortical areas (Rektor et al. 1994, 1998, 2001a; Lamarche et al. 1995; Bareš and Rektor 2001; Ikeda et al. 1992); but is in contrast with the nearly ubiquitous cortical distribution of P3-like potentials (Baudena et al. 1995; Halgren et al. 1995a, b; Parent et al. 2001). When looking at the behavioural significance of the tested protocols, there is a substantial difference between them in terms of the motor function. In the oddball protocol, the task consists of the identification and consecutive counting of the rare stimuli; the movement itself is not a goal but only a kind of confirmation of the cognitive activity. In the oddball protocol, the movement

Fig. 5a, b The distribution of the generators of the P3-like potentials, the Bereitschaftspotentials, and the Contingent Negative Variation in the basal ganglia in the right (a) and left hemisphere (b). *Left*: the position of all electrode contacts in the BG. *Right*: the contacts where the generators were localised. Based on the Talairach and Tournoux Atlas (1988). 1. vP3, 2. vCNV, 3. aCNV, 4. aP3, 5. aP3c, 6. BP, 7. CNV

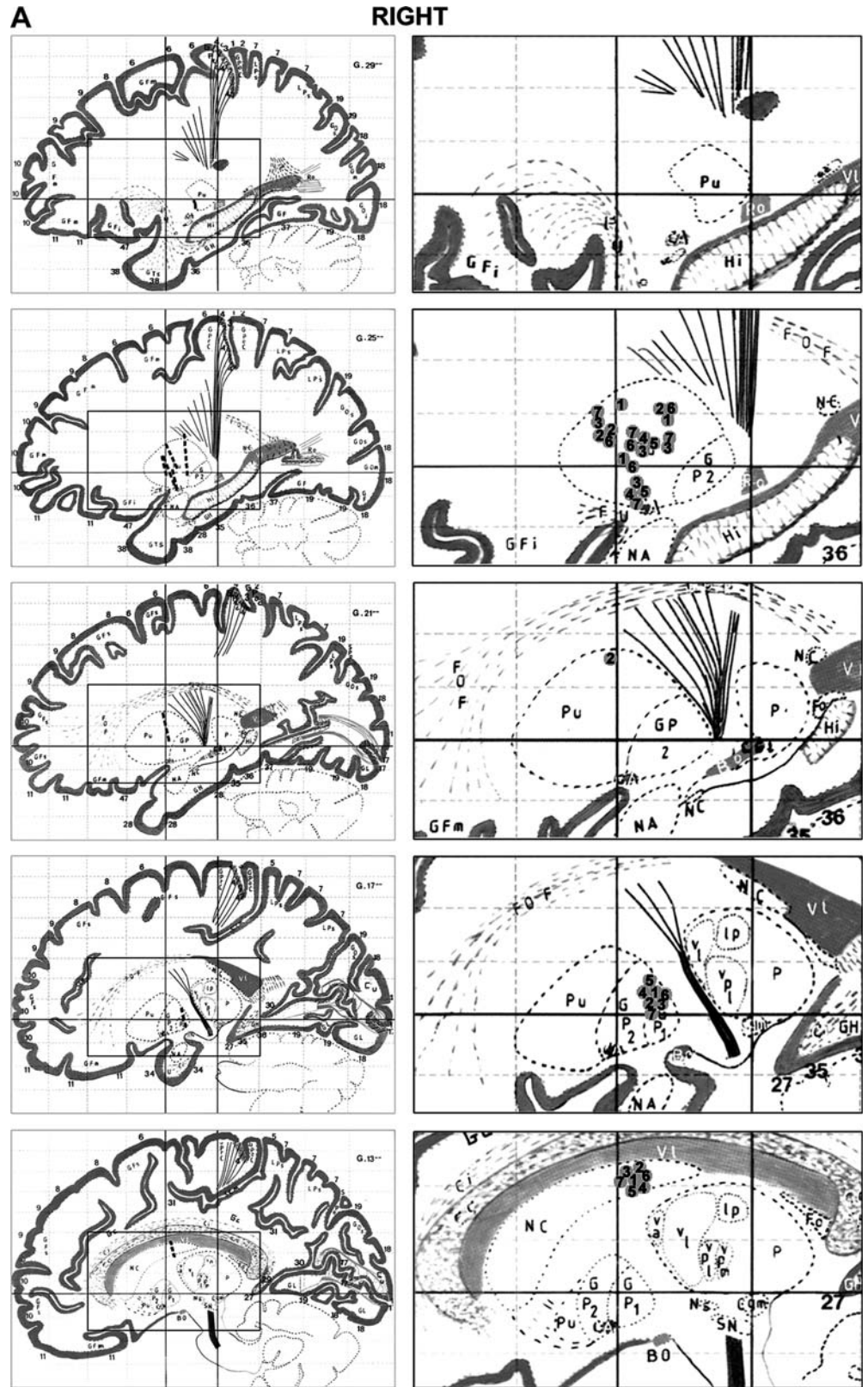
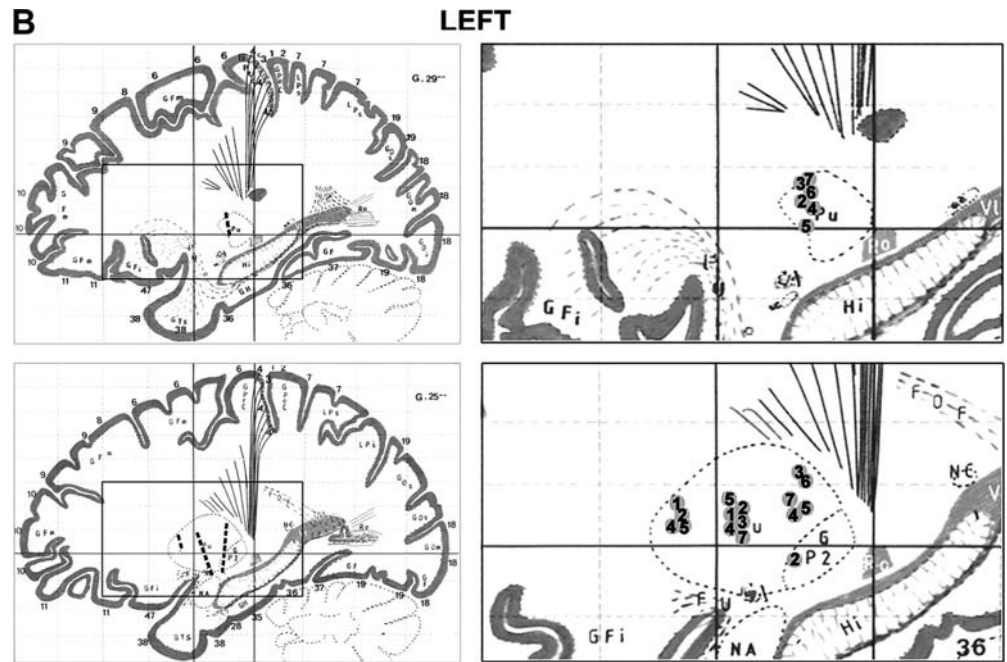


Fig. 5a, b (continued)



does not play a substantial role. This was also shown by the nearly identical occurrence and characteristics of auditory P3-like potentials both with and without a movement. In contrast, in the BP and CNV protocols, the task consisted of the performance of a movement. The processing of movement-related cognitive activities in the CNV and BP tasks in the motor/premotor cortex, which is directly involved in the preparation and execution of the motor activity, is not surprising. The cognitive processing of movement-related activity in the BG-motor/premotor cortex loop fits well with the original model of the segregated processing of information in individual BG-thalamocortical loops. On the other hand, the distributed occurrence of the cognitive processing of sensory information represented by P3-like potentials in all cortical areas does not fit well with the closed parallel model of cortico-basal ganglionic-thalamo-cortical circuits. Recent intracranial recordings have shown the participation of widespread areas of the frontal and parietal association cortex, in addition to the cingulate and mesial temporal regions, in tasks that generate scalp P300 potentials. The hippocampus, superior temporal gyrus, and possibly the superior-posterior parietal area, appear to constitute focal generators of the P3b wave. A widespread distribution of ERP, elicited by the CNV paradigm over multiple cortical regions and in the posterior thalamus, was also observed. The intracranial recordings support the view that multiple cortical and BG regions are activated during the P300 time window (Kropotov et al. 1992a, b; Baudena et al. 1995; Brázdil et al. 1999; Bareš 2001; Rektor 2002). Baudena et al. (1995) have proposed that although the generators are distributed in many frontal cortical fields, they are localised to small regions within each field. Our recordings could indicate that these small regions in each field

are active or inactive in relation to the nature of the task (Fig. 2).

It seems, in contrast to motor-related cognitive activity, that the cognitive processing of sensory information is not processed in segregated BG-frontocortical circuits. It may instead correspond to a variable and task-dependent internal organisation of BG-cortical systems, as suggested by Parent and Cicchetti (1998). Our conclusions about the cortico-subcortico-cortical processing of various cognitive activities are based on the analysis of unique data, but the design of this study did not enable unequivocal proofs. We hope that new data could provide new arguments that might be valuable in the ongoing discussion about the role of the cortico-subcortico-cortical loops.

When looking at the topography of recording sites inside the BG in our study, we were unable to reveal a focal concentration of any type of recorded potentials. The functional topography of cognitive potentials inside the BG is rather unclear (Figs. 4 and 5); the various potential generators are mutually intermingled. It is true that we were not able to systematically map the entire putamen, and that only a few recordings from the caudate and the pallidum were obtained. Nevertheless, according to known regional functional differentiation (Joel 2001), the recording of various potentials on the consecutive leads of an electrode passing through various parts of the putamen should have shown some topographic organisation of cognitive potentials, but this was not the case. Instead, we recorded cognitive potentials all over the putamen, as well as various potentials on the same lead or nearby contacts. A depth electrode contact is submerged in the neuronal tissue, and thus records from its immediate vicinity. This means that the neuronal pools generating various potentials are either very close to each other or even

overlapping, or that some neurons are active in several tasks. Kropotov and Ponomarev (1991) recorded a visually evoked P300 component from the pallidum when the eliciting stimulus was relevant, independent of patient response—whether the patient counted silently or pressed a button. In multi-unit recordings, Kropotov (1992a) observed separate neuronal populations according to the response evoked in an oddball paradigm—there were stimulus-related and response-related multi-units. Some neurons reacted in connection with the pressing of a button, others in connection with silent counting. The stimulus-related multi-unit responses were suppressed when the stimuli were behaviourally meaningless (Kropotov et al. 1992b). A similar situation was observed in animals. In the monkey putamen some cells produced activity after a visual trigger. Other cells responded to auditory clicks, but only if they triggered movement (Kimura 1986; Kimura et al. 1990). In the cat striatum, there are neurons that are activated during the presentation of visual signals which prepared animals for the execution or withholding of a movement (Takada et al. 1998).

We presume that the studied cognitive processes are produced in clusters of neurons that are organised in the putamen differently than the known functional topography, e.g. of motor functions. This organisation may form a substrate for an integrative function of the BG. However, the restricted number of recording sites did not enable us to uncover the internal organisation of the studied phenomena in the BG.

The latencies of P3-like potentials were slightly shorter in the BG for all but one paradigm. The difference between the latencies of all potentials in the BG and in the cortex was insignificant (Fig. 3). The BG activity was not driven from the frontal cortex.

Our data establish the existence of cognitive activities in the BG in parallel with cortical motor and non-motor areas in all of the tested paradigms. When comparing the frequency of all the cognitive potentials in the explored cortical areas with their frequency in the BG, a significantly higher occurrence in the BG was displayed. Until the 1980s, the BG were seen as funnels of information of diverse origin, with the neostriatal nuclei being considered important integrative centres (Goldman-Rakic and Selemon 1990). Reliable anatomical tracing techniques enabled the model of parallel processing in the BG-thalamocortical loops in the late 1980s. Nevertheless, more recent concepts have suggested that the BG form open systems of mutually interconnected nuclei, pathways, and cortical areas (Joel 2001). The BG may be viewed as a widely distributed network, with a highly patterned set of collaterals (Parent et al. 2001). We suggest that in addition to the specific functions organised in the circuits, the BG may play an integrative role in cognitive information processing, both in motor and in non-motor tasks. This role seems to be non-specific in terms of stimulus modality and in terms of the cognitive context of the task. It is known that the striatum receives prominent, topographically organised inputs from virtually all cortical areas. There is an anatomical as well as functional convergence with a substantial reduction of neurons along the cortico-basal ganglia-thalamo-cortical loop

(Cummings 1993). The functional output from the loop is a modulation—either an inhibition or an excitation—of cortical activity. Based on our data, we suggest the following mechanism: the BG form a non-specific system that progressively converges data concerning various functions from various parts of the cortex, the converged data are processed in the BG and positively or negatively modulate the cortex. The BG are the site at which information from various functional systems (sensory, attentional, memory) may be processed in a mutual context. This contextual modulation may be important for the functioning of the individual cortical areas that are the target of the loop. As the main targets are prefrontal and premotor areas, this hypothesis might help explain why a BG disturbance is followed by a functional impairment of the prefrontal functions, such as the executive function disturbance in parkinsonian syndromes, or behavioural and emotional disturbances related to the BG lesions (Cummings 1993; Dubois et al. 1994). Our observations coincide with Graybiel's suggestion that the BG operate in conjunction with the cortex in forebrain neural processing at the highest level, and are in a position to influence the activity states of such forebrain systems (Graybiel 1997).

Conclusions

All of the studied cognitive potentials were generated in the BG; the occurrence in frontal cortical areas was more selective.

In the motor/premotor cortex, the frequency of all P3-like potentials elicited in the oddball paradigm was lower than in the BG; nevertheless, the occurrence of BP, CNV, and P3-like potentials elicited in the CNV paradigm did not significantly differ. The cognitive processing of motor tasks in the BG-motor/premotor cortex loop fit well with the original model of segregated information processing in the motor basal ganglia-thalamocortical loop.

The frequency of all but one potential was significantly higher in the BG than in the DLPFC/lateral OF or in the cingulate/medial OF cortices.

The occurrence of cognitive sensory information processing in all of the cortical areas does correspond to a variable and task-dependent internal organisation of BG-cortical systems.

The distribution of cognitive potentials in the BG was not displayed in accordance with the known regional functional topography. Cognitive potentials were recorded from all over the putamen. We presume that the cognitive processes we studied were produced in clusters of neurons that are organised in the putamen differently than the known functional organisation, e.g. of motor functions.

The BG, specifically the striatum, may play an integrative role in cognitive information processing, in motor as well as in non-motor tasks. This role seems to be non-specific in terms of stimulus modality and in terms of the cognitive context of the task.

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