Neuropsychologia 48 (2010) 2009–2017

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Visuo-motor and cognitive procedural learning in children with basal ganglia pathology

C. Mayor-Dubois[a,*], P. Maeder[b], P. Zesiger[c], E. Roulet-Perez[a]

[a] Pediatric Neurology and Neurorehabilitation Unit, University Hospital, Lausanne, Switzerland
[b] Radiology, University Hospital, Lausanne, Switzerland
[c] Faculty of Psychology and Educational Sciences, University of Geneva, Switzerland

ARTICLE INFO

Article history:
Received 17 August 2009
Received in revised form 24 March 2010
Accepted 25 March 2010
Available online 1 April 2010

Keywords:
Serial Reaction Time
Probabilistic Classification Learning
Child
Basal ganglia pathology

ABSTRACT

We investigated procedural learning in 18 children with basal ganglia (BG) lesions or dysfunctions of various aetiologies, using a visuo-motor learning test, the Serial Reaction Time (SRT) task, and a cognitive learning test, the Probabilistic Classification Learning (PCL) task. We compared patients with early (<1 year old, $n = 9$), later onset (>6 years old, $n = 7$) or progressive disorder (idiopathic dystonia, $n = 2$). All patients showed deficits in both visuo-motor and cognitive domains, except those with idiopathic dystonia, who displayed preserved classification learning skills. Impairments seem to be independent from the age of onset of pathology. As far as we know, this study is the first to investigate motor and cognitive procedural learning in children with BG damage. Procedural impairments were documented whatever the aetiology of the BG damage/dysfunction and time of pathology onset, thus supporting the claim of very early skill learning development and lack of plasticity in case of damage.

1. Introduction

According to the conception of multiple memory systems (Squire, 1992; Squire, Knowlton, & Musen, 1993; Squire & Zola-Morgan, 1988), procedural learning is generally defined as "knowing how" to do things (for review, Knowlton & Moody, 2008). It is part of non-declarative memory and refers to a progressive improvement of motor or cognitive performance through practice or repetition. The procedural learning system includes perceptual and motor skill learning as well as habit learning, which refers to the gradual acquisition of stimulus-response associations. It contrasts with declarative memory ("knowing that"), a flexible system responsible for the conscious retrieval of information (Cohen & Squire, 1980). These different memory systems are subserved by distinct neuroanatomical networks (Squire, 1992; Squire et al., 1993). While declarative memory is clearly assumed by the medial temporal lobes and the diencephalon, procedural learning is mainly supported by the striatum (putamen and caudate nuclei), with the participation of the cerebellum, the frontal cortex and other cortical areas, depending on the nature of the task (Doyon et al., 1997; Packard & Knowlton, 2002; Poldrack, Prabhakaran, Seger, & Gabrieli, 1999).

Dissociations between procedural learning and declarative learning systems were reported, with normal motor procedural learning being observed despite severe amnesia due to medial temporal lobe lesions (Brooks & Baddeley, 1976; Corkin, 1968; Damasio, Eslinger, Damasio, Van Hoesen, & Cornell, 1985; Gabrieli, Corkin, Mickel, & Growdon, 1993; Milner, 1962; Tranel, Damasio, Damasio, & Brandt, 1994) and impaired procedural learning together with preserved declarative memory in patients with basal ganglia damage like Parkinson's (Haaland, Harrington, O'Brian, & Hermanovicz, 1997; Harrington, Haaland, Yeo, & Marder, 1990; Sarazin et al., 2002) and Huntington diseases (Gabrieli, Stebbin, Singh, Willingham, & Goetz, 1997; Schmidtke, Manner, Kaufmann, & Schmolck, 2002; Willingham, Koroshetz, & Peterson, 1996). Even if the participation of declarative memory or executive function in optimal skill learning is likely (Curran, 1997; Foerde, Poldrack, & Knowlon, 2007; Knowlton, Squire, & Gluck, 1994; Packard & Knowlton, 2002; Poldrack et al., 2001; Smith & McDowall, 2004), it appears that conscious recollection is not a necessary component of the process.

The basal ganglia, which include the striatum, globus pallidus, subthalamic nucleus and substancia nigra, are involved in movement control and planning but also in the regulation between motivational, cognitive and motor components of behavior (Bédard et al., 2003; Saint-Cyr, Taylor, & Lang, 1988). Lesions or dysfunction of these structures typically lead to either loss of postural adjustment, rigidity and bradykinesia (as seen in parkinsonism), or to abnormal movements like chorea, athetosis, dystonia and tics (Adams & Victor, 2001).

Procedural learning has mostly been investigated in its motor facet with the Serial Reaction Time test (SRT, Nissen & Bullemer,

* Corresponding author. Tel.: +41 21 31 435 63; fax: +41 31 435 72.
E-mail address: Claire.Mayor@chuv.ch (C. Mayor-Dubois).

0028-3932/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropsychologia.2010.03.022

1987). In this task, participants have to respond as quickly as possible to a stimulus appearing in a specific location. Faster reaction times are observed for the reoccurring but not for the random sequences of stimuli, the participant being unaware of the repetitive structure of the task. This task does not depend on declarative memory since patients with amnesia show preserved learning skills (Nissen & Bullemer, 1987). Functional neuroimaging studies with healthy subjects show striatal activations in SRT learning in association with premotor cortex and supplementary motor area (Grafton, Hazeltine, & Ivry, 1995; Rauch et al., 1997). Performance in SRT tasks is impaired in patients with Huntington disease (Knopman & Nissen, 1991; Willingham & Koroshetz, 1993) and in Parkinson disease, although the nature and extent of the deficit are found to vary across studies (Doyon et al., 1997; Jackson, Jackson, Harrison, Henderson, & Kennard, 1995; Muslimovic, Post, Speelman, & Schmand, 2007; Pascual-Leone et al., 1993; Smith & McDowall, 2004, 2006; Stefanova, Kostic, Ziropadja, Markovic, & Ocic, 2000).

Procedural learning was initially thought to support only motor learning but progressively, its role in cognitive learning, such as associative learning has been recognized (Packard & Knowlton, 2002). This cognitive procedural component has been investigated with a probabilistic classification task (Shohamy et al., 2004) adapted from the original «Weather Prediction» Task (Knowlton, Mangels, & Squire, 1996), in which the participant has to learn the association between a combination of cues and a given result (=outcome). Healthy subjects show increased activation in the right caudate nucleus in this associative learning compared to baseline (Poldrack et al., 1999). Patients with focal (Kéri, Beniczky et al., 2002) or more diffuse degenerative lesions of basal ganglia (Knowlton, Mangels, et al., 1996; Knowlton, Squire, Paulsen, Swerdlow, & Swenson, 1996) perform poorly in this task, unlike patients with medial temporal lobe or diencephalic pathology (Eldridge, Masterman, & Knowlton, 2002; Knowlton, Mangels, et al., 1996; Knowlton et al., 1994), cerebellar disease (Witt, Nuhsman, & Deuschl, 2002) or frontal lobe lesions (Knowlton, Mangels, et al., 1996).

Studies of procedural learning in children are sparse and concern either infants in their first year of life or school-aged children. It has been suggested that during development, children move from a largely procedural to a more declarative knowledge (Karmiloff-Smith, 1994). Automatic, non-conscious learning, acquired through repetition, is thought to be very important for the acquisition of motor and language skills and is viewed as a more primitive system from the phylogenetic and ontogenetic point of view (Nelson, 1987; Reber, 1993). A simplified SRT task – the visual expectancy task – has indeed shown reliable anticipatory responses in infants as young as 3 months old for simple sequence patterns (Haith & McCarty, 1990) and from 5 months old for longer sequences (Smith, Loboschefski, Davidson, & Dixon, 1997). This indicates that sequence learning is already present very early in development and possibly increases during the first year of life. Studies with SRT tasks show no evidence of age-related improvements from 4 to 10 years old (Meulemans, Van Der Linden, & Perruchet, 1998; Thomas & Nelson, 2001), as well as no difference from childhood to adulthood (Meulemans et al., 1998), suggesting age invariance of procedural learning skills beyond infancy. If learning performance is similar across life-span and if the neural structures underlying these learning skills are the same in adults and children, then it would imply that basal ganglia lesions would affect procedural learning in children just like in adults. However, procedural learning has never been studied in children with basal ganglia pathology in order to test this hypothesis.

The few existing paediatric studies on procedural learning have focused on children with diffuse brain pathology like traumatic brain injury (Ward, Shum, Wallace, & Boon, 2002) or various kinds of brain development disorders: in genetic syndromes, such as Williams syndrome (Vicari, 2001a, 2001b), in autism (Gidley Larson & Mostofsky, 2008; Mostofsky, Goldberg, Landa, & Denckla, 2000) or in specific learning disorders like dyslexia (Howard, Howard, Japikse, & Eden, 2006; Stoodley, Ray, Jack, & Stein, 2008; Vicari et al., 2005). Procedural learning impairments – but preserved declarative memory – has been reported in Williams syndrome and in most studies on children with autism or dyslexia, whereas the reversed pattern of performance has been found in children with traumatic brain injury. These results indicate that both memory systems can also be dissociated in children.

The only studies addressing procedural learning in a developmental disorder involving the basal ganglia, were carried out on patients with Gilles de la Tourette syndrome. This syndrome is thought to arise from a fronto-striatal dysfunction and consists of a severe and chronic tic disorder starting during childhood, and frequently associates cognitive and psychiatric disturbances (for review: Leckman, Bloch, Scahill, & King, 2006). Results obtained in children and adults showed preserved perceptivo-motor learning (Marsh, Alexander, Packard, Zhu, & Peterson, 2005), but impaired cognitive procedural learning (Kéri, Szlobodnyik, Benedek, Janka, & Gadoros, 2002; Marsh et al., 2004). Children with chorea due to congenital or acquired conditions or children with focal basal ganglia damage have never been studied.

We investigated 18 children aged 8–15 years with lesions or a dysfunction of the basal ganglia, by giving them a classical SRT task and a probabilistic classification task.

The first aim of our study was to investigate procedural visuo-motor sequence learning and cognitive (classification) learning skills in children with basal ganglia pathology by comparing their learning skills with those of healthy, control children. We expected learning deficits in the clinical group compared to the control group, and similar procedural learning deficits in children as in adults with basal ganglia damage, since their procedural memory system is considered to be already differentiated early in development. The second aim was to investigate a possible plasticity of the procedural learning system, by comparing congenital or early acquired pathologies with later acquired ones in terms of their impact on the SRT and classification tasks. Finally, we wondered if dissociations between visuo-motor and cognitive skills could be observed, as shown in some adults (Foerde et al., 2008).

2. Methods

2.1. Participants

Eighteen patients (9 girls, 9 boys) aged 8–15 years (mean = 11.5) were recruited via our paediatric neurology outpatient clinic. Criteria for study participation was a minimum age of 8 years, normal cognitive development (see below) and either combined neurological and radiological, or only clinical signs of uni- or bilateral basal ganglia pathology of various aetiology (Table 1). Neurological signs included choreic movements, dystonia, hemiparesis and tics. Five patients with clear neurological signs at initial consultation were included, although abnormal movement had disappeared at the time of neuropsychological assessment, because of spontaneous evolution or medication. These 18 patients constituted the basal ganglia (BG) group.

Age of pathology onset ranged from prenatal to 13 years old. Four patients had early acquired damage (before 1 year old) and five had a neurodevelopmental dysfunction. These 9 patients were defined as the early acquired lesion/dysfunction group. Seven patients had a lesion/dysfunction acquired after the age of 6 years and constituted the late acquired lesion group. Two children had progressive disease (clinical onset at respectively 7 and 9 years old) with a diagnosis of idiopathic dystonia of unknown etiology (DYT1 negative).

Two patients had unilateral lesions of basal ganglia; the 16 others had clinically or MRI documented bilateral involvement. Only four patients had additional lesion outside basal ganglia. All MRI were reviewed by the radiologist (PM). Six patients had no MRI (no clinical indication or refusal).

Fifteen patients had comprehensive neuropsychological testing for clinical purposes (Table 1). All patients had normal intelligence, defined by a Verbal Reasoning Index superior to 85 at the Wechsler Intelligence Scale, 4th edition (Wechsler, 2007), or based on a single subtest of logico-deductive reasoning for a few children (3), who had no academic difficulties and were recruited for research purposes only (Table 1).