The role of the basal ganglia in cognition is still uncertain. This case study investigates the partial neuropsychological profile of a 20-year-old patient with a perinatal left putaminal lesion. This pathology is relatively rare and little is known of its cognitive effects. The focuses of our neuropsychological assessment were working memory, executive functions, analysis of spontaneous speech and implicit skill learning. The patient’s executive functions did not attain the normal range, and working memory was also partially impaired. In addition, the temporal features of her speech revealed an increased pause/signal time ratio. Finally, in an implicit skill learning task, the patient showed general motor skill learning, but no sequence specific learning. Together these findings suggest that the frontal/subcortical circuit between the putamen and frontal motor areas plays a role in higher cognitive processing such as executive functions, working memory, as well as in first-order sequence learning.

Keywords: putamen, cognition, neuropsychology, working memory, implicit learning

The basal ganglia are a set of interconnected subcortical structures composed of the caudate and lentiform nuclei (putamen and globus pallidus), the substantia nigra, and the sub-thalamic nucleus (Kandel, Schwartz and Jessell, 2000). Early hypotheses viewed the basal ganglia as a funnel, through which information from various cortical regions is transported to the motor
cortex by way of the ventrolateral thalamus (Alexander, DeLong and Strick, 1986). Later evidence, however, suggested the existence of segregated basal ganglia-thalamocortical channels entailing the maintained separation of motor and association influences, thus precluding the consolidation of information from the various motor and association inputs (Alexander, DeLong and Strick, 1986). Further revisions to this hypothesis led to the inclusion of multiple circuits linking the basal ganglia with frontal regions (Alexander, DeLong and Strick, 1986), and today there is strong evidence in support of this claim and against the information funneling perspective (Middleton and Strick, 2000). Moreover, the association of the basal ganglia with motor skills is largely recognized as only partially accurate, as the basal ganglia are involved in both movement and cognition (Middleton and Strick, 2000).

The basal ganglia’s role in cognition is suggested by the existence of circuits connecting the basal ganglia to non-motor regions in the frontal lobe (dorsolateral prefrontal cortex, lateral orbitofrontal cortex, and anterior cingular cortex) associated with a variety of cognitive functions (Alexander, DeLong and Strick, 1986; Middleton and Strick, 2002). Additionally, a wealth of evidence is afforded by studies linking damage to the basal ganglia with indirect cognitive effects in frontal brain regions. Lesions of the basal ganglia, for example, have been associated with cognitive deficits similar (but not identical) to those observed in focal frontal lesions. These include deficits in working memory, long-term memory retrieval, verbal fluency performance, and attention, as well as impairments in executive functions like concept formation, mental set shifting, and inhibition of responses (Cummings, 1993). The disturbance of some of these functions has also been observed in patients with Parkinson’s Disease and Huntington’s Disease – which are characterized by basal ganglion degeneration (Brandt et al., 1996; McPherson and Cummings, 1996) – and neuroimaging studies have shown that lesions in the putamen or globus pallidus can result in a relative hypometabolism in the frontal lobe (LaPlane et al., 1984; Strub, 1989). Apart from the aforementioned studies, isolated putamen lesions have also been associated with ADHD and ADHD traits (Max et al., 2002) and obsessive-compulsive disorder (Daniele et al., 1997).

The basal ganglia are also thought to play a crucial role in language processes like grammar, fluency, sentence-level comprehension, and production (Alexander, 1989; Crosson, 1992; D’Esposito et al., 1995; Gurd and Bamford, 1997; Nadeau and Crosson, 1997; Troyer et al., 2004; Ullman, 2001). Of interest to the present study, evidence from ganglion lesions suggests that both the putamen and the caudate are involved in setting rate, volume, and initiation of speech (Gurd and Bamford, 1997). Despite the fact that speech tempo, a common neuropsychological measure of language production, is unimpaired in patients with Parkinson’s Disease (Ackermann and Ziegler, 1991), an increased speaking rate has been observed in patients with Wilson’s Disease (Uhlhaas and Singer, 2006), which is associated with basal ganglia, in particular putamen abnormalities (King et al., 1996). Additionally, verbal working memory has been found to be impaired in focal putamen lesions (Giroud et al., 1997; Sullivan et al., 1991) and in Parkinson’s disease after pallidotomy (Alegret et al., 2003; Troster, Woods and Fields, 2003), and both Huntington’s disease (Ho et al., 2002) and bilateral lentiform lesions (Haaxma et al., 2007; LaPlane et al., 1984) are associated with greater deficits in letter (phonemic) fluency than semantic fluency, a result which is also observed in subjects with frontal lobe lesions.
The basal ganglia are also associated with implicit skill learning (Doyon et al., 2009; Hikosaka et al., 1999; Hikosaka et al., 2002; Keele et al., 2003; Kincses et al., 2008). Implicit skill learning occurs when information is acquired from an environment of complex stimuli without conscious access either to what was learned or to the fact that learning occurred (Reber, 1993). In everyday life, this learning mechanism supports the temporal organization of behavior, the formation of high-order associations, and the prediction of future events (Keele et al., 2003; Nemeth et al., 2010; Robertson, 2007).

Neuropsychological studies revealed that medial temporal lobe (MTL) impairment has little effect on implicit learning (Dennis and Cabeza, 2010; Reber and Squire, 1994, 1998). In contrast, basal ganglia and cerebellar disorders (e.g. Parkinson disease, Huntington’s disease, cerebellar degeneration) showed impairments in implicit learning (Brown et al., 2003; Pascual-Leone et al., 1993; Westwater et al., 1998). Neuroimaging and transcranial magnetic stimulation (TMS) studies have also revealed that the striatum and cerebellum are critical contributors to implicit learning performance (Keele et al., 2003; Peigneux et al., 2000; Torriero et al., 2004). Although the global role of the striatum in implicit skill learning is unquestionable (Doyon et al., 1997; Peigneux et al., 2000), the putamen’s involvement on its own is still to be investigated (Rauch et al., 1997).

THE AIM OF THE STUDY

The aim of the present study was to describe the detailed cognitive profile of a patient with an isolated left putamen lesion examining a large-scale of neuropsychological functions. Based on aforementioned studies we examined executive functions, short-term and working memory, speech analysis and implicit skill learning. The primary contribution of our study is that only little data is available regarding the cognitive effects of focal putamen lesions because in previous studies putamen lesion was often associated with other brain lesions as well, e.g. impairments of the globus pallidus, nucleus caudatus, etc. (Crosson, 1992; Damasio et al., 1982; Nadeau and Crosson, 1997). We expected decreased performance in tasks involving basal ganglia and fronto-striatal circuits.

METHODS

Neurological and neuroradiological description of the patient

The patient was a 20-year-old left-handed Hungarian Caucasian female born in normal delivery after a normal pregnancy. Her family history was negative for consanguinity or neurological diseases. After the delivery, the development and the usage of her right extremities were observed to be retarded. By the age of 2, an abnormal posture of the right extremities had developed. Continuous physiotherapy maintained a limited function of the right arm and leg. She reported a cramp-like feeling and had an abnormal posture of the upper arm, forearm and fingers. She displayed involuntary movements, whereby her right foot would turn inwards.
and the right toes would curl; these movements were aggravated by physical stimuli and relieved by sleep.

The MRI demonstrated a T2 hyperintensity in the left putamen, and hypointensity on the FLAIR and T1 images (Fig. 1). This lesion is consistent with a perinatal lesion. Her dystonia was improved by oral baclofen and botulinum toxin infiltration.

Subjects

The patient and 5 healthy control subjects were matched for age, education (third-year undergraduates), handedness and gender. All subjects, including the patient, performed in the normal IQ range by the Raven Progressive Matrices Test (between 46 and 53 raw score) (Raven, Raven and Court, 2004) and had a maximum score (30) on Mini-Mental State Examination (Folstein, Folstein and McHugh, 1975). This investigation was approved by the local ethical committee of the University of Szeged. Participants were informed about the methods and aims of the study, and gave their written informed consent.

Neuropsychological tests

Six major neuropsychological functions were investigated: verbal (letter and semantic) fluency, phonological short-term memory, visuo-spatial short-term memory, working memory, speech production and implicit skill learning. Tests were administered in the same order to every subject.

Verbal (letter and semantic) fluency tasks. Verbal fluency is a common neuropsychological measure of executive functioning relying on the spontaneous production of words within a fixed time interval (Troyer et al., 1998; Troyer, Moscovitch and Winocur, 1997). There are

Figure 1. MRI images of the patient. A: Flair sequences, B: T1 weighted coronal sequences, C: T2 weighted images. The arrows indicate the lesion.
two types of verbal fluency tasks: letter fluency and semantic (or “category”) fluency. For letter fluency, words must be produced according to phonemic constraints (e.g., exemplars beginning with a specified letter). For semantic fluency, words must be produced according to semantic constraints (e.g., exemplars which belong to a particular semantic category, such as “animal”). The letter fluency task is a powerful tool to detect frontostriatal pathology, while category fluency tasks are presumed to correspond more with temporal lobe deficits (Troyer et al., 1998). In both tasks, verbal fluency is defined as the number of words correctly generated within 60 seconds.

**Phonological short-term memory.** Verbal short-term memory (or “phonological loop” capacity) was measured with a digit span test and a word recall test. The digit span test involves the presentation of spoken sequences of digits for immediate serial recall. Four sequences are presented for each length, starting with three-digit sequences; if three sequences of a particular length are correctly recalled, the sequence length increases by one. Digits are presented at the rate of one per second, and the maximum length at which three sequences are correctly recalled provides a measure of digit span. The word recall and morphologically complex word recall tests are equivalent to the digit span test, with the exception that two-syllable words or morphologically complex words are used in place of digits. All words are controlled for frequency, concreteness, and ease of pronunciation. No words are repeated (see Racsmány et al., 2005).

**Visuo-spatial short-term memory.** Visuo-spatial short-term memory (or “visuospatial sketchpad”) was measured by the Corsi Block Tapping Test (Lezak, 1995). In this nonverbal task, nine three-dimensional black cubes are arranged on a blackboard and the subject must tap the cubes in the same order as the experimenter. Similarly to the digit span and word span tests, the length of the sequence increases by one after three out of four successful repetitions.

**Working memory.** The term ‘working memory’ refers to the ability to hold and manipulate information simultaneously over short periods of time (Baddeley, 1992). Working memory was measured via a backward digit span test and a reading span test. The backward digit span test employs the same procedure as the digit span and word span tests, but in this task the participant has to recall the sequence of spoken digits in reverse order. Working memory capacity was further measured by the Hungarian version of Daneman and Carpenter’s Reading Span Task (Daneman and Carpenter, 1980). In this test, subjects are required to read aloud increasingly longer sequences of sentences and to recall the final word of all the sentences in each sequence in serial order. A subject’s working memory capacity is defined as the longest sequence length at which they are able to recall the final words (see Janacsek et al., 2009; Racsmány et al., 2005).

**Speech analysis.** To investigate speech production, the experimenter engaged in a guided conversation with each subject. While subjects were able to respond freely, each was asked the same questions. These conversations were recorded and phonetically transcribed, and an oscillogram was created. The articulation rate, the speech tempo, and the pause ratio were measured (Feldstein and Bond, 1981; Hoffmann et al., 2010). The articulation rate was de-
fined as the total number of phonemes produced (by the subject) during the conversation divided by the total conversation time (subject production only) with all pauses omitted. The speech tempo is similar to the articulation rate, except that pauses are included in the total conversation time. The pause ratio is the ratio of the duration of all pauses to the total conversation time attributable to the subject, including all pauses (Hoffmann et al., 2010).

Implicit Skill Learning – The Serial Reaction Time (SRT) task was used to measure implicit skill learning. The SRT task is a four-choice reaction time task containing a hidden repeating sequence that the subject comes to implicitly predict and learn (Nissen and Bullemer, 1987). This widely used task is connected to the activation of striatum (Peigneux et al., 2000).

During the SRT task, subjects see a stimulus (asterisk or dot) appearing at different visual locations arranged horizontally in a seemingly random pattern and have to press the response keys corresponding to those locations as quickly as possible (Fig. 2). After pushing the correct button the target stimulus appears above another line out of the four. Unbeknownst to the subjects, the appearance of the target stimuli follows a serial order (e.g. 4231324321, where numbers refer to different locations on the screen). The SRT task consisted of 12 blocks with 12 sequences in each blocks. The last block was a random block in which the visual cue no longer followed a repeating pattern. There was a one minute pause between blocks.

The reaction time (RT) is the dependent measure of primary interest in the SRT task, because the accuracy rates usually demonstrate ceiling effects (see Negash et al., 2007). Gradual reduction in reaction times across repeated (sequential) blocks is expected to occur. This reduction is due to the participants’ growing expertise in learning not only the sequence but also in learning the visuomotor association between the position of the visual cue and the required motor response (Poldrack et al., 2005; Robertson, 2007). A more specific measure of learning in this task can be obtained by comparing performance on the repeated sequence blocks against performance on the random block. Any response time advantage gained by having learned the motor response will remain during the random block, and the resulting difference

*Figure 2. The classical SRT task developed by Nissen and Bullemer (1987)*
in response times as compared to the blocks containing repeated sequences is a consequence of the subject having learned the pattern implicitly. When the sequence is unexpectedly substituted with a random sequence, the subject is going to have an inclination to respond according to the pattern learned during trials containing repeated sequences. This impulse causes reaction times to increase in random trials compared to repeated sequence trials, as the subject must (implicitly) correct for this tendency (Robertson, 2007). Therefore Knopman and Nissen (1991) identified two learning measures: the RT difference between the first and the last pattern blocks (P1 and P11 in Fig. 3A–B, where P refers to pattern blocks), which indicates general motor skill learning and sequence learning together, and the RT difference between the last pattern block and the random block (P11 and R in Fig. 3A–B, where R refers to random block), assessing sequence learning separately. These measures are commonly used in the SRT research (e.g. Green et al., 1997; Negash et al., 2007; Westwater et al., 1998). Our analyses followed these studies.

RESULTS

Verbal Fluency. The performance of the patient in the letter fluency task was 6 standard deviations (SD) smaller compared to that of the normal controls, whereas in the semantic fluency task there was no difference (see Table 1).

Short-Term and Working Memory. Patient’s performance in the word span task and backward digit span test was within 1 SD of controls’ mean score, while in the reading span and digit span tasks was lower than that of control subjects (by 8, 2.6 and 1.7 SDs, respectively). Patient performance in the visuo-spatial short-term memory task was identical to that of controls.

Speech Analysis. Monotonous in intonation and interspersed with frequent and long pauses, the patient’s speech is best described as languid. The speech tempo was 1 SD slower and the pause ratio was 7 SDs higher than the controls’. In contrast, the patient’s articulation

<table>
<thead>
<tr>
<th>Test</th>
<th>Patient</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Letter fluency (words / 1 min)</td>
<td>7.0</td>
<td>15.3 ± 1.26</td>
</tr>
<tr>
<td>Semantic fluency (words / 1 min)</td>
<td>25.0</td>
<td>27.1 ± 6.37</td>
</tr>
<tr>
<td>Digit span</td>
<td>4.0</td>
<td>6.2 ± 1.3</td>
</tr>
<tr>
<td>Word span</td>
<td>4.5</td>
<td>4.8 ± 0.45</td>
</tr>
<tr>
<td>Morphologically complex word span (2 syllable)</td>
<td>4.5</td>
<td>4.4 ± 0.55</td>
</tr>
<tr>
<td>Morphologically complex word span (3 syllable)</td>
<td>3.0</td>
<td>4.2 ± 0.45</td>
</tr>
<tr>
<td>Backward digit span</td>
<td>4.0</td>
<td>4.8 ± 0.84</td>
</tr>
<tr>
<td>Reading span</td>
<td>2.33</td>
<td>4.6 ± 0.28</td>
</tr>
<tr>
<td>Corsi block test</td>
<td>5.0</td>
<td>5 ± 0.7</td>
</tr>
<tr>
<td>Articulation rate (sound/sec)</td>
<td>12.8</td>
<td>14.3 ± 2.2</td>
</tr>
<tr>
<td>Speech tempo (sound/sec)</td>
<td>9.4</td>
<td>12.4 ± 2.1</td>
</tr>
<tr>
<td>Pause/signal time ratio (%)</td>
<td>26.6</td>
<td>18 ± 1.1</td>
</tr>
</tbody>
</table>
rate was within 1 SD compared to the controls mean. Moreover, grammatical errors did not appear more often than for controls.

**Implicit skill learning.** As is typical in the SRT task, the accuracy levels remained high over the whole experiment. The percentage of correct responses amounted 98% of the trials in all participants. Hence, we focused analyses on reaction times. Median reaction times (RTs) for correct responses within 4 standard deviations (SDs) were calculated separately for each block for each participant. As is shown in Figure 3A, the patient is overall slower than the control group, but similarly to controls, shows a generally decreasing reaction time across blocks.

![Figure 3A](image_url)

**Figure 3.** A) Means of median RTs are displayed for control group (filled square) and median RTs for the patient (open square). B) Difference scores of overall skill learning (P1–P11) and sequence learning (R–P11) are displayed. Error bars indicate SDs, computed for control group only. P – pattern, R – random

As Figure 3B shows, the difference between the first and the last pattern blocks is high for both groups (223 ms for controls, 180 ms for patient). The patient’s learning score is within 1 standard deviation of controls’ score, suggesting intact overall skill learning. In contrast, the difference between the last pattern and the random block was large for controls (145 ms) and 4 SDs smaller for patient (10 ms), suggesting sequence specific learning for the control group only.

**DISCUSSION**

To the best of our knowledge, this study is the most extensive examination of cognitive functioning in a patient with a focal left putamen lesion to date. We employed a more comprehensive test of working memory system than was used in Sullivan (Sullivan et al., 1991), Giroud (Giroud et al., 1997) or Crosson (Crosson, 1992), and additionally performed an analysis of
speech tempo, which to the best of our knowledge has never been looked at in any focal putamen lesion studies. Our investigation revealed cognitive deficits in verbal fluency, working memory, and speech production.

Consistent with other investigations of patients with striatonigral degeneration, our patient either barely reached or failed to reach the standard for normal controls on our tests of executive functioning. Impaired verbal short-term and working memory tasks are consistent with earlier studies of perinatal lesions (Sullivan et al., 1991), while normal performance on the Corsi Block-Tapping Task suggests that the left putamen is not involved in visuo-spatial working memory. The temporal analysis of speech revealed an increased pause ratio. As the articulation rate was normal, this finding cannot be explained in terms of a motor impairment. We propose that the increased pause ratio, in combination with impaired letter fluency, points to the involvement of the left putamen in lexical access. In both the letter fluency task and in spontaneous speech, words must be selected from the mental lexicon, for which the temporal lobe is thought to be responsible (Hickok and Poeppel, 2007). Given that the mental lexicon of our patient was not impaired and her articulation rate was normal, these results point to lexical access as the functional cause of the deficit, and in turn point to the focal lesion of the left putamen as the source of the impairment in lexical access. As lexical access is strongly associated with the frontal lobes, our results are consistent with Gurd and Bamford (1997), who proposed that the basal ganglia acts as an interface between the frontal and temporal cortical regions. Integrating our findings with this hypothesis, the left putamen may be considered to play a key role in modulating lexical access between the frontal and temporal lobes (see also Crosson, 1992; Nadeau and Crosson, 1997).

Compared to studies concerning the more extensive striatal involvement (Doyon et al., 1997; 1998), our research confirms the key role of putamen in implicit sequence learning. The explanation of this phenomenon in this patient’s case is the impairment of the fronto-basal ganglia circuit. It is a well-known fact that motor functions – mostly movements – rely on serial ordering and many cognitive functions (e.g. working memory) do so as well. The patient shows a deficit in this ability, which is probably similar to that observed in cerebellar impairment (Desmond and Fiez, 1998; Schmahmann, 1998; Schmahmann and Sherman, 1998).

In conclusion, while the putamen has long been associated with motor skills, the results of our case study also support that it may also have a significant functional role in the frontostriatal circuit. The primary contribution of our study is that it examined a focal putamen lesion well complementing previous models on the role of basal ganglia in cognitive functions. However, further studies are needed to address the question of possible differences between focal lesions acquired in adulthood and early focal brain lesions which may affect the development of a large-scale neuronal network related to multiple cognitive functions.

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