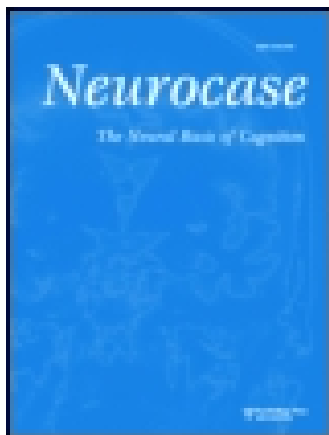


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# Basal Ganglia Lesions and the Theory of Fronto-Subcortical Loops: Neuropsychological Findings in Two Patients with Left Caudate Lesions

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## Abstract

Basal ganglia lesions have a high prevalence for associated behavioural impairments. However, the exact pattern of cognitive impairments and its relationship to individual basal ganglia lesion have rarely been investigated by means of a detailed neuropsychological and lesion study. Furthermore, different mechanisms have been proposed as relevant for the observed cognitive deficits; among these, the hypothesis of fronto-subcortical loops (Alexander *et al.*, 1986) has made predictions regarding the relationship between the damage of particular striato-frontal circuits and the resulting behavioural impairment which await clinical confirmation. We present a study of two subjects who suffered a MRI-documented focal left basal ganglia hematoma. The two patients differed in their lesions; in one patient (PJ) large parts of the caudate nucleus were destroyed whereas in the other (AS) mainly the pallidum and putamen were lesioned and the caudate suffered only minor damage. In the acute phase, the behavioural and neuropsychological abnormalities were similar in both cases and included mainly abulia, an impairment of executive and attentional functions, and a severe amnesic syndrome. After several months many functions were restored in AS, whereas PJ's abilities remained largely defective. Based on these data and on previous case studies several conclusions are drawn. Left caudate lesions induce marked and long-lasting behavioural and neuropsychological impairments comprising predominantly drive, executive control, attention, and memory. The extent of lesion in the head of the caudate nucleus is the critical factor regarding the severity and the outcome of the syndrome, whereas damage to the putamen and pallidum is less crucial for cognitive functions. A subset of behavioural alterations, among them abulia, attentional and frontal-executive dysfunctions, can well be attributed to lesions of the anterior cingulate circuit and the dorsolateral-frontal circuit at the basal ganglia level. Other impairments, most importantly the prominent amnesic syndrome, are more difficult to interpret on the grounds of this hypothesis and may be related to other pathomechanisms.

## Introduction

It has been amply documented that the basal ganglia (BG) not only mediate motor function, but also participate in neural activities subserving behavioural, cognitive and personality functions (Laplane *et al.*, 1989; Dubois *et al.*, 1995; Abdullaev *et al.*, 1998). In a recent review, Bhatia and Marsden (1994) found that 46% of all patients with BG lesions presented with various behavioural disorders, among them abulia, disinhibition, confusional states, disturbances of speech, or depression. However, the specific neurobehavioural role of anatomically defined entities of the BG is less well established, as is the mechanism of cognitive impairments following BG lesions. Behavioural alterations following focal lesions of the globus pallidus and putamen have been described as mainly being associated with inertia, stereotyped activities or compulsions (Laplane *et al.*, 1984; Laplane *et al.*, 1989; Strub, 1989;

Bhatia and Marsden, 1994; Dubois *et al.*, 1995). Lesions of the caudate nucleus (CN) are most likely among all BG lesions to cause behavioural alterations (Bhatia and Marsden, 1994). Knowledge about the behavioural role of the CN has been derived from several sources. It is well-known that degeneration of the CN plays an important role in the cognitive loss of Huntington's (Berent *et al.*, 1988; Lawrence *et al.*, 1998) and Parkinson's disease (Holthoff-Detto *et al.*, 1997; Rinne *et al.*, 2000), and possibly also in obsessive compulsive disorder (Baxter *et al.*, 1992) and cognitive aging (Garraux *et al.*, 1999; Rubin, 1999). Vascular lesions damaging the CN, mostly by way of so-called striatocapsular lesions, have revealed a wide range of behavioural alterations, including abulia (Trillet *et al.*, 1990), disinhibition, and a variety of affective and personality disorders (Stein *et al.*, 1984;

Richfield *et al.*, 1987; Mendez *et al.*, 1989; Caplan *et al.*, 1990; Starkstein *et al.*, 1991; Bokura and Robinson, 1997; Kumral *et al.*, 1999). Furthermore, case studies of CN lesions in the dominant hemisphere have listed aphasia and apraxia as a possible sequelae (Naeser *et al.*, 1982; Alexander *et al.*, 1987; Richfield *et al.*, 1987; Willmes and Poeck, 1993; Kumral *et al.*, 1999), and neglect after right-sided CN damage (Caplan *et al.*, 1990; Kumral *et al.*, 1999). Finally, impairments of memory, attention and executive functions have also been observed (Stein *et al.*, 1984; Mendez *et al.*, 1989; Caplan *et al.*, 1990; Markowitsch *et al.*, 1990; Canavero and Fontanella, 1998; Kumral *et al.*, 1999). Notably, many of these reports were based on clinical impression, rather than on systematic assessment procedures.

The BG are important constituents of the fronto-subcortical circuits, neuronal loops connecting the BG in a reciprocal and topographically organized manner with the thalamus and with divisions of the frontal cortex (Alexander *et al.*, 1986; Mega and Cummings, 1994; Middleton and Strick, 2000). The model of fronto-subcortical circuits (FSC) explains the cognitive impairment associated with BG or thalamic lesions as resulting from disturbed connectivity among cortico-subcortical networks, and has made detailed claims as to causal relationship between specific cognitive deficits and the disruption of particular loops (Mega and Cummings, 1994). Among these circuits, three have been suggested to play a crucial role in the regulation of human behaviour and cognition, each dedicated to specific functions. The dorsolateral prefrontal circuit subserves 'executive functions', the ability to organize behavioural responses to solve complex problems, activate memory, direct oneself independent from environmental contingencies, and shift and maintain cognitive sets. The lateral orbitofrontal circuit mediates emphatic, civilized and socially appropriate behaviour, and is also involved in the regulation of mood. The anterior cingulate circuit mediates motivated behaviour; loss of drive, akinetic mutism and indifference are the behavioural consequences of its damage. Previous studies of patients with BG lesions, particularly of the CN, have often noted 'frontal' behaviour, such as apathy, disinhibition, or a major affective disturbance, and have suggested that these abnormalities result from a disconnection of fronto-subcortical loops (Mendez *et al.*, 1989; Caplan *et al.*, 1990; Degos *et al.*, 1993; Bhatia and Marsden, 1994; Mega and Cummings, 1994), however, without explaining the relationship between impaired behaviour and subcortical lesion in greater detail. Thus, the FSC-hypothesis represents an explanatory model which awaits confirmation from clinical case studies.

Despite the wealth of clinical observations suggesting that lesions of the BG are associated with significant behavioural impairments, there are several methodological difficulties. Previous studies of patients with focal basal ganglia lesions were mostly conducted as group studies, carrying the known disadvantages resulting from heterogeneous patient populations, different lesion etiologies and considerable anatomical variability. Furthermore, observations of altered

patient behaviour were largely anecdotal and often lacked a systematical exploration. Also, little is known about the long-term cognitive outcome of vascular BG lesions. Bokura and Robinson (Bokura and Robinson, 1997) have described a significant intellectual impairment in a group of patients with chronic vascular CN lesions using the MMSE (Folstein *et al.*, 1975), an instrument which does not allow a detailed assessment of cognitive functions. Also, only a few reports contain exact neuroanatomical lesion studies. Due to these weaknesses, and motivated by the claims of FSC-hypothesis, it was felt that a detailed study of selected patients with well-documented focal BG lesions could help to clarify some of these problems. We describe the behavioural and neuropsychological impairments of two subjects who suffered a vascular lesion of the left BG region. Special emphasis was placed on the selection of patients, a comprehensive assessment of neuropsychological functions, and close observation of behavioural abnormalities. Furthermore, patients were followed over a substantial period of time to investigate the long-term course of disease. It was also sought to achieve a detailed analysis of the relationship between the individual behavioural pattern and the underlying BG lesion. From these data, an attempt was made to clarify how well the observed impairments are compatible with the postulated neuropsychiatric alterations as predicted by the theory of FSC (Alexander *et al.*, 1986; Mega and Cummings, 1994), and to decide specifically which fronto-subcortical systems may be defective in our patients.

## Case reports

In May 1998 two right-handed patients, AS (female, age 58) and PJ (male, age 56) were admitted to our clinic with a spontaneous hematoma in the left BG. AS was a multilingual secretary and PJ an owner of a small plumber's firm. Both subjects had an unremarkable medical history except for longstanding hypertension. In both subjects an initial neurological examination showed meningeal signs, a minimal paresis of the right face, arm and leg, slight dysarthria and word-finding difficulties. These symptoms all resolved completely within a few days. MRI demonstrated a bleeding located in the left basal ganglia region, but no other brain lesion. Angiography was negative in both subjects.

## Patient behaviour

Shortly after disease onset, AS and PJ were both abulic. They showed a profound lack of spontaneous activities, rarely expressed thoughts or asked questions. During conversation they produced sparse, laconic verbal output and had prolonged answering latencies. To keep the conversation going, the dialogue needed continuous support via repetitive requests and proposals from the examiner. Both patients often needed motivational assistance during psychometric testing, exhibited blunt and indifferent affect and never appeared preoccupied regarding their disease.

Several weeks after disease onset, spouses and family members reported that abulia had somewhat improved. Other mental changes remained basically unchanged. AS, who was premorbidly known for her energy, drive and initiative, was described by her sons as now being slow, poorly motivated, lacking concern for her household and social activities, emotionally flat, absent-minded, unable to make plans, with severe memory problems and a loss of social interests. During both follow-ups she explicitly denied any form of mental impairment and stated that she felt well and unchanged. PJ had successfully run a small firm with several employees. Now his wife described him as unable to take care of his business due to lack of initiative, drive and endurance. He was perseverating, indifferent, inattentive, uninterested, emotionally unconcerned, and severely forgetful. Similar to AS he seemed unable to detect a difference between his present and premorbid functional state. Over a period of 22 months PJ gained about 15 kgs of weight. Apart from the observed loss of drive, both patients exhibited no other symptoms typical for depression. Other behavioural changes like psychosis, mania, paranoia, altered sexual behaviour, compulsivity or disinhibition were not found. No patient showed spontaneous confabulations or motor abnormalities.

## Brain lesions

Standard MRI studies were performed in the acute and chronic disease state. In AS, the hemorrhage was located in the globus pallidus and putamen, crossing the anterior limb of the internal capsule and reaching the cranial part of the head of the caudate (Fig. 1a–e). The main portion of PJ's bleeding (Fig. 2a–e) was located in the head of the caudate, extending to the anterior limb of the internal capsule and the lentiform nucleus. Rupture of the hematoma to the anterior horn of the lateral ventricle suggests that the head of the CN and the anterior portion of the internal capsule were lesioned in both subjects.

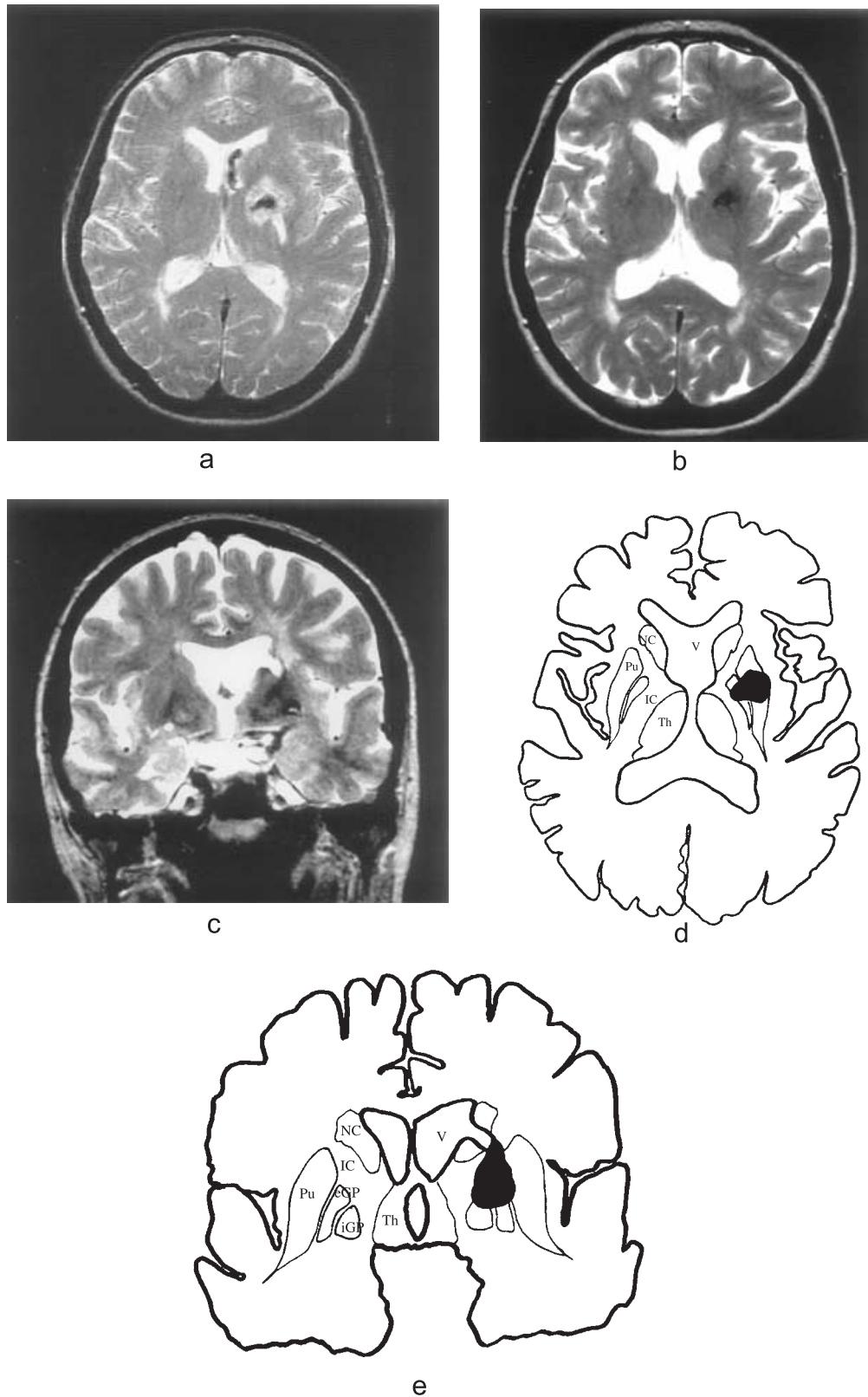
## Methods

### *Neuropsychological assessment*

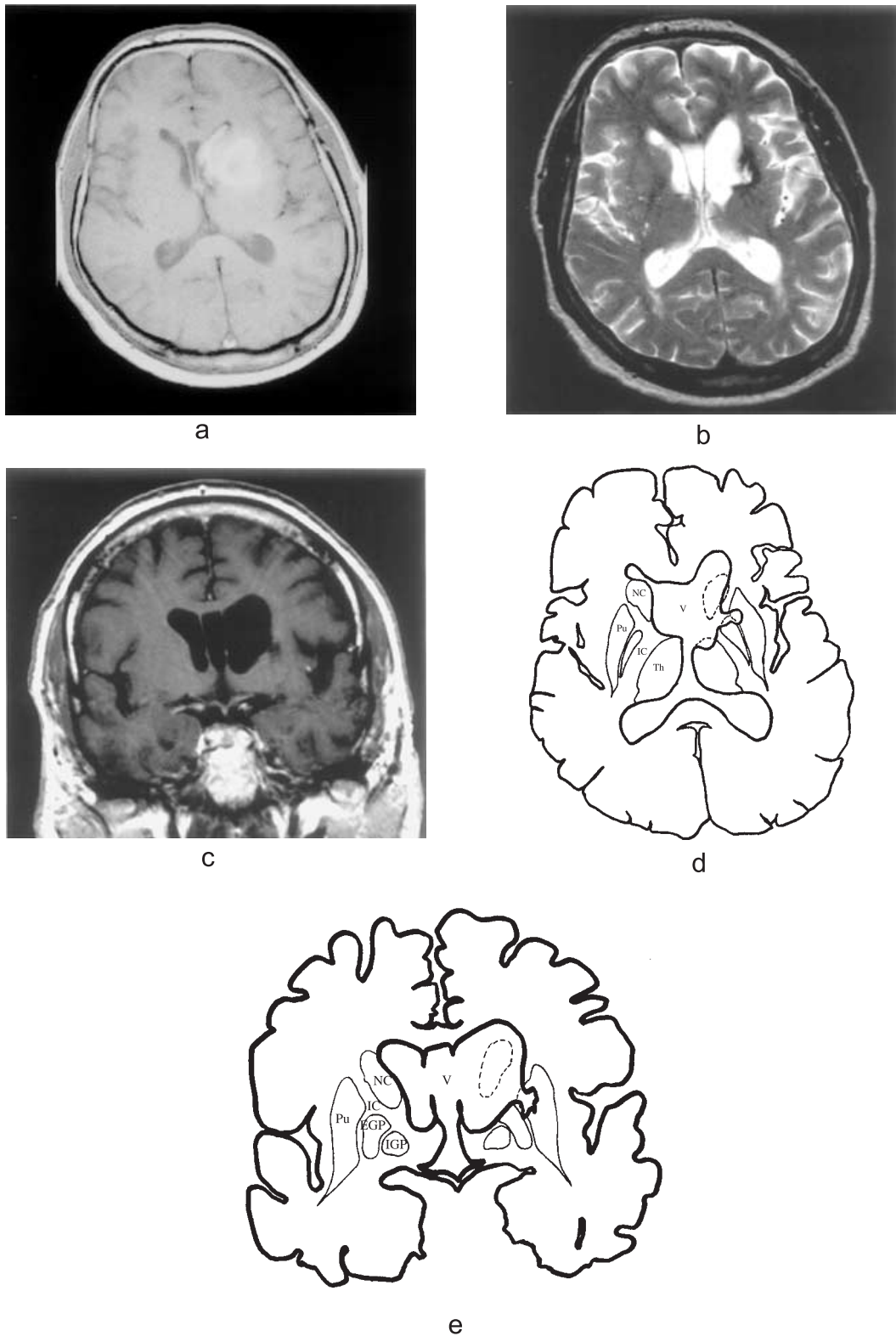
Both subjects gave their informed consent to participate in the study. Assessments were performed in the acute phase and on two follow-up occasions. AS was tested on day 7, day 54 and day 680, and PJ on day 13, day 70 and day 665 post-disease onset. Dependent on the individual patient's cooperation and fatigue, as many tests as possible were repeated during follow-up, with an emphasis on individual tests with previously poor results.

*Premorbid verbal intelligence* was estimated using a multiple choice vocabulary test (Lehrl, 1977). *Language and speech* was assessed using the Aachener Aphasia test (AAT; Huber *et al.*, 1983), a language battery comprising a 5-point rating scale for spontaneous speech, and five subtests, the token-test, oral repetition, written language, confrontation

naming, and comprehension. *Arithmetical functions* were assessed using a reduced form of the EC301 battery (Deloche *et al.*, 1994). This standardized assessment battery covers arithmetical and numerical skills like counting, enumeration, number transcoding, evaluation of quantities, access to arithmetical facts and algorithms for written operations; the Graded Difficulty Arithmetic Test (GDAE; Jackson and Warrington, 1986) was used to test the ability to perform mental additions and subtractions of increasing difficulty under time pressure. *Memory* was tested using several tasks. A German version of the California Verbal Learning Test (Delis *et al.*, 1987), the Münchner Gedächtnistest (MGT; Ilmberger, 1988) was used to tap the learning, spontaneous and cued recall, and recognition abilities of a 16-item word list. The ability to draw and recall figural material was tested with the Rey Complex Figure Test (Lezak, 1995) and the Visual Design Learning Test (RVDLT; Lezak, 1995). Recognition memory for words and faces was assessed using the Recognition Memory Test (RMT; Warrington, 1984). Verbal and spatial span memory was tested with the Digit Span and with Corsi's (Milner, 1971) Block Tapping Test. Several *frontal-executive functions* were evaluated, among them tasks tapping predominantly psychomotor speed and set shifting abilities (TMT, Trail Making tests form A and B; Spreen and Strauss, 1991), sorting and categorizing abilities (WCST, Wisconsin Card Sorting Test; Heaton *et al.*, 1993). Non-verbal inductive reasoning was tested using two non-verbal subtests of the Verbal and Spatial Reasoning Test (VESPAR; Langdon and Warrington, 1995); here subjects have to either pick the item among four shapes that in some way falls in a different category (spatial odd one), or pick one of four alternatives that has a spatial relationship similar to a given pair of shapes (spatial analogy). The Goldenberg Test of Flexibility (Goldenberg, 1993) was used to assess the ability to learn figural information and to suppress proactive interference. In this test, a subject is presented with two sets of 9 cards, each carrying a different coloured symbol. Three cards of each set also have a black dot on their back. Set 1 of the test consists of a learning trial during which subjects have to learn which symbol is associated with a black dot on its back. Next, the cards are presented 5 times in random sequence and subjects have to indicate from memory which card has a black dot on its back; subjects are informed about their decision (right-wrong), and correct answers are scored. In set 2, the subject is informed that the black points are now on different cards which are shown initially; then the cards are presented as in set 1. The idea behind the task is that the subject has to learn a given association, and on a later occasion when a new memory is built up, has to suppress the familiarity and to react with a false positive response. In each set, 2 points are given for a correctly answered trial, and 1 point is subtracted for a false positive answer, resulting in a maximum possible score per set of 30 points; an age correction is performed. The Action Program Test (APT; Wilson *et al.*, 1996) was used to assess both subjects' ability to develop an action plan in order to solve a problem. In this task, five steps



**Fig. 1a–e (patient AS).** (a) MRI of the acute hemorrhage in the left lateral BG region (putamen and pallidum). Blood in the lateral ventricle indicates that the head of the caudate nucleus has been perforated. (b) MRI-study showing chronic lesion in the posterolateral basal ganglia region. (c) Cystic defect in the anterior part of the internal capsule extending through head of the caudate nucleus and reaching the frontal horn of the lateral ventricle. (d and e) Schematic reconstruction of axial and coronal cuts showing shape and extension of the chronic lesion drawn in black. Superposition of normal location of basal ganglia from corresponding cuts of a brain atlas (Mai *et al.*, 1997). Main damage in the lentiform nucleus. Pu = putamen, EGP = external globus pallidus, IGP = internal globus pallidus, TH = thalamus, NC = nucleus caudatus, IC = internal capsule, V = ventricle.



**Fig. 2a–e (patient PJ).** (a) Acute hemorrhage in the left BG area. (b and c) Chronic, partly cystic lesion with hemosiderin imbibition located in the head of the caudate nucleus, anterior limb of the internal capsule and medial part of the nucleus lentiformis in the axial and coronal plane. Massive dilatation of left frontal horn due to destruction of caudate nucleus. (d and e) Schematic reconstruction of axial and coronal cuts showing associated e-vacuo dilatation of frontal horn in the area of the original hemorrhage. Superposition of normal location of the basal ganglia from corresponding cuts of a brain atlas (Mai *et al.*, 1997). Pu = putamen, EGP = external globus pallidus, IGP = internal globus pallidus, TH = thalamus, NC = nucleus caudatus, IC = internal capsule, V = ventricle.

have to be planned in order to solve a simple practical problem; subjects are presented with a large beaker with a removeable lid, a thin transparent tube at the bottom of which is a small cork. The beaker is two-thirds full of water. Further tools are a metal, L-shaped rod which is not long enough to reach the cork, and a small screw top container with the top unscrewed. Subjects are asked to get the cork out of the tube using any of the objects but without lifting the tube or the beaker. To solve the problem subjects have to work out that the key to the problem is to use the water to make the cork float to the top of the tall tube, and then how to work out how to get the water out of the beaker and into the tube. This involves removing the lid with the metal 'hook', screwing the top onto the small container, filling the small container with water, pouring it into the tube and repeating this procedure until the cork floats to the top of the tube. There is no time limit for the task, but if a subject is unable to progress through any of the five stages, then a prompt is given. Verbal divergent thinking was tested measuring the ability to name category members (animals, food items) during 1 minute (Lezak, 1995). Figural fluency, productivity and response variability were tested using the Design Fluency Test (Jones-Gotman and Milner, 1977); here patients have to produce as many novel nonsense designs in a given time. This test is performed in two trials; during free condition the subject is asked to invent as many abstract designs as possible in 5 minutes. During the second, fixed condition which lasts 4 minutes, only four-line drawings are allowed. In both conditions, perseverations or rule breakings (scribbling, producing nameable items) are forbidden and the total number of designs, of novel designs, perseverations and rule breakings is counted. Three *attentional functions*, namely alertness, divided attention, and visuospatial attention were tested. Alertness and divided attention were assessed on a computer-based, standardized battery using visual and auditory stimuli (Zimmermann and Fimm, 1993). On the alertness task, the time is measured which is needed to press a key after a visual stimulus (cross) appears on the screen. Four blocks of 40 stimuli each are given, in one the simple reaction time is measured for a sole visual cue (tonic or intrinsic alertness), and in the other an acoustic warning precedes each visual stimulus (phasic alertness). Divided attention was assessed with a dual-task paradigm. Subjects have to react to 100 visual stimuli (a rectangle which appears at times in a changing matrix of crosses) and at the same time monitor a sequence of high and low tones and recognize whenever a tone is followed by a tone of identical frequency. In this paradigm reaction times, correct responses, anticipations, misses and errors are recorded. A searchboard task tested visuospatial attention and exploration (Kimura, 1986). In this non-verbal task the patient sits in front of a board of 22 × 20 inches, on which are 86 drawings of familiar objects. Twenty stimulus cards are put one by one in the centre of the board without naming them. The patient, whose head is aligned with the board centre, is asked to find the object match as quickly as possible and point to it. Search times (scored with a stop watch) and the half of the board where the match is

located (left vs. right) are recorded. Stimuli are balanced across both searchboard halves, eight stimuli occur in one position, 4 in 2, and 8 in 3 positions, the rest of stimuli are distractors. Visual search performance is scored in number of items found and in mean search time (secs), both per searchboard half (left vs. right).

## Results

### *Neuropsychological results in the acute state*

Psychometric test results are summarized in Table 1.

#### *Intelligence*

Estimated premorbid verbal intelligence was average in AS and PJ.

#### *Language*

Language in AS and PJ was characterized by normal performance on subtests of the AAT tapping comprehension, naming, repetition, reading and writing. Thus, aphasia as commonly defined could be ruled out in both cases. However, discourse and spontaneous speech were abnormal in the acute stage; both subjects had severely reduced output of spontaneous speech, and rarely initiated conversation. Verbal responses were sparse, slow, usually with long response latencies, and often absent. Verbal fluency was also defective.

#### *Arithmetical functions*

Untimed basic calculation and number processing was undisturbed in both patients, including counting, number transcoding, mental calculation, magnitude comparisons, number placement on an analogue scale, and quantity estimation, with the exception of some errors in complex calculation procedures (AS and PJ) and perseverative errors (PJ). By contrast, both patients performed subnormally on the timed mental arithmetics task.

#### *Frontal-executive functions*

Both subjects had severely reduced psychomotor speed on the TMT, especially when set shifting abilities were required as in part B. Fluency scores were profoundly reduced in the verbal and in the figural domain. On the design fluency test, the percentage of perseverative errors was high and the novel output score low; PJ also committed rule breakings. Card sorting was also defective: AS achieved a reduced category score, and committed numerous perseverative and also non-perseverative errors; PJ achieved only a single category. On the Action Program test AS found the required solutions without prompting, but needed an abnormally long period (180 secs) to start her initial step. PJ had problems with action planning as evident from the abnormally long period to solve step 2. On this task, he perseverated attempts to scoop water from the large beaker with an unscrewed and therefore leaky container without interruption over a period of more than 4 minutes. He needed two prompts and an abnormally long

**Table 1.** Neuropsychological findings in patients AS and PJ

	AS 1	AS 2	AS 3	PJ 1	PJ 2	PJ 3	Maximum score
<i>IQ and language</i>							
Time post-disease onset (days)	7	54	680	13	70	665	
Premorbid intelligence (MWT)							
Correct	29			27			37
Estimated IQ	108			100			
<i>Language</i>							
<i>Aachener Aphasia Test</i>							
<i>Spontaneous speech</i>							
Communicat. behaviour	4	5	5	4	5	5	5
Articulation/prosody	5	5	5	4	5	5	5
Automatic language	5	5	5	5	5	5	5
Semantic structure	5	5	5	4	5	5	5
Phonemic structure	5	5	5	4	5	5	5
Syntactic structure	5	5	5	5	5	5	5
Token Test (errors)	0			3	0		50
Repetition	150			142	150		150
Written language	90			88	90		90
Naming	120			107	120		120
Comprehension				108	116		120
<i>Arithmetical functions</i>							
Time post-disease onset (days)	7	54	680	13	70	665	
GDAE	6*			7*	12		
<i>EC 301</i>							
Counting	2			2			2
Enumeration	6			0**			6
Number writing	12			12			12
Number reading	12			12			12
Mental calculations	16			16			16
Analogue scale	10			10			10
Magnitude comparison	46			48			48
Written calculation	11*			10*			15
Quantity estimation	8			6			10
<i>Executive functions</i>							
Time post-disease onset (days)	7	54	680	13	70	665	
<i>TMT</i>							
Trail A (sec)	85**	53*	67*	75**	50*	42	
Trail B (sec)	265**	99*	103*	360**	240**	137*	
<i>Verbal semantic fluency</i>							
Animals/minute	5**	14*	17	5**	8*	8*	
Food items/minute	0**	6**	10*	3**	14*	12*	
<i>Design Fluency</i>							
<i>Free condition</i>							
Total designs	10*	13		18	21		
Novel designs	5**	13		10*	9*		
Perseverative errors (%)	5**	0		6*	11**		
Rule breakings	0	0		2*	1		
<i>Fixed condition</i>							
Total designs	8*	11*		10*	13*		
Novel designs	1**	10*		6*	8*		
Perseverative errors (%)	7**	1		1	3		
Rule breakings	0	0		3*	2*		
<i>WCST</i>							
Categories	4*	4*	6	1**		3**	6
Perseverative errors	21*	16	20	0		61**	
Non perseverative errors	36**	32**	14	23**		4*	
<i>APT</i>							
Total time to solve problem	150**			410**			
Step 1 in second	80**			10			
Step 2 in second	112**			268**			
Step 3 in second	114**			390**			
Step 4 in second	116**			395**			
Step 5 in second	146**			405**			
Rule breakings	0			1*			
Prompts given	0			2**			

(continued)



Table 1. (continued)

	AS 1	AS 2	AS 3	PJ 1	PJ 2	PJ 3	Maximum score
<b>VESPAR Reasoning Test</b>							
Spatial odd one	19			12*			25
Spatial analogy	20			8**			25
<b>Goldenberg Test of Flexibility</b>							
Set I							
Hits	11	10	15	10	9	14	
False alarms	4	1	0	13	11	6	
Score	23*	19**	30	12**	7**	22**	30
Set II							
Hits	9	15	13	7	14	13	
False alarms	6	0	3	14	10	7	
Score	16**	30	23*	4**	18**	19**	30
<b>Memory</b>							
Time post-disease onset (days)	7	54	680	13	70	665	
Digit span							
Forward	6			4*	5*		
Backward	3			2*	3		
Corsi block span							
Uncrossed	4*			4*			
Crossed	5			4*			
<b>MGT</b>							
Verbal learning (sum)	20**	35*	52	9**	28**	25**	80
Short delay free recall	1**	10	10	0**	0**	5**	16
Short delay cued recall	0**	11	13	0**	2**	5**	16
Long delay free recall	1**	8*	11	0**	5**	6*	16
Long delay cued recall	0**	11	13	0**	5**	6*	16
Recognition	10**	14	16	9**	16	16	16
False positives	1	0	0	5*	8**	1	16
<b>Rey-Osterrieth Complex Figure</b>							
Copy	36	33	33	20**	28**	27**	36
Immediate recall	9.5**	13**	16*	5**	16*	12.5**	36
Delayed recall	7.5**	14**	16.5*	1**	11.5**	13.5**	36
<b>RVDLT</b>							
Learning (sum)	28	33		11*	32		75
Recognition	12	13		9	12		15
False positive	2	0		10	2		
<b>RMT</b>							
Faces	42		46	44		34**	50
Words	43		48	30**		48	50
<b>Attention</b>							
Time post-disease onset (days)							
Alertness							
Tonic alertness							
Median reaction time	594**	408**	592**	313**	295**	299*	
SD reaction time	141**	124**	163**	121**	107**	54	
Phasic alertness							
Median reaction time	474**	389**	600**	394**	280**	241	
SD reaction time	142**	98**	152**	201**	48	35	
Divided Attention							
Median reaction time	1051**	803**	885**	692	561	804**	
SD of reaction time	366**	163**	229**	436**	194	238	
Correct	17	26	26	28	19	27	50
Anticipations	0	0	0	2	2	0	
Misses	15**	5*	5*	0	6*	3*	
Errors	0	2	2	53**	32**	18**	
<b>Visual Exploration</b>							
Searchboard							
Search time on right (sec)	5.4	8.3		21.2	15		
Search time on left (sec)	2.9	8		5.9	6.7		
Items found on right	7	10		8	9		30
Items found on left	13	10		12	11		30

Note. MWT = Mehrfachwahl-Wortschatz-Intelligenztest, GDAE = Graded Difficulty Arithmetic Test, TMT = Trail Making Test, WCST = Wisconsin Card Sorting Test, APT = Action Program Test, MGT = Münchner Gedächtnistest, RVDLT = Rey Visual Design Learning Test, RMT = Recognition Memory Test, TAP = Test zur Aufmerksamkeitsprüfung, SD = Standard deviation.

\*Indicates score between 11<sup>th</sup> and 25<sup>th</sup> percentile or moderately impaired performance.

\*\*Indicates score below 10<sup>th</sup> percentile or severely impaired performance.

performance time to complete the test. AS and PJ were both severely impaired at the Goldenberg test which requires the learning of new figural associations, set-shifting performance and inhibition of proactive interference. Both patients did better on the spatial reasoning task, with the exception of PJ's score on the spatial analogy task which was below average.

### Memory

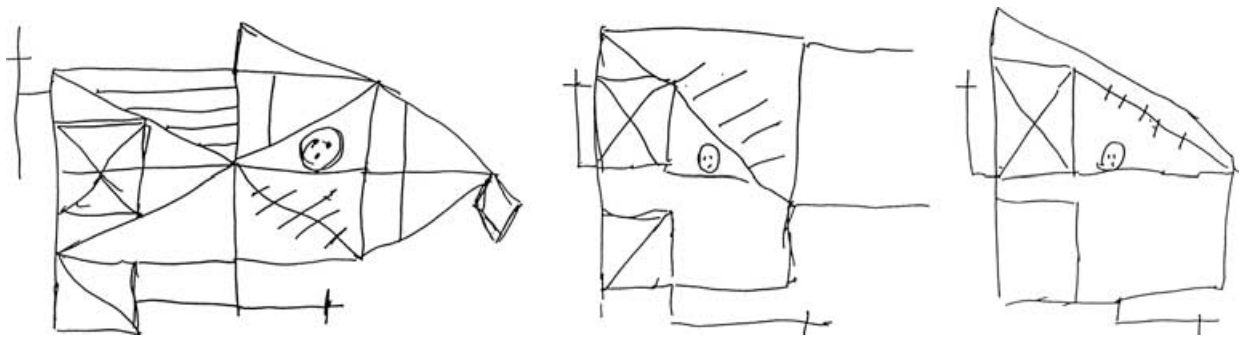
Both subjects had a marked deficit of episodic verbal and figural memory. On the MGT AS and PJ gained only flat and inconsistent learning curves; after presentation of a distractor list, short and long delay spontaneous recall were both severely defective. Both were unable to profit from semantic cues. Recognition was also impaired; here PJ produced many errors of commission. On the recall sections of the Rey Figure test both patients scored below the tenth percentile (Figs. 3 and 4). AS's achievement on visual design learning (RVDLT) was intact, whereas PJ scored in the defective range, again with many false positive errors. Recognition memory for words and faces (RMT) was well preserved in AS, whereas PJ recognized faces well and words poorly on this task. AS also reached normal scores on both span tasks, whereas PJ had a subnormal digit span.

### Tests of attention

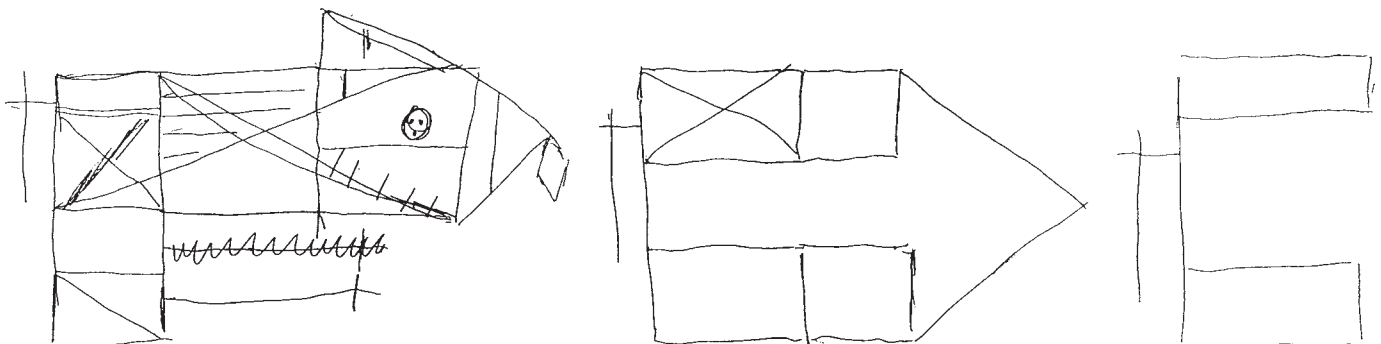
Tonic and phasic alertness, as tested by a simple reaction time task, were markedly reduced in both subjects. Especially AS was profoundly slow on the alertness task; PJ's reaction times were faster, but still in the defective range, and he did not benefit from the warning tone. Both patients were slow and inaccurate on the divided attention task where they had to react simultaneously to visual and acoustic stimuli; here AS had numerous misses and PJ committed a large number of errors. The prolonged reaction times and large standard deviations on both RT-tasks indicate the occurrence of many 'lapses of attention' and an instability of attentional performance over the duration of the test. Although no overt symptoms of neglect were evident in AS and PJ, both displayed a systematic bias of visuospatial exploration towards the ipsilesional side on the searchboard task.

### Neuropsychological follow-up

The outcome of both neuropsychological follow-up assessments after 2 months (AS2, PJ2) and 22 months (AS3, PJ3) is summarized in the Table. AS showed a steady improvement of memory, now acting at subnormal to normal levels on



**Fig. 3.** Performance of patient AS on Rey Complex Figure Task showing intact copying (left), but severe impairment of short (middle) and long delay (right) recall abilities on day 6 post onset.



**Fig. 4.** Performance of patient PJ on Rey Complex Figure Task (day 13 post onset) showing disorganized copy with qualitative errors (left), as well as poor short (middle) and long term (right) recall abilities.

verbal learning and spontaneous recall; her recall abilities of the Rey complex figure remained defective. Executive functions were partly restored except for a lasting impairment of psychomotor speed, set shifting and flexibility. Visuospatial exploration showed a complete recovery and a loss of the left-sided bias. Alertness and divided attention remained severely impaired.

PJ recovered quickly from his initial language impairment. He also showed some improvement on the verbal span test, and on the ability to learn lists of words or designs. However, his performance remained defective on spontaneous verbal and figural recall, and also on recognition tests, where he continued to produce errors of commission. Performance on the RMT was remarkably inconsistent; while recognizing faces in the normal range during the acute phase, his performance dropped drastically on the second follow-up. Recognition of words showed exactly the inverse pattern with a severe impairment in the acute stage and high scores during follow-up. There was also some improvement of his psychomotor speed, on both fluency tasks, on card sorting, flexibility and on arithmetic under time pressure. PJ's bias on visuospatial exploration remained unchanged. Alertness and divided attention showed improvements of speed, however, at the cost of many errors.

In sum, in the acute state AS and PJ presented with abulia, an impairment of spontaneous speech and fluency, a dysexecutive syndrome, impairment of memory, biased spatial attention, and a disorder of attention. Compared to AS, PJ's deficits were clearly more pronounced. Follow-up assessments revealed that PJ's recovery was insignificant, with most abilities remaining in the defective range. Compared with PJ, several impairments had subsided in AS; however, her figural memory and attention both remained severely disturbed. Thus, both patients revealed a similar profile of impairment shortly after their brain lesion, but unlike PJ, AS showed a more substantial amount of recovery over time.

## Discussion

This study describes the behavioural alterations found in two patients with a focal lesion in the left BG area. AS and PJ were both right-handed, middle-aged persons of average premorbid intelligence who were premorbidly known as behaviourally unimpaired subjects. They had no prior neurologic history and had experienced their first episode of a cerebrovascular disease. With these background variables, our patients represent a well-suited cohort for a neuropsychological case study. In both subjects, MRI showed a striatocapsular brain lesion involving, among other structures, the head of the CN. In PJ damage to the CN was extensive, whereas AS had a small caudate lesion extending to the globus pallidus and putamen. Since there was no cortical damage, it can be concluded that the BG lesion caused the observed behavioural and neuropsychological changes. Remarkably, both patients' somatic symptoms were minor and rapidly vanishing, as compared to their prominent behavioural impairment. The

following discussion will analyze the behavioural and neuropsychological findings and evaluate the effect of the underlying brain lesion on the deficit pattern and disease outcome. Finally we will discuss to what extent the FSC-hypothesis can capture the range of behavioural phenomena of our patients.

## *Patient behaviour*

The most striking behavioural alteration of AS and PJ was their ubiquitous abulia, which led to a pronounced personality change. Both patients presented with a marked reduction of psychic self-activation, but remained reactive to external stimulation. Abulia (or psychic akinesia) has been mentioned in many CN cases (Mendez *et al.*, 1989; Bhatia and Marsden, 1994; Kumral *et al.*, 1999), and also in patients with striatal lesions (Strub, 1989). Its character resembles the type of inertia and lack of spontaneity found in subjects with prefrontal (Fuster, 1989), bilateral paramedian (Gentilini *et al.*, 1987; Crews *et al.*, 1996), or anterior thalamic lesions (Ghika-Schmid and Bogousslavsky, 2000). Abulia as observed in AS and PJ is in marked contrast to the disinhibited, agitated and restless behaviour described in a different variant of CN patients (Richfield *et al.*, 1987; Mendez *et al.*, 1989; Caplan *et al.*, 1990; Kumral *et al.*, 1999), and to a further subgroup presenting mainly with depression (Mendez *et al.*, 1989; Caplan *et al.*, 1990). The present cases also show that persistent abulia may be the consequence of a unilateral lesion, and need not result from bilateral BG damage (Laplaine *et al.*, 1984; Richfield *et al.*, 1987; Trillet *et al.*, 1990; Canavero and Fontanella, 1998). Other behavioural abnormalities were a marked indifference to the consequences of their disease. Altered self-awareness and indifference regarding one's handicap or brain disorder is a well known feature found after frontal brain lesions (Fuster, 1989; Prigatano and Schacter, 1991), and has also been described following lesion of the caudate (Pozzilli *et al.*, 1987; Kawamura *et al.*, 1988; Canavero and Fontanella, 1998). PJ also experienced an alteration of his eating habits towards bulimia. At present, it remains unclear why CN lesions may produce quite different personality changes and affective disorders as listed in this compared to previous case studies.

## *Neuropsychological impairments*

### *Language*

Different language abnormalities have been observed in patients with left CN lesions, mostly dysarthria and nonfluent, global or transcortical motor variants of aphasia (Kumral *et al.*, 1999). Other findings comprise fluent aphasia (Cambier *et al.*, 1979), word finding difficulties, stuttering (Caplan *et al.*, 1990), abnormalities of discourse (Cambier, 1979), verbal paraphasia and perseverations (Puel *et al.*, 1984; Kreisler *et al.*, 2000), and agraphia (Cambier *et al.*, 1979; Kumral *et al.*, 1999). However, absence of language impairment has also been noted in many CN cases (Mendez *et al.*, 1989; Bhatia and Marsden, 1994; Nadeau and Crosson, 1997;

Kumral *et al.*, 1999). Aphasia testing in PJ showed that language recovered quickly after an initial period during which he produced paraphasias and was dysnomia. However, it is known that standard aphasia testing of patients with BG lesions may be insensitive to subtle deficits in more cognitively demanding aspects of language (Copland *et al.*, 2000a). Therefore, the findings of our study do not preclude the presence of other, higher-level deficits such as in semantic activation, processing of lexical ambiguities or discourse processing as found in other studies of patients with dominant subcortical lesions (Chenery *et al.*, 1999; Copland *et al.*, 2000b; Copland *et al.*, 2001). Neurologically, it has been noted that mostly large ischemic lesions including the CN, the anterior limb of the internal capsule and the lentiform nucleus are associated with aphasia, which is often associated with hemiplegia (Damasio *et al.*, 1982; Bhatia and Marsden, 1994; Kumral *et al.*, 1999), findings not apparent in AS and PJ. Lack of aphasia in AS and PJ also indicates intactness of the perisylvian region, since co-occurring lesions of the dominant perisylvian cortex have been claimed as the actual cause of aphasia in patients with striatocapsular lesions (Weiller *et al.*, 1990; Weiller *et al.*, 1993; Willmes and Poeck, 1993; Godefroy *et al.*, 1994).

Of note, AS and PJ presented with a marked reduction of spontaneous and conversational speech. In the context of preserved linguistic functions, and combined with poor verbal fluency, this impairment of language has the hallmarks of 'dynamic aphasia' (Luria and Tsvetkova, 1967), a disorder of communicative language. Dynamic aphasia is seen by most authors as a prelinguistic, conceptual disorder due to a general loss of spontaneity or thought ('Antriebsmangel der Sprache', Kleist, 1934), an impairment of verbal planning (Costello and Warrington, 1989), or a disordered selection between competing verbal response options (Robinson *et al.*, 1998), and not as true aphasia. It is almost invariably found with left frontal, particularly fronto-mesial lesions. The present findings add dynamic aphasia to the spectrum of language disorders following CN lesions; together with the observed poor verbal fluency, the CN may be seen as a possible lesion site for disorders of the generative aspects of language (Mega and Alexander, 1994).

#### *Executive functions*

AS and PJ both suffered from a severe frontal-executive deficit. Executive functions which appeared most impaired during psychometric testing were response initiation and response selection, cognitive flexibility, problem solving abilities, divergent thinking, error control, and the suppression of previously established, habitual response schemata. Typical errors were perseverative responses, false positive errors and rule breakings (PJ). Executive problems became particularly apparent with tasks offering no or only little structured response schema, or requiring spontaneous flexibility such as the Action Program Test, or the type of fluency tasks that were used. In contrast, performance was better on tests requiring 'reactive' flexibility, or offering a multiple-choice

response format like the VESPAR. Time pressure had a particularly deleterious effect on performance, as evident, e.g. from arithmetical operations which were largely unimpaired when performed without time limit, as opposed to the GDAE. Both patients were also impaired in answering complex problems by appropriate calculation procedures. During arithmetical operations, two different types of procedural deficits have been identified – one due to frontal-executive difficulties (Semenza *et al.*, 1997), the other due to memory problems (Girelli and Delazer, 1996). In the first type, procedural deficits are attributed to poor planning and monitoring mechanisms (Semenza *et al.*, 1997; Mantovan *et al.*, 1999), whereas difficulties in storing and/or retrieving a complex sequence from long-term memory are involved in the second type. The qualitative error analysis suggests that at least PJ's deficit may be attributed to difficulties in executing a complex, multi-step procedure rather than to the retrieval of the appropriate algorithm. Errors indicative of frontal-executive dysfunction were also found in the dot-counting task, where PJ produced erroneous results due to repeated perseveration of counting steps. Overall, these findings are in line with previous studies of CN patients (Mendez *et al.*, 1989; Degos *et al.*, 1993; Kumral *et al.*, 1999) and of other BG lesions (Laplaine *et al.*, 1984; Mendez *et al.*, 1989; Strub, 1989; Caplan *et al.*, 1990; Kumral *et al.*, 1999) suggesting that frontal-executive deficits represent a hallmark of focal BG lesions. A further aspect of frontal dysfunction is the observed attentional impairment which will be discussed separately below.

#### *Memory*

Both patients had a severe disorder of episodic, short and long term memory encompassing both verbal and figural materials. Memory disorders have been observed in previous CN cases (Stein *et al.*, 1984; Mendez *et al.*, 1989; Caplan *et al.*, 1990; Kumral *et al.*, 1999), and have mostly been described as anterograde, short-term memory loss. PJ's and AS' memory disorder was characterized by poor encoding and defective spontaneous free and cued recall, particularly of non-contextually embedded or abstract information, such as e.g. lists of words or designs, or the complex figure (Figs. 3 and 4). Recognition was adequate in AS, whereas PJ's verbal and figural recognition was defective, with a high rate of false alarms.

Two main hypotheses can be discussed to explain both subjects' memory impairment, one anatomic, and one cognitive. First, the observed impairment of memory may be due to damage to primary structures mediating memory functions. This would give the CN a role as a principal structure of memory, such as the hippocampal formation, the diencephalon or the basal forebrain nuclei. At present, knowledge from clinical and experimental studies about the role of the caudate nucleus does not allow such a designation. A further anatomical explanation relates the observed impairment of memory to a 'strategic lesion' in the anterior limb of the internal capsule, as discussed below. Second, AS and PJ's may have developed amnesia secondary to their attentional or executive

impairment. Several findings support the second explanation. Lapses of focused and sustained attention were evident from both subjects' incongruous learning curves (MGT, RVDLT), and from PJ's dissociation of verbal and figural recognition scores across both testings. Also, PJ's poor digit and block span measures indicate an impairment of attention and working memory. It is evident that some of the mnemonic deficits were clearly related to a reduction of executive control, particularly those dependent on the effortful and strategic aspects of memory, such as encoding, the employment of semantic cues, spontaneous recall, the ability to suppress non-relevant information or confabulatory responses, or to monitor recognition processes. Poor use of self-employed encoding strategies, impaired active memory search, sensitivity to interference, confabulations, and a nonselective recognition approach are all in line with the presence of an impaired executive control of memory functions (Shimamura *et al.*, 1991; Gershberg and Shimamura, 1995). Based on an information processing model which claims that memory tasks are fulfilled by component processes and the 'cognitive effort' conferred by these processes, it seems fair to conclude that AS and PJ's impairment of memory was functionally related to coexisting attentional, motivational and executive components. Previous studies have shown that these component processes rely on the integrity of the frontal lobes and are reduced in patients with dorsolateral frontal lesions (Shimamura *et al.*, 1991; Incisa della Rocchetta and Milner, 1993; Gershberg and Shimamura, 1995). The present findings suggest that the impairment of memory found after CN lesions is secondary to the executive impairment of these patients. However, the anatomical and the cognitive hypothesis may not be mutually exclusive. Overall, we conclude that CN damage can lead to extensive, global episodic memory impairment.

### Attention

Different functions and systems have been subsumed under the notion of attention, among them alertness and arousal, as well as focused, sustained and divided attention (van Zomeren and Brouwer, 1994). As documented by computer-based measurements, AS and PJ both exhibited a pronounced and persistent reduction of attentional resources, particularly of alertness, and of divided attention. Also, both patients failed to profit from a warning tone during the phasic task, possibly due to poor control mechanisms over their reaction and an increased readiness to react to irrelevant stimuli (Zimmermann and Fimm, 1993). Though not tested formally, sustained attention and concentration appeared also reduced during test sessions. Deficits of attention have been mentioned in patients with CN lesions (Mendez *et al.*, 1989; Canavero and Fontanella, 1998) and have also been found in Huntington's disease (Sprengelmeyer *et al.*, 1995; Lawrence *et al.*, 1998) and in patients with lesions of the BG (Copland *et al.*, 2000b). Thus, a disruption of fronto-striatal mechanisms may produce attentional deficits and secondary deficits inducing the activation of other cognitive domains which are strongly attention-based, such as memory and problem solving. Our findings

confirm the existence of a disorder of arousal and divided attention following CN lesions which is in many aspects similar to the attentional impairment following frontal brain regions (Fuster, 1989; Foster *et al.*, 1994; Godefroy *et al.*, 1996). A further deficit regards lateralized visual exploration in the extrapersonal space. Though none of the patients showed any clinical sign of hemineglect, both subjects displayed an attentional bias for the detection of stimuli contralateral to their brain lesion. Neglect or biased spatial attention following the lesions of the BG has previously been documented (Caplan *et al.*, 1990; Weiller *et al.*, 1990; Kumral *et al.*, 1999; Fimm *et al.*, 2001). Overall, our observations support the concept that the BG are important structures mediating different forms of attention.

### Lesion location and outcome of disease

Both patients' brain lesion was located in the left BG. However, the exact lesion location within the left BG was not identical in AS and PJ. AS' lesion bears the form of a striatocapsular hemorrhage with its main part in the putamen and pallidum, and with a small extension to the head of the CN (Fig. 1b and c). PJ's lesion shows the inverse pattern with its main portion located in the head of the caudate and minor involvement of the lentiform nucleus (Fig. 2b and c). A schematic reconstruction of the chronic lesion reveals that a substantially larger amount of the left caudate, particularly the head area, is damaged in PJ (Fig. 2d and e) as compared to AS (Fig. 1d and e). Neither was the severity of cognitive losses identical in both patients, with PJ's behaviour and neuropsychological functioning appearing far more defective than AS'. Also, a long-term follow-up examination after more than 20 months revealed that more cognitive recovery had taken place in AS, whereas most of PJ's impairments remained unchanged. We suggest that this discrepancy in the severity of long-term cognitive impairment is related to the difference of the patients' underlying brain lesion. After the mass effect of the acute bleeding had subsided in AS, her cognitive outcome was presumably better because her lesion predominantly affected the putamen and pallidum, whereas PJ's performance was more defective due to its main location in the caudate. In contrast, AS' reaction time on a simple alertness task was abnormally slow and showed only little recovery; she also had many misses on the divided attention task. Her slowness may be due to the fact that non-cognitive, motor circuits linked to the putamen were disrupted to a greater degree than PJ's, who suffered only minor damage to the lentiform nucleus and whose reaction times were less pathologic.

In sum, these findings suggest that the extent of CN lesion, particularly in the head of the caudate nucleus, seems to be critical for the severity and persistence of the observed behavioural abnormalities in our patients. This observation underlines the importance of the CN for cognition and behaviour; it also shows that damage to other structures of the BG are less dangerous for the integrity of cognition, a

notion which is well in line with other studies (Bhatia and Marsden, 1994; Gurd and Bamford, 1997).

### *Lesions of the CN and the hypothesis of fronto-subcortical circuits*

Different hypotheses have been put forward to explain the origin of cognitive impairment caused by BG lesions (Alexander *et al.*, 1987; Cappa and Vallar, 1992; Nadeau and Crosson, 1997). A detailed comparison and appraisal of these models is far beyond the scope of this paper. The FSC-hypothesis is a theory based on neuroanatomical and neurochemical findings which outlines the neural connections between the BG and the frontal cortex (Alexander *et al.*, 1987; Houk and Wise, 1995; Middleton and Strick, 2000). This model predicts that damage to individual loops is followed by specific behavioural effects (Mega and Cummings, 1994; Lawrence *et al.*, 1998). Since the BG are important constituents of all three 'cognitive' loops, AS' and PJ's case provide an opportunity to test the predictions of the FSC hypothesis on the basis of their lesions and clinical findings. To verify these claims, we will discuss the essentials of our patient data in the context of a clinical framework of this model (Mega and Cummings, 1994).

Abulia, dynamic aphasia, and frontal-executive impairment are the conditions which can be best explained by the FSC-hypothesis. According to this model, abulia and dynamic aphasia are the result of a disruption of the anterior cingulate-prefrontal circuit which subserves drive, motivation, and response initiation. This behavioural pattern resembles asponaneity, poor response initiation, mutism or reduced verbal generative ability following medial frontal lesions (Costello and Warrington, 1989; Ziegler *et al.*, 1997; Robinson *et al.*, 1998), suggesting a functional equivalence of CN damage and frontomesial lesions. Furthermore, the alterations subsumed under the notion of a frontal-executive deficit are consistent with a dysfunction of the dorsolateral prefrontal circuit, which in our cases evidently results from a disconnection between the BG and the prefrontal cortex. The summary of the 'prefrontal' syndrome as derived by Fuster (Fuster, 1989) from primate studies lists defective problem solving, impaired planning and control of interference, poor initiation of goal-directed behaviour, reduced or abnormal disease awareness, poorly focused and maintained attention, disorders of visual search, and slowness as its most important constituents. Other descriptions (Mesulam, 1986; Stuss and Benson, 1986; Shallice and Burgess, 1991) agree with this characterization. Thus, from a phenomenological perspective, abulia and executive dysfunction following CN lesions are well in accord with the proposed disruption of two circuits. Interestingly, the FSC-hypothesis does not mention forms of attentional dysfunction as typically associated with lesions of a loop (Mega and Cummings, 1994). Based on the view that attentional impairments have often been reported in patients with frontal brain damage (Fuster, 1989; Foster *et al.*, 1994; Godefroy *et al.*, 1996), one could propose similar deficits of

attention resulting from lesions of the dorsolateral-prefrontal or the anterior cingulate circuit, or of a combined lesion of both loops.

The FSC-hypothesis offers a less straightforward, indirect explanation for an amnesic syndrome caused by a BG lesion. Memory impairment is explained as resulting from a frontal-executive deficit causing a reduction of the organizational, motivational and set-shifting abilities which are required during complex mnestic processes. More recent reports have established a major role of 'frontal' functions in memory, regarding, e.g. the temporal organization of information, source memory, or sensitivity to interference (Shimamura *et al.*, 1991; Gershberg and Shimamura, 1995; Wheeler *et al.*, 1995). Overall, AS' and PJ's cognitive profile supports the hypothesis of an 'executive' memory impairment (Mega and Cummings, 1994) which is augmented by a profound dysfunction of attentional mechanisms.

An alternative mechanism causing memory and executive impairment in our patients is proposed by the concept of a 'strategic' lesion in the internal capsule. Severe, nonresolving multimodal memory disorders have been found after lesions of the capsular genu and anterior limb of the internal capsule (Kooistra and Heilman, 1988). The putative mechanism is an interruption of the inferior and anterior thalamic peduncles which connect the thalamus with frontal and temporal cortical areas in a reciprocal fashion (Markowitsch *et al.*, 1990; Schnider *et al.*, 1996). Thus, a strategically placed lesion in the internal capsule may result in a loss of thalamic input to the Papez circuit and basolateral limbic circuit, and also to the frontal cortex, combined with a deprivation of the thalamus from cortical input, most importantly from the temporo-limbic system. Functional brain imaging studies in these cases show a focal reduction in perfusion most prominent in the ipsilateral inferior and medial frontal cortex (Tatemichi *et al.*, 1992). Similar to AS and PJ, patients with the capsular genu syndrome present with abulia, psychomotor retardation, blunting of affect, unconcern, and executive impairment (Madureira *et al.*, 1999; Chukwudelunzu *et al.*, 2001).

The least stringent account given by the FSC-hypothesis is the one given for neglect or aphasia following CN damage. Though neglect following BG lesions has been observed (Caplan *et al.*, 1990; Weiller *et al.*, 1990; Kumral *et al.*, 1999; Fimm *et al.*, 2001), it is not clear which loop specifically mediates spatial attention, and it appears that other functional networks (Mesulam, 1981; Posner and Petersen, 1990) may provide a better explanation than the FSC-model. Also, there is no straightforward explanation for aphasia as related to a disconnection of FSC. If not produced by co-occurring lesions in the perisylvian cortex (Weiller *et al.*, 1990; Godefroy *et al.*, 1994), several models of subcortical structures participating in language functions become explanatory candidates (for a recent review see Crosson *et al.*, 1997, or Wallech, 1997). However, none of the models claiming a quasi-linguistic competence of the BG bears functional or anatomical resemblance to the concept of FSC. Aphasia associated with a left CN lesion can only be explained by

a model claiming damage to the existence of circuits linking the perisylvian cortex with the BG; at present, only some of these subsystems have been described (Middleton and Strick, 1996), and none of them is outlined in the FCS-hypothesis (Mega and Cummings, 1994).

## Conclusions

The present study provides a detailed description of the behavioural abnormalities associated with a focal left BG lesion including the CN. Overall, several findings of patients AS and PJ, specifically their abulia, attentional and executive deficit can apparently be explained by a disturbance of the anterior cingulate and dorsolateral prefrontal circuits. Also, a mechanism resulting from a disordered orbitofrontal circuit causing disinhibition, personality and mood changes, as found in other patients with CN lesions (Mendez *et al.*, 1989; Caplan *et al.*, 1990), can be construed. These findings are in favour of the FSC-model. The backtracking of other deficits to a disconnection of cortico-striatal loops is less compelling. This is particularly true for 'non-frontal' cognitive impairments like aphasia associated with CN lesions. Also, the exact mechanism for the observed episodic memory impairment remains debatable, the candidates being a weakness of systems executing and supporting memory functions, and an anatomical variant.

Due to methodological limitations this study can only partly resolve the issue of the neural substrate which underlies the cognitive deficits after a disconnection of frontostriatal circuits. Our findings are based on standard clinical-neuropsychological investigations which do not allow us to disentangle the complex organization of striato-cortical loops, and which are not specifically designed to test individual loops. Also, some chosen designations for deficits following FSC-lesions like 'abulia' or 'dysexecutive syndrome' are broad behavioural terms which certainly need further differentiation. Some of the listed discrepancies and problems with this approach may also stem from the fact that the FSC-hypothesis is anatomical by its character, and therefore little is known about how cognitive acts are actually performed in the loop system. Without knowing its functional architecture better it will remain difficult to understand how a lesion of an identical brain structure causes one syndrome in a group of patients and a different syndrome in another group of subjects, such as in cases of CN lesions causing abulia as opposed to disinhibition or depression. Alternative strategies and further research will be required to study functions within and between the corticostriatal circuitry.

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## Basal ganglia lesions and the theory of fronto-subcortical loops: Neuropsychological findings in two patients with left caudate lesions

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### Abstract

Basal ganglia lesions have a high prevalence for associated behavioural impairments. However, the exact pattern of cognitive impairments and its relationship to individual basal ganglia lesion have rarely been investigated by means of a detailed neuropsychological and lesion study. Furthermore, different mechanisms have been proposed as relevant for the observed cognitive deficits; among these, the hypothesis of fronto-subcortical loops (Alexander *et al.*, 1986) has made predictions regarding the relationship between the damage of particular striato-frontal circuits and the resulting behavioural impairment which await clinical confirmation. We present a study of two subjects who suffered a MRI-documented focal left basal ganglia hematoma. The two patients differed in their lesions; in one patient (PJ) large parts of the caudate nucleus were destroyed whereas in the other (AS) mainly the pallidum and putamen were lesioned and the caudate suffered only minor damage. In the acute phase, the behavioural and neuropsychological abnormalities were similar in both cases and included mainly abulia, an impairment of executive and attentional functions, and a severe amnesic syndrome. After several months many functions were restored in AS, whereas PJ's abilities remained largely defective. Based on these data and on previous case studies several conclusions are drawn. Left caudate lesions induce marked and long-lasting behavioural and neuropsychological impairments comprising predominantly drive, executive control, attention, and memory. The extent of lesion in the head of the caudate nucleus is the critical factor regarding the severity and the outcome of the syndrome, whereas damage to the putamen and pallidum is less crucial for cognitive functions. A subset of behavioural alterations, among them abulia, attentional and frontal-executive dysfunctions can well be attributed to lesions of the anterior cingulate circuit and the dorsolateral-frontal circuit at the basal ganglia level. Other impairments, most importantly the prominent amnesic syndrome, are more difficult to interpret on the grounds of this hypothesis and may be related to other pathomechanisms.

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### Primary diagnosis of interest

Neuropsychological deficits following left caudate lesions

### Author's designation of case

AS, PJ

### Key theoretical issue

- Fronto-subcortical loops

*Key words:* basal ganglia; caudate nucleus; cognitive impairment; fronto-subcortical loops

### Scan, EEG and related measures

MRI

### Standardized assessment

Psychometric assessment

### Other assessment

Lesion analysis

### Lesion location

- Head of left caudate nucleus

### Lesion type

Hemorrhage

### Language

English