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**CONTRIBUTION DU STRIATUM ET DU CERVELET DANS L'APPRENTISSAGE**  
**VISUOMOTEUR**

Thèse  
présentée  
à la Faculté des études supérieures  
de l'Université Laval  
pour l'obtention  
du grade de Philosophiae Doctor (Ph.D.)

École de psychologie  
FACULTÉ DES SCIENCES SOCIALES  
UNIVERSITÉ LAVAL  
QUÉBEC

DÉCEMBRE 1997

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## Résumé

Les travaux rapportés dans cette thèse ont pour objectif principal de mieux comprendre le rôle du striatum et du cervelet dans l'apprentissage d'habiletés visuomotrices et, plus particulièrement, d'approfondir l'apport spécifique de chaque structure dans cette forme de mémoire. La première étude a pour but de vérifier l'hypothèse selon laquelle le striatum serait impliqué dans la phase d'automatisation des apprentissages. La performance de deux sous-groupes de patients atteints de la maladie de Parkinson (MP), respectivement porteurs de lésions striatales unilatérale et bilatérale, est comparée à celle d'un groupe de sujets témoins à l'aide de la technique de double-tâche. Conformément aux hypothèses, les résultats démontrent que seule une atteinte bilatérale du striatum affecte d'une façon significative la capacité d'effectuer une seconde tâche de nature visuospatiale lors de l'exécution d'une habileté visuomotrice apprise, suggérant ainsi que cette structure participe aux phases avancées de l'acquisition d'habiletés. La deuxième expérience vise à étudier la contribution spécifique du striatum et du cervelet dans l'apprentissage visuomoteur. Pour ce faire, la performance de deux groupes de patients ayant la MP ainsi que celle d'un groupe de patients, porteurs d'une lésion circonscrite au cervelet (CE), sont respectivement comparées à celle de deux groupes de sujets témoins appariés, à l'aide d'une version aléatoire de la tâche de séquence visuelle répétée et d'une nouvelle version de la tâche de tracé-miroir. Pour la première fois, les résultats montrent une double dissociation fonctionnelle entre ces deux structures. Alors que le striatum semble davantage gérer un apprentissage associatif de type perceptivomoteur, le cervelet est particulièrement nécessaire à la mise en séquence de mouvements appris. De nature exploratoire, la troisième étude s'intéresse à la participation du striatum et du cervelet dans la capacité d'adaptation à un changement contextuel à l'aide d'un schème expérimental d'apprentissage d'habiletés. Les résultats suggèrent que les patients parkinsoniens porteurs d'une dysfonction striatale bilatérale, et non ceux ayant une lésion au cervelet, ne peuvent généraliser l'habileté acquise à un autre contexte où ils doivent modifier une partie du plan moteur pour effectuer la tâche. Ensemble, ces données suggèrent non seulement que le striatum et le cervelet participent à l'acquisition

incrémentielle d'habiletés visuomotrices, mais également que ces structures diffèrent quant aux mécanismes privilégiés lors de l'apprentissage d'habiletés visuomotrices.

## Résumé

Trois études ont été réalisées afin de mieux connaître la contribution du striatum et du cervelet dans l'apprentissage d'habiletés visuomotrices. Tel qu'attendu, les résultats de l'Expérience I confirment que le striatum participe à la phase d'automatisation des apprentissages. Les résultats obtenus lors d'une seconde étude démontrent, pour la première fois, une double dissociation fonctionnelle entre le striatum et le cervelet lors de l'apprentissage d'habiletés visuomotrices. D'un côté, le striatum serait impliqué dans l'apprentissage associatif de type perceptivomoteur alors que l'intégrité du cervelet serait particulièrement importante dans les apprentissages nécessitant la mise en séquence de mouvements appris. Bien qu'exploratoires, les résultats de la troisième expérience suggèrent que les patients porteurs d'une dysfonction striatale bilatérale, et non ceux ayant une lésion au cervelet, montrent une difficulté à s'adapter à un changement contextuel lors de l'exécution d'une nouvelle épreuve d'apprentissage visuomoteur. De façon générale, en plus de démontrer que le striatum est impliqué lors de l'automatisation d'habiletés visuomotrices, les données de cette thèse suggèrent que le rôle du striatum et du cervelet diffère quant aux mécanismes privilégiés lors de l'apprentissage d'habiletés visuomotrices.

## AVANT-PROPOS

J'aimerais remercier chaleureusement mon directeur de thèse, le Dr Julien Doyon, qui, au cours des sept dernières années, m'a constamment appuyé dans mes démarches. Je tiens aussi à souligner la générosité et le professionnalisme avec lesquels il m'a enseigné une multitude de connaissances passionnantes tout au long de mes études graduées. J'aimerais également exprimer ma reconnaissance à l'égard des patients et des sujets témoins qui ont participé aux études de la présente thèse de même qu'à toutes les personnes qui m'ont aidé au recrutement de ces derniers. Je tiens à témoigner ma gratitude envers les membres de mon comité de thèse, les docteurs Paul Bédard, François Doré et Yves Lacouture qui, par leurs champs de spécialisation respectifs, m'ont aidé à faire en sorte que cette thèse contribue à l'avancement des connaissances dans le domaine de la mémoire. J'aimerais adresser un remerciement spécial à Joanne Roy pour son aide à plusieurs niveaux de la thèse et, plus particulièrement, pour sa vivacité intellectuelle qui m'a souvent poussée au dépassement. Je ne saurais passer outre la contribution importante du Dr Rhonda Amsel en ce qui a trait à la qualité des analyses statistiques réalisées dans cette thèse. Je tiens aussi à exprimer toute mon affection à mes ami-e-s et collègues de laboratoire de même qu'à tous les membres du «Groupe de Recherche en Réadaptation Physique» du centre François-Charon avec qui j'ai partagé ces années inoubliables. Enfin, je réserve mon plus beau remerciement à mon épouse, Caroline, à mes parents, Mamie et Robert de même qu'à ma belle-famille, qui, malgré les tempêtes, m'ont toujours fourni un amour inconditionnel. Cette thèse est dédiée à la mémoire de ma grand-mère, Simonne qui, un jour à la fois, me procure une présence spirituelle m'aidant à saisir le jour.

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## CHAPITRE I

### CONTRIBUTION DU STRIATUM ET DU CERVELET DANS L'APPRENTISSAGE D'HABILETÉS VISUOMOTRICES

La mémoire dite non-déclarative réfère à un ensemble d'habiletés et d'habitudes reposant sur un apprentissage implicite (Squire, 1992; voir Squire & Knowlton, 1995, pour une recension des écrits). Dans ce système de mémoire, l'information acquise n'est pas accessible volontairement, mais est observée seulement lorsque le sujet s'engage de nouveau dans l'exécution d'une tâche. Parmi l'ensemble hétérogène de processus que regroupe cette forme de mémoire (ex., apprentissage d'habiletés, amorçage, conditionnement classique simple et apprentissage associatif), figure l'apprentissage d'habiletés de type procédural qui consiste en l'acquisition graduelle d'une habileté par la pratique, c'est-à-dire suite à l'exposition répétée à une activité spécifique.

Récemment, de nombreux chercheurs ont tenté d'identifier les substrats neuroanatomiques impliqués dans l'acquisition d'habiletés visuomotrices ou autres. De façon générale, les résultats des travaux effectués dans notre laboratoire et ailleurs, et ce, tant chez l'animal que chez l'humain, suggèrent que le striatum (ex., Doyon, Gaudreau, Laforce, Castonguay, Bédard, Bédard & Bouchard, 1997a; Doyon, Karni, Song, Adams, Maisog, Ungerleider, 1997b; Doyon, Owen, Petrides, Sziklas & Evans, 1996; voir aussi Butters, Salmon & Heindel, 1994; Doyon, 1997; Gabrieli, 1995; Graybiel & Kimura, 1995; Moscovitch, Vriezen & Goshen-Gottstein, 1993; Salmon & Butters, 1995; Schultz, Apicella, Romo & Scarnati, 1995a; Schultz, Romo, Ljungberg, Mirenowicz, Hollerman & Dickinson, 1995b; White, 1997, pour une recension des écrits), le cervelet (ex., Doyon et al., 1997a, 1996; voir aussi Bloedel, 1992; Bloedel & Bracha, 1997; Bloedel, Bracha, Shimansky & Milak, 1996; Doyon, 1997; Leiner, Leiner & Dow, 1993; Thach, 1996, pour une recension des écrits), ainsi que certaines régions corticales associées (Doyon et al., 1997a, 1997b, 1996; Grafton, Hazeltine & Ivry, 1995; Grafton, Woods & Mike, 1994; Hazeltine, Grafton & Ivry, 1997; Jenkins, Brooks, Nixon, Frackowiak & Passingham, 1994; Passingham, Jueptner, Frith, Brooks & Frackowiak, 1995; Rao, Harrington, Haaland, Bobholz, Binder, Hammeke, Frost, Myklebust, Jacobson, Bandettini & Hyde, 1995; Seitz, Canavan, Yaguez, Herzog, Tellmann, Knorr, Huang & Homberg, 1994; voir aussi Doyon, 1997; Moscovitch et al., 1993, pour une recension des écrits), participent à cette forme d'apprentissage.

Malgré le nombre impressionnant de recherches qui indiquent que le striatum et le cervelet participent à l'apprentissage d'habiletés, plusieurs questions demeurent. Par exemple, il existe peu de données qui permettent d'identifier le(s) stade(s) d'apprentissage dans lequel(lesquels) ces structures participent (Doyon et al., 1997a, 1996; Grafton, Mazziotta, Presty, Friston, Frackowiak & Phelps, 1992; Grafton et al., 1994; Jenkins et al., 1994; Seitz et al., 1994; Seitz, Roland, Bohm, Greitz & Stone-Elander, 1990). De plus, très peu de travaux ont tenté d'explorer la nature des mécanismes d'apprentissage qui sont privilégiés par l'une et l'autre de ces structures lors de l'acquisition d'habiletés (Pascual-Leone, Grafman, Clark, Stewart, Massaquoi, Lou & Hallett, 1993). Ainsi, l'objectif principal des études présentées dans cette thèse est donc d'éclaircir la contribution distincte du striatum et du cervelet dans l'apprentissage d'habiletés de types visuomotrices et, plus particulièrement, d'approfondir l'apport spécifique de chaque structure dans cette forme de mémoire.

La première étude fait suite aux travaux de Doyon et collaborateurs (1997a), lesquels ont montré que les patients qui souffrent d'une dysfonction bilatérale du striatum affichent une difficulté dans les phases plus avancées d'une tâche d'apprentissage de séquence visuelle répétée. À l'aide de la technique de double-tâche (voir Chapitre III), elle a pour but d'explorer la possibilité que le striatum soit particulièrement important lors de la phase d'automatisation des apprentissages (Anderson, 1990, 1996). Basées sur les modèles fonctionnels du striatum (Flowers, 1978; Marsden, 1982, 1987; Marsden & Obeso, 1994; Robertson & Flowers, 1990; Schmidt, 1975; Willingham & Koroshetz, 1993), du cervelet (Albus, 1971; Boylls, 1980; Braitenberg, 1961, 1967; Braitenberg & Onesto, 1961; Eccles, 1969; Gilbert, 1975; Gilbert & Thach, 1977; Inhoff, Diener, Rafal & Ivry, 1989; Inhoff & Rafal, 1990; Ito, 1993; Ivry & Keele, 1992; Leiner et al., 1993; Llinas, 1981; Marr, 1969; Paulin, 1993; Pellionisz-Llinas, 1979, 1980; Schmahmann, 1996; Thach, Goodkin & Keating, 1992; voir Bloedel, 1992; Bloedel & Bracha, 1997; Thach, 1996, pour une recension des écrits) et sur ceux qui tentent d'intégrer l'apport de ces deux structures (Akshoomoff, Courchesne, Press & Iragui, 1992; Burton, 1990; Houk & Wise, 1995; Ivry, 1996; Jueptner, Frith, Brooks, Frackowiak & Passingham, 1997; Pascual-Leone et al., 1993; Wise & Houk, 1994), les deuxième et troisième expériences

visent plus spécialement à étudier la contribution distincte du striatum et du cervelet dans l'apprentissage visuomoteur. Ainsi, la deuxième étude s'intéresse à la contribution de ces structures dans l'apprentissage associatif de type perceptivomoteur de même que dans la mise en séquence de mouvements appris, et ce, à l'aide d'une version aléatoire de la tâche de séquence visuelle répétée et d'une nouvelle version de la tâche de tracé-miroir (voir Chapitre IV). Finalement, toujours en utilisant la tâche de tracé-miroir, la troisième expérience porte sur la participation du cervelet et, en particulier, du striatum, dans l'adaptation à un changement contextuel lors de l'exécution d'une tâche d'apprentissage d'habiletés visuomotrices (voir Chapitre V).

## CHAPITRE II

### RÔLE DU STRIATUM ET DU CERVELET DANS L'APPRENTISSAGE D'HABILETÉS

## Théories contemporaines de la mémoire

Une pléthore d'études dans le domaine des neurosciences cognitives ont permis jusqu'à présent d'accumuler de nombreuses données concernant les processus, ainsi que les structures, impliqués dans la mémoire. De façon générale, ces travaux se regroupent sous deux conceptualisations distinctes (voir Nadel, 1992, pour une discussion plus détaillée). La première propose que cette fonction fasse appel à un système unitaire opérant selon certains processus précis. Par contre, la seconde pose l'hypothèse selon laquelle la mémoire est formée de systèmes multiples, dont les composantes possèdent à leur tour des règles d'opérations indépendantes. Malgré le fait que quelques auteurs aient récemment questionné la pertinence scientifique d'une telle division théorique (Pitarque, Algarabel & Meseguer, 1992; Roediger & McDermott, 1993; Schacter, 1995; Scherry & Schacter, 1987), un nombre grandissant de recherches provenant de divers domaines corrobore l'approche selon laquelle il existe plusieurs systèmes de mémoire distincts (ex., Nadel, 1992; Squire & Knowlton, 1995, pour une recension des écrits).

Les chercheurs qui adoptent la notion de système de mémoire unitaire (Anderson, 1983a, 1990; Hintzman, 1984; Humphreys, Bain & Pike, 1989; Jacoby, 1983a, 1983b; Roediger, 1984; Roediger & Blaxton, 1987a, 1987b; Roediger & McDermott, 1993; Roediger, Rajaram & Srinivas, 1991; Toth, Reingold & Jacoby, 1994) se sont particulièrement intéressés aux règles de fonctionnement entre les différents processus d'encodage, de storage et de récupération de l'information. Ainsi, plusieurs auteurs ont fourni des résultats qui sont en accord avec une telle conception de la mémoire en étudiant, par exemple, l'efficacité de l'organisation du matériel à mémoriser dans une tâche de rétention (Bower, Clark, Lesgold & Winzenz, 1969), l'effet de l'autorépétition sur le maintien de la trace mnésique (Craik & Watkins, 1973), l'importance du contexte dans la mémorisation (Einstein & Hunt, 1980) ou encore les niveaux de traitement impliqués dans l'encodage en mémoire (Craik & Lockhart, 1972).

Il est intéressant de souligner que, dans le cas de la mémoire de travail (Baddeley, 1986, 1992, 1993, 1994), certaines découvertes majeures ont nécessité la transformation d'un modèle unitaire en un modèle à composantes multiples. Tel que le mentionne

Baddeley (1994), le modèle actuel de la mémoire de travail a évolué à partir du «modal model» des années soixante selon lequel il existait un seul réservoir à court terme qui agissait en tant que système de mémoire de travail. Le «modal model» le plus influent, celui d'Atkinson et Shiffrin (1968), proposait alors l'existence d'un réservoir unitaire à capacité limitée, qui était responsable d'un large éventail de phénomènes mnésiques essentiels tels que l'empan et l'effet de récence dans le rappel libre. Cependant, ce modèle expliquait difficilement comment les patients qui présentaient des troubles de mémoire à court terme pouvaient démontrer un apprentissage normal en mémoire à long terme. Aussi, à l'aide d'une série d'expériences basées sur la technique de double-tâche, Baddeley et Hitch (1974) ont montré que même si l'on sature les capacités en mémoire de travail à l'aide d'une série de chiffres, par exemple, les sujets obtiennent tout de même des résultats dans la moyenne lorsqu'ils sont interrogés sur une seconde tâche verbale effectuée simultanément, indiquant ainsi la présence d'une capacité cognitive jusqu'ici sous-estimée. Compte tenu de ces résultats, Baddeley et Hitch (1974) ont proposé d'abandonner l'idée d'une conception unitaire de la mémoire de travail au profit d'un modèle tripartite (Baddeley, 1986). Tel qu'on le connaît aujourd'hui, ce modèle se compose de trois modules: 1) la boucle articulatoire, qui représente la mémoire active de l'information sous une forme propre au langage, 2) la tablette visuospatiale, qui permet de maintenir active une image mentale de stimuli visuels ou auditifs et 3) l'unité de gestion centrale, qui agit en tant que module de coordination entre les divers processus de la mémoire à court terme.

Malgré l'intérêt que représente la conceptualisation unitaire de la mémoire, il existe actuellement un nombre croissant de recherches tant chez l'animal que chez l'humain qui corroborent une seconde option selon laquelle ce processus se compose de plusieurs systèmes distincts (voir Nadel, 1992; Schacter, 1987; Squire & Knowlton, 1995, pour une recension exhaustive). Les résultats qui corroborent cette position proviennent d'études effectuées dans plusieurs domaines différents tels que l'enregistrement électrophysiologique cellulaire (Paller, 1990), les travaux comportementaux effectués chez les rongeurs et les primates non-humains (McDonald & White, 1993; Packard, Hirsh & White, 1989; Petri & Mishkin, 1994; Squire, 1992; voir White, 1997, pour une recension

des écrits), la psychologie cognitive chez les sujets sains (Graf & Schacter, 1987; Tulving, 1995) ou encore la neuropsychologie clinique chez les populations présentant des troubles de mémoire tels que l'amnésie [AMN] (Cohen & Squire, 1980; Heindel, Butters & Salmon, 1988), la maladie d'Alzheimer [MA] (Bondi & Kaszniak, 1991; Heindel, Salmon, Shults, Walicke & Butters, 1989), la maladie d'Huntington [MH] (Bylsma, Brandt & Strauss, 1990; Heindel et al., 1988; Knopman & Nissen, 1991; Willingham & Koroshetz, 1993), et la maladie de Parkinson [MP] (Doyon et al., 1997a; Ferraro, Balota & Connor, 1993; Frith, Bloxham & Carpenter, 1986; Harrington, York Haaland, Yeo & Marder, 1990; Pascual-Leone et al., 1993; Saint-Cyr, Taylor & Lang, 1988). D'autres recherches qui vont dans le même sens que cette notion ont été réalisées dans le cadre d'études pharmacologiques (Danion, Zimmerman, Willard-Schroeder, Grange & Singer, 1989; Nissen, Knopman & Schacter, 1987), d'imagerie cérébrale à l'aide de techniques modernes telles que la tomographie par émission de positrons (TEP) (Doyon et al., 1996; Grafton et al., 1995; Rauch, Savage, Brown, Curran, Alpert, Kendrick, Fischman & Kosslyn, 1995; Squire, Ojemann, Miezin, Petersen, Videen & Raichle, 1992) et l'imagerie par résonance magnétique fonctionnelle (IRMf) (Doyon et al., 1997b; Rauch, Whalen, Savage, Curran, Kendrick, Brown, Bush, Breiter & Rosen, 1997).

De façon générale, les recherches recensées ci-dessus corroborent une classification opposant tantôt la mémoire déclarative à la mémoire non-déclarative (Squire, 1992; Squire & Knowlton, 1995), les représentations individuelles aux représentations relationnelles ou la mémoire procédurale à la mémoire déclarative (Cohen, Eichenbaum, Deacedo & Corkin, 1985; Cohen & Squire, 1980), la formation d'habitudes à la mémoire cognitive (Mishkin, Malamut & Bachevalier, 1984), la mémoire sémantique (faits) vs épisodique (événements) (Tulving, 1972, 1983), la mémoire de référence à la mémoire de travail (Honig, 1978; Olton, Becker & Handelmann, 1979) ou encore la mémoire sémantique à la mémoire cognitive (Warrington & Weiskrantz, 1982). De plus, certains auteurs distinguent à leur tour chaque composante en plusieurs sous-systèmes (voir Squire, 1992; Squire & Knowlton, 1995). Cependant, tout comme dans le cas des taxonomies générales de la mémoire présentées plus haut, il existe selon les auteurs des différences majeures au niveau des sous-divisions. Dans le domaine non-déclaratif, par exemple, la

classification récente de Shacter et Tulving (1994) suggère que la mémoire procédurale comprend des mécanismes tels que les habiletés motrices, les habiletés cognitives, le conditionnement simple et l'apprentissage associatif simple. Ainsi, contrairement à Squire et Knowlton (1995), pour qui l'amorçage est une subdivision du système de mémoire non-déclaratif, Schacter et Tulving (1994) conçoivent l'effet d'amorçage perceptif ou «priming» comme un système spécifique de mémoire et ne le considèrent donc pas comme une subdivision de la mémoire non-déclarative. Toutefois, quoique plusieurs taxonomies aient été présentées pour rendre compte des multiples types de mémoire qui ont été identifiés jusqu'à présent, celle qui fait davantage l'unanimité parmi les chercheurs (voir Nadel, 1992), et qui sera utilisée dans cette thèse, oppose la mémoire déclarative à la mémoire non-déclarative (Squire, 1992; Squire & Knowlton, 1995).

### Taxonomie révisée de la mémoire

Squire (1992), et plus récemment, Squire et Knowlton (1995), ont proposé l'existence de deux systèmes de mémoire fonctionnellement distincts: la mémoire déclarative et la mémoire non-déclarative (voir Figure 1). Selon cette classification, la mémoire déclarative permet d'encoder et surtout de récupérer à l'aide du rappel ou de la reconnaissance diverses informations sous forme de mots, d'images ou d'événements. La récupération se fait de manière consciente ou explicite. La mémoire déclarative se divise à son tour en deux sous-systèmes. D'abord, la mémoire des faits ou sémantique, qui réfère à des connaissances plus générales telles que la grammaire, le vocabulaire, la signification des gestes et des événements, les règles sociales et la signification des objets. Puis, la mémoire des événements ou épisodique, qui a pour rôle d'emmagasiner des informations sur les expériences personnelles et les relations qui existent entre ces événements; c'est en quelque sorte une mémoire «autobiographique» (Fortin & Rousseau, 1989).

De son côté, la mémoire non-déclarative réfère à un ensemble d'habiletés et d'habitudes reposant sur un apprentissage implicite. Dans ce système, l'information acquise n'est pas accessible volontairement, mais est observée seulement lorsque le sujet

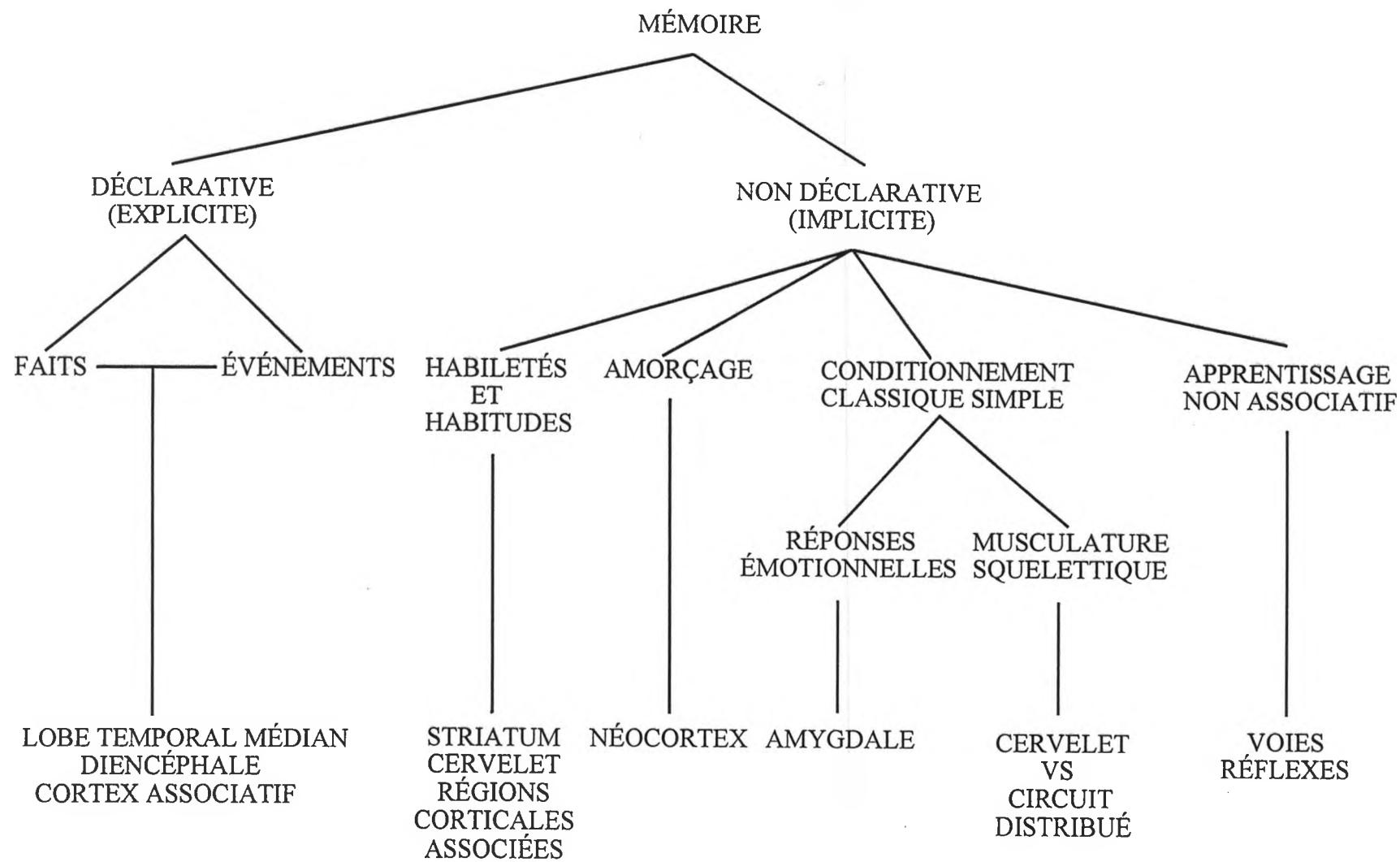


Figure 1. Taxonomie de la mémoire adaptée de Squire et Knowlton (1995).

s'engage de nouveau dans l'exécution d'une tâche (Squire, 1992). Le système de mémoire non-déclarative regroupe un ensemble hétérogène de processus mnésiques tels que l'apprentissage d'habiletés dites procédurales, l'amorçage («priming»), le conditionnement classique et l'apprentissage non-associatif. Parmi ces divers processus, il est important de préciser que les travaux rapportés dans cette thèse se concentrent sur l'apprentissage non-déclaratif de type procédural, qui consiste en l'acquisition graduelle d'une habileté par la pratique, c'est-à-dire suite à l'exposition répétée à une activité spécifique (Cohen & Squire, 1980; Heindel et al., 1989; Martone, Butters, Payne, Becker & Sax, 1984; Saint-Cyr et al., 1988). En d'autres termes, ce type d'apprentissage réfère à la mémoire du «comment faire les choses» (Anderson, 1983a). Des études récentes effectuées chez le singe et chez l'humain (Karni, 1996; Karni, Meyer, Rey-Hipolito, Jezzard, Adams, Turner & Ungerleider, *in press*) suggèrent que cette forme d'apprentissage se déroule selon deux phases, c'est-à-dire une phase rapide qui survient tôt dans l'apprentissage et dans laquelle il est possible d'observer une amélioration importante dans la performance des sujets (et ce même à l'intérieur d'un seul bloc d'essais), puis, une phase plus lente qui apparaît plus tard dans l'apprentissage, et dans laquelle les améliorations dans la performance s'échelonnent sur plusieurs sessions, voire même plusieurs semaines. Enfin, l'habileté acquise peut être de nature cognitive (ex., Laforce, Gaudreau, Castonguay, Bédard & Doyon, 1993a; Saint-Cyr et al., 1988), visuoperceptive (ex., Martone et al., 1984) ou visuomotrice (ex., Doyon et al., 1997a; Heindel et al., 1989).

Le rôle de la plupart des structures corticales et sous-corticales impliquées dans ces systèmes de mémoire a été inférée à l'aide de corrélations anatomo-fonctionnelles, et ce, tant chez les primates non-humains que chez les humains. De façon générale, les études indiquent que les structures médiales du lobe temporal (amygdale, hippocampe, cortex rhinal [entorhinal et périrhinal] et gyrus parahippocampique), les noyaux dorso-médians et ventral antérieur du thalamus, le prosencéphale basal et les régions ventromédiales du cortex préfrontal constituent les bases neuroanatomiques du système de mémoire déclarative (Mishkin, 1982; Petri & Mishkin, 1994; Squire, 1987, 1992;

Suzuki, 1996). D'autre part, il semble que plusieurs systèmes anatomiques soient impliqués dans la mémoire non-déclarative.

En ce qui concerne l'apprentissage non-déclaratif de type procédural (aussi appelé apprentissage d'habiletés), plusieurs données provenant de divers domaines tels que la neurophysiologie (Joseph & Barone, 1987; Miyashita, Hikosaka, Lu & Miyachi, 1995; Mushiake, Inase & Tanji, 1990, 1991), les études lésionnelles (Miyashita, Sakai & Hikosaka, 1996) et neuroanatomiques chez les primates non-humains (Alexander & Crutcher, 1990; Middleton & Strick, 1994; Schmahmann, 1996) ainsi que les études d'imagerie cérébrale chez les sujets contrôles (Doyon et al., 1997a, 1996; Grafton et al., 1995, 1994; Hazeltine et al., 1997; Jenkins et al., 1994; Karni, Meyer, Jezzard, Adams, Turner & Ungerleider, 1995; Passingham et al., 1995; Rao et al., 1995; Seitz et al., 1994; voir Moscovitch et al., 1993; Wessel, Hermsdorfer, Deger & Herzog, 1995, pour une recension des écrits) suggèrent que les régions corticales motrices des lobes frontaux participent à ce type de mémoire, particulièrement dans la modalité motrice ou visuomotrice. Toutefois, malgré plusieurs recherches sur le sujet, la nature de la contribution frontale dans ce processus demeure encore obscure (Doyon et al., 1996; Passingham et al., 1995). Par contre, il existe un plus grand consensus quant à la participation du striatum, structure télencéphalique faisant partie des ganglions de la base (voir Figure 2) ainsi que celle du cervelet, situé à la face postérieure du tronc cérébral (voir Figure 3), dans l'apprentissage d'habiletés (Doyon et al., 1997a, 1996; Grafton et al., 1995, 1992, 1994; Graybiel, 1995; Graybiel & Kimura, 1995; Hazeltine et al., 1997; Jenkins et al., 1994; Leiner et al., 1993; Passingham et al., 1995; Rao et al., 1995; Seitz et al., 1994; voir aussi Bloedel, 1992; Butters et al., 1994; Doyon, 1997; Moscovitch et al., 1993; Salmon & Butters, 1995; Thach, 1996; White, 1997, pour une recension des écrits). Pour cette raison, le présent chapitre traite principalement du rôle de ces deux dernières structures dans l'acquisition d'habiletés.

Aussi, avant même de débuter l'exploration du rôle du striatum et du cervelet dans l'apprentissage d'habiletés visuomotrices, il est important de souligner que, jusqu'à maintenant, les recherches suggèrent que ces deux structures fassent partie de deux circuits neuroanatomiques distincts (voir Figure 4) (Asunama, Thach & Jones, 1983;

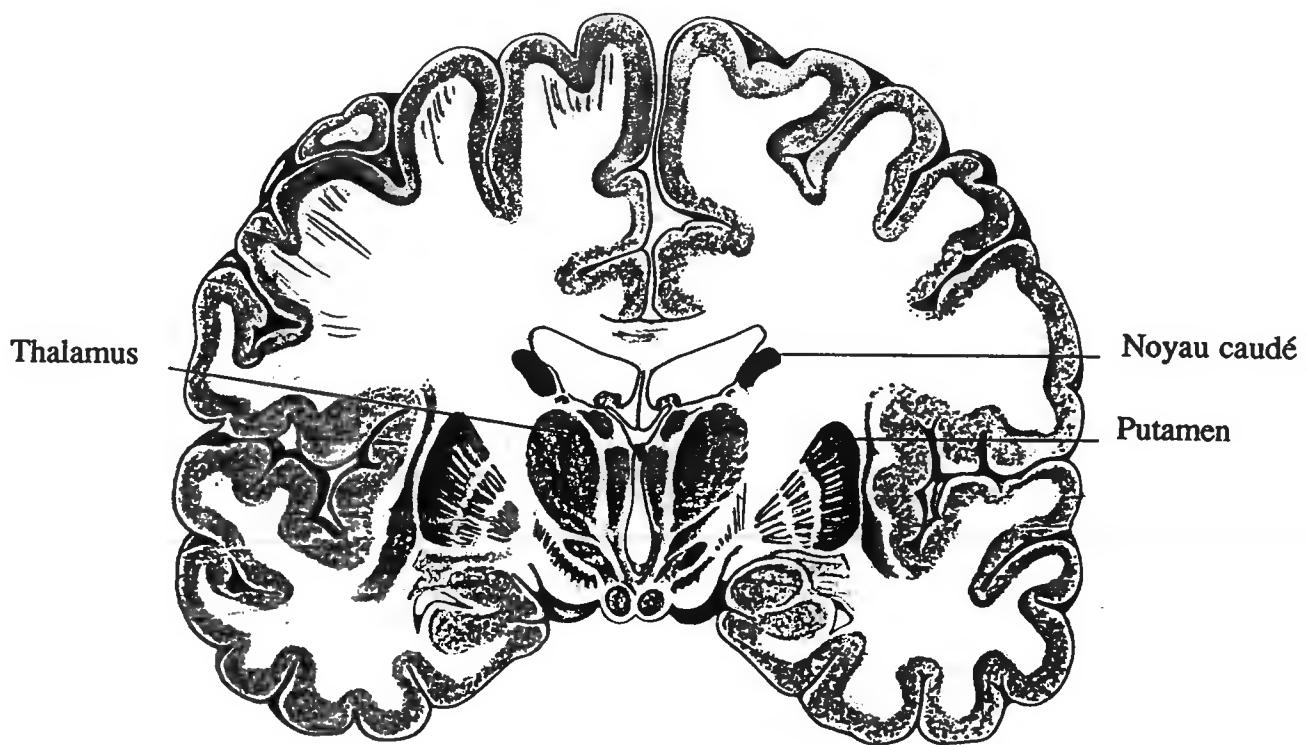


Figure 2. Cette coupe coronale d'un cerveau humain présente les ganglions de la base ainsi que certaines structures environnantes. Il est possible de distinguer le striatum qui se compose du noyau caudé et du putamen. (Adaptée de Kandel, Schwartz & Jessel, 1991).

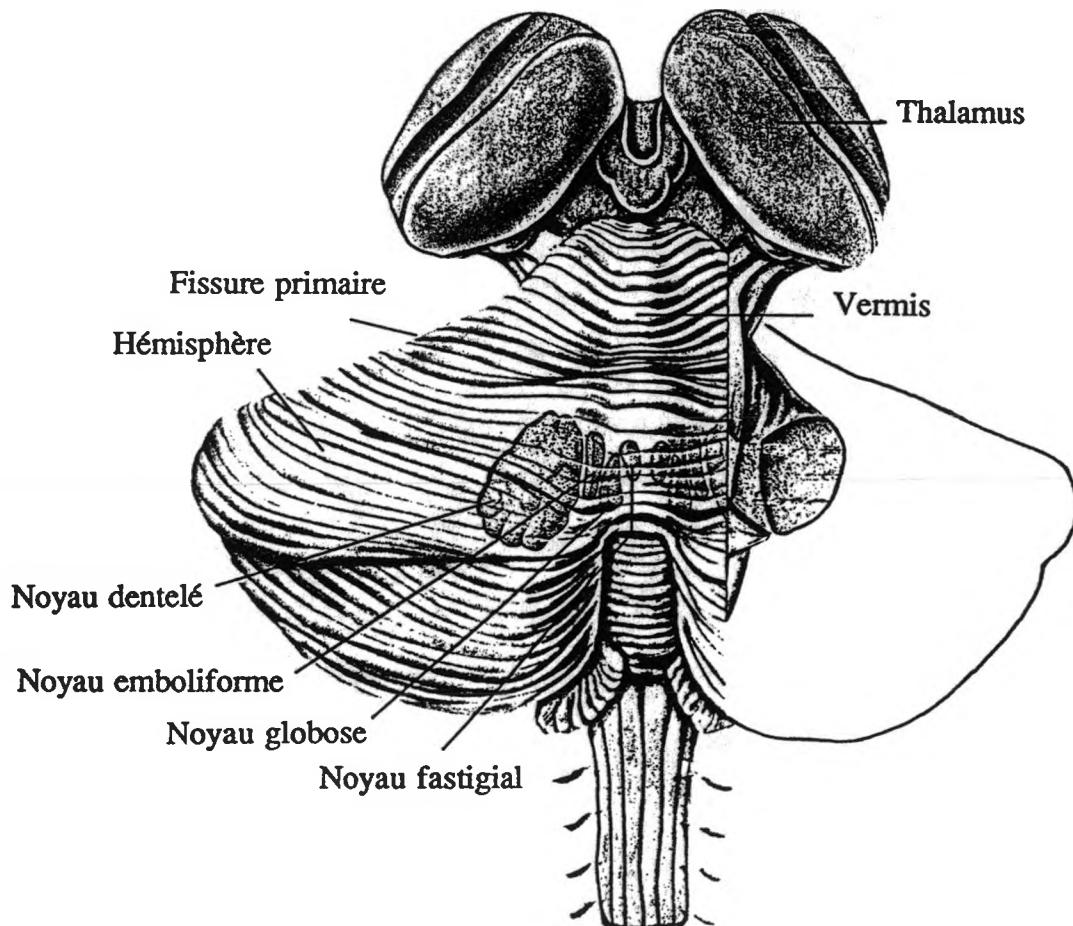


Figure 3. Vue dorsale du cervelet présentant, à la fois, les hémisphères cérébelleux et les noyaux profonds du cervelet. Sur cette figure, les hémisphères cérébraux de même qu'une partie de l'hémisphère cérébelleux droit ont été réséqués afin d'illustrer les structures sous-jacentes. (Adaptée de Kandel et al., 1991).

# Néo-Cortex Cérébral

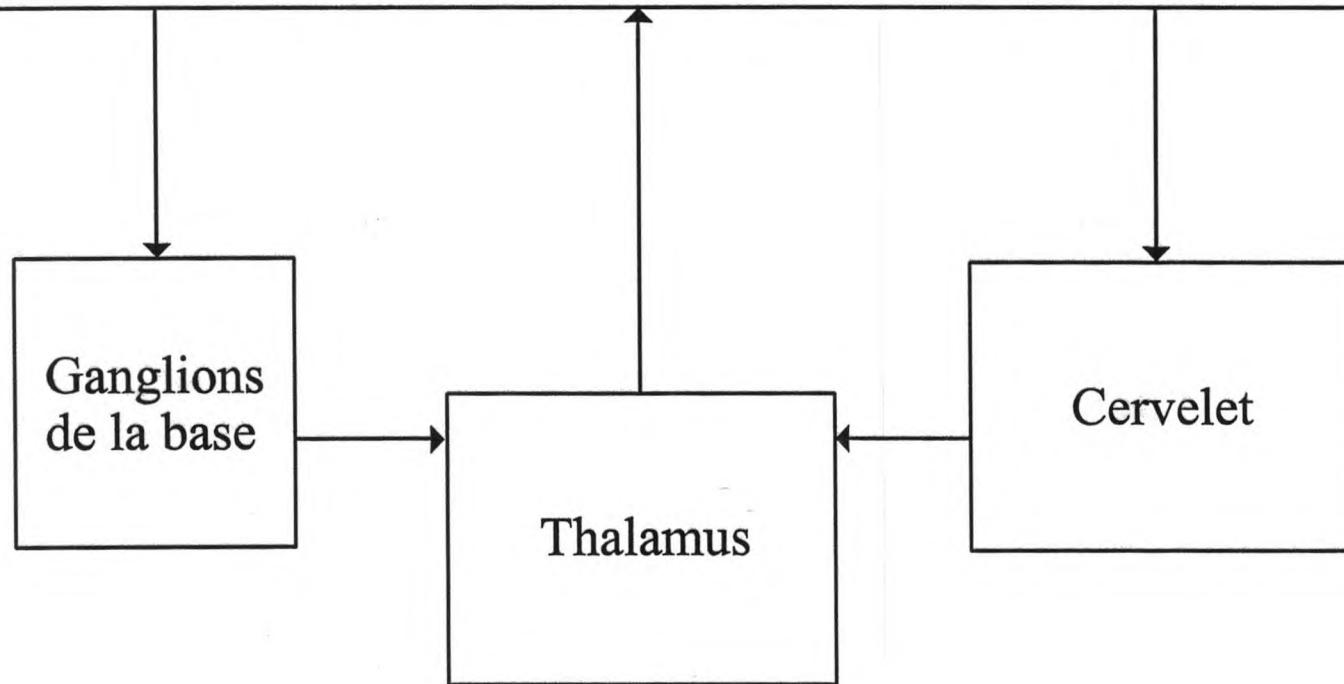


Figure 4. Schéma anatomique simplifié des circuits cortico-striatal et cortico-cérébelleux. Tout comme le striatum, le cervelet est un site d'efférences en provenance de diverses régions du cortex cérébral. (Adaptée de Leiner, Leiner & Dow, 1986).

Kemp & Powell, 1971; Leiner, Leiner & Dow, 1986; Middleton & Strick, 1994; Percheron & Filion, 1991; Percheron, François, Yelnik, Fénelon & Talbi, 1993; Sakai, Inase & Tanji, 1996; Yamamoto, Yoshida, Kishimoto & Oka, 1992). Dans le cas du circuit cortico-striatal, par exemple, les recherches d'Alexander et Crutcher (1990) ont permis de montrer que le striatum contient cinq circuits (moteur, oculomoteur, limbique, dorsolatéral préfrontal et orbitofrontal latéral) qui se distinguent, d'une part, par les afférences cortico-striatales et, d'autre part, par les sites de projection au niveau des lobes frontaux (voir Wichmann & DeLong, 1996, pour une revue critique). De la même façon, une recension récente effectuée par Schmahmann (1996) a démontré que le cervelet fait partie d'un système en boucle qui reçoit de plusieurs régions corticales associatives et paralimbiques, et qui projettent à plusieurs de ces mêmes régions. Considérant l'importance des informations fournies par l'ensemble de ces travaux, l'auteur tient donc à préciser explicitement que l'utilisation des termes «striatum» et «cervelet» dans cette thèse est effectuée tout en prenant en considération que ces structures font partie de circuits neuroanatomiques distincts impliquant plusieurs autres structures corticales et sous-corticales. La prochaine section de ce chapitre présente l'ensemble des études portant strictement sur le rôle du striatum dans l'apprentissage. Une section spécialement réservée aux études sur la contribution du cervelet est ensuite proposée. La troisième section traite quant à elle des recherches qui ont comparé directement le rôle du striatum et du cervelet dans l'apprentissage implicite, et ce, dans le cadre d'une même étude. Enfin, basée sur les connaissances présentées dans ces trois premières sections, la dernière rassemble les données suggérant la possibilité d'une contribution distincte du striatum et du cervelet dans l'apprentissage d'habiletés.

Considérant le plan de travail proposé ci-dessus, il est important de préciser que les travaux présentés dans la troisième section, c'est-à-dire celle qui recense les recherches qui tentent d'explorer l'apport de ces deux structures lors de l'acquisition d'habiletés, auraient pu tout aussi bien être cités, respectivement, dans les première et deuxième sections de ce chapitre. En effet, plusieurs études décrites dans ces sections contiennent des données qui corroborent le rôle respectif de chaque structure dans l'apprentissage d'habiletés. Cependant, afin de faire ressortir une nouvelle tendance qui existe dans le

domaine quant à l'étude de la véritable nature de la contribution de ces deux structures dans l'apprentissage d'habiletés implicites, l'auteur a jugé pertinent de résérer une section spéciale aux études qui ont pour but de comparer le rôle du striatum et du cervelet dans ce type de mémoire. Ainsi, un tel plan facilite le transition logique avec la dernière section du chapitre, laquelle soulève la possibilité d'une dissociation entre le rôle de ces deux structures au niveau de l'apprentissage d'habiletés visuomotrices.

Enfin, bien que les chercheurs oeuvrant dans ce domaine aient étudié la contribution de ces structures à l'aide de divers types de tâches (cognitives, visuoperceptives, ou visuomotrices), cette thèse traite davantage de l'acquisition d'habiletés visuomotrices. En ce sens, seules les études portant sur cette dernière forme d'apprentissage sont recensées. De plus, étant donné que les études expérimentales rapportées dans ce relevé de littérature ont été effectuées, en grande partie, à l'aide de versions de la tâche séquence visuelle répétée (Nissen & Bullemer, 1987), une attention particulière est portée aux résultats qui ont été obtenus à l'aide de cette épreuve.

### Contribution du striatum dans l'apprentissage d'habiletés motrices

Tel que mentionné plus haut, plusieurs données récentes corroborent la participation du striatum dans l'apprentissage implicite d'habiletés. Cette affirmation est appuyée par des résultats obtenus dans divers domaines de recherche tant chez l'animal (Aosaki, Graybiel & Kimura, 1994a; Aosaki, Tsubokawa, Ishida, Watanabe, Graybiel & Kimura, 1994b; Apicella, Scarnati, Ljungberg & Schultz, 1992; Brotchie, Iansek & Horne, 1991a, 1991b; Graybiel, Aosaki, Flaherty & Kimura, 1994; McDonald & White, 1993; Petri & Mishkin, 1994; Phillips, Malamut, Bachevalier & Mishkin, 1988; Reading, Dunnett & Robbins, 1991; Saint-Cyr, Taylor, Trépanier & Lang, 1992; Wang, Aigner & Mishkin, 1990; voir Graybiel & Kimura, 1995; Schultz et al., 1995a, 1995b; White, 1997, pour une recension des écrits) que chez l'humain (Bylsma et al., 1990; Corkin, Growdon & Koroshetz, 1992; Ferraro et al., 1993; Grafton et al., 1995, 1992; Harrington et al., 1990; Hazeltine et al., 1997; Heindel et al., 1988, 1989; Knopman & Nissen, 1991; Metz, Singh, Gabrieli, Willingham, Dooley, Jiang, Chen & Cooper, 1993; Rauch et al., 1995,

1997; Roy, Saint-Cyr, Taylor & Lang, 1993; Saint-Cyr & Taylor, 1992; Saint-Cyr et al., 1988; Seitz & Roland, 1992; Willingham & Koroshetz, 1993; voir aussi Butters et al., 1994; Doyon, 1997; Gabrieli, 1995; Moscovitch et al., 1993; Salmon & Butters, 1995, pour une recension des écrits).

Par exemple, au niveau neurophysiologique, Brotchie et al. (1991a, 1991b) ont observé une population de cellules du pallidum qui affichent une double activation durant les phases d'une séquence de mouvements lorsqu'ils sont bien appris. De façon générale, les résultats montrent que la première activation survient après le premier geste de la séquence tandis que la seconde précède le mouvement subséquent. Parmi les caractéristiques de cette activité phasique des neurones, il semble également que ces derniers participent à la remise à zéro de l'activité neuronale du système. Basés sur ces résultats, les auteurs ont conclu que ces doubles potentiels d'action reflètent la présence d'indices internes générés par le striatum dans le but d'exécuter correctement un mouvement en séquence. À l'aide d'une tâche de conditionnement classique, Graybiel et Kimura (1995) ont récemment obtenu des données physiologiques chez le primate en action qui suggèrent aussi que le complexe striatal affiche une habileté à développer des programmes moteurs. Les auteurs mentionnent qu'une des caractéristiques particulières du fonctionnement de ce complexe est la plasticité synaptique du mécanisme d'apprentissage. En effet, il semble qu'une population de neurones appelés les «Tonically Active Neurons» (TAN's), participerait non seulement à l'élaboration de programmes moteurs, mais permettrait également de les modifier en fonction d'une nouveauté contextuelle.

D'autres données appuyant le rôle du striatum dans l'apprentissage visuomoteur nous viennent des études lésionnelles effectuées chez les primates non humains. Dans ces travaux, il a été démontré que le cortex inférot temporal (IT) projette à la queue du noyau caudé, à la portion ventrale du putamen et à la portion rostrale du striatum (incluant la tête du noyau caudé), et qu'une lésion affectant soit le cortex IT ou les structures des noyaux de la base qui reçoivent ces afférences influence l'apprentissage d'une habileté de type visuelle (Kemp & Powell, 1970; Saint-Cyr et al., 1988; Van Hoesen, Yeterian & Lavizzo-Mourey, 1981). Buchwald, Rakic, Wyers, Hull et Heuser (1962) ainsi que Herz

et Peeke (1971), par exemple, ont montré qu'une forte stimulation du striatum ou de la queue du noyau caudé affecte l'acquisition incrémentielle d'une tâche de discrimination visuelle. D'autres chercheurs utilisant la technique lésionnelle ont aussi obtenu des résultats suggérant qu'une lésion bilatérale du cortex IT (Mishkin, 1954), de la queue du noyau caudé (Divac, Rosvold & Szwarcbart, 1967) ou de la portion ventrale du putamen et de la matière blanche adjacente (Buerger, Gross & Rocha-Miranda, 1974) produit un déficit d'apprentissage à cette même tâche. Finalement, Phillips et al. (1988) ont montré qu'une lésion du cortex IT ou de ses sites de projections au niveau du striatum (Wang et al., 1990) provoque un problème d'apprentissage à une tâche de discrimination visuelle concurrente, comportant un intervalle de 24 heures entre les essais et mesurant la formation d'habitudes (c'est-à-dire, la formation d'un lien automatique [non-conscient] entre un stimulus et une réponse).

Pour leur part, les résultats de plusieurs travaux effectués chez le rat ont montré qu'une lésion de la région dorsolatérale du striatum produit un déficit lors de l'acquisition incrémentielle d'une association stimulus-réponse (S-R) à une version du test du labyrinthe radial («win-stay») (Packard et al., 1989; Packard & White, 1990; voir White, 1997, pour une recension des écrits)<sup>1</sup>. Plus récemment, McDonald et White (1993) ont fourni des éclaircissements concernant le rôle du striatum dans l'apprentissage en utilisant, ici encore, la tâche d'apprentissage du labyrinthe radial chez le rat. Leurs résultats indiquent que le circuit neuronal, dont le striatum fait partie, pourrait être considéré comme un système d'apprentissage associatif simple qui permettrait aux stimuli neutres de produire différentes réponses suite au renforcement répété d'une association entre un stimulus et une réponse. Toujours selon ces auteurs (voir White, 1997, pour une recension des écrits), la portion dorsale du striatum serait essentielle pour l'acquisition d'une telle association.

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<sup>1</sup> Cependant, il est à noter que cette dernière implique la présence d'une récompense sous forme de nourriture et que l'animal n'est pas entraîné à réaliser de nouveaux apprentissages moteurs. Ainsi, ce déficit peut aussi être interprété comme un trouble au niveau de l'apprentissage d'une association entre un stimulus et une récompense (Petrides, 1987, 1996; Sziklas & Doyon, 1997). Malgré cela, dans le but de respecter l'interprétation originale de ces auteurs, l'appellation S-R sera utilisée tout au long de cette thèse pour décrire la nature du déficit chez le rat.



Bien que certaines réticences aient été émises quant à la validité de l'hypothèse selon laquelle le striatum joue un rôle important dans l'apprentissage incrémentiel (Gaffan, 1996; Wise, 1996), plusieurs démonstrations convaincantes de la contribution du striatum dans l'acquisition d'habiletés ont été effectuées à l'aide de diverses populations cliniques présentant une dysfonction striatale telle que dans la MH et la MP (Bylsma et al., 1990; Corkin et al., 1992; Ferraro et al., 1993; Harrington et al., 1990; Heindel et al., 1988, 1989; Knopman, 1991; Knopman & Nissen, 1991; Nissen & Bullemer, 1987; Roy et al., 1993; Saint-Cyr & Taylor, 1992; Saint-Cyr et al., 1988; Willingham & Koroshetz, 1993; voir Butters et al., 1994; Salmon & Butters, 1995, pour une recension des écrits). Ces populations de patients représentent un intérêt particulier pour les chercheurs pour une raison bien précise. Dans la MH, par exemple, on remarque une atrophie des noyaux gris centraux, et en particulier du noyau caudé (Brandt, 1991; Willingham & Koroshetz, 1993). Pour sa part, la MP est une maladie neurodégénérative qui affecte les cellules dopaminergiques de la substance noire *pars compacta* et qui altère le taux d'efférences dopaminergiques au striatum (ex., Marsden, 1982). Cette dernière se caractérise notamment par quatre symptômes classiques: les tremblements au repos, la rigidité, la bradykinésie (lenteur à initier et à exécuter le mouvement) et l'instabilité posturale. Elle est également la plus fréquente des manifestations causées par une atteinte des noyaux gris centraux de l'encéphale (Spence & Mason, 1983), et plusieurs auteurs confirment d'ailleurs que les patients souffrant de la MP représentent la population clinique la plus adéquate pour étudier l'effet d'une dysfonction striatale chez l'humain (Harrington et al., 1990; Marsden, 1982; Saint-Cyr et al., 1988).

Ainsi, afin d'étudier le rôle du striatum dans l'apprentissage implicite, Heindel et ses collègues (1988) ont évalué la performance de sujets témoins, de patients ayant la MH, la MA, et AMN à un test de reconnaissance verbale et à une tâche d'apprentissage visuomoteur soit la poursuite rotative. Dans cette épreuve d'apprentissage, les sujets devaient maintenir le contact entre un stylo de métal et une cible circulaire située sur un disque en rotation. Les données ont montré que les patients des groupes MA, AMN, ainsi que les sujets contrôles, ont augmenté significativement leur temps de contact avec la cible au cours des six blocs d'essais alors que les patients ayant la MH n'ont montré que

peu ou pas d'apprentissage. De plus, les patients des groupes MA et MH ont obtenu sensiblement la même performance à l'épreuve de reconnaissance alors que le groupe ayant la MH a réussi significativement mieux le test de rappel verbal. Dans l'ensemble, ces résultats suggèrent qu'une dysfonction striatale peut amener une double dissociation entre l'apprentissage d'habiletés visuomotrices et la mémoire déclarative. Une année plus tard, Heindel et son groupe (1989) ont tenté de reprendre la même expérience à l'aide de groupes ayant la MH et la MA, en y ajoutant également un groupe de patients parkinsoniens déments et non-déments. Tout comme dans la première étude, les résultats obtenus par les patients des groupes MH et MA suggèrent une double dissociation entre l'apprentissage d'habiletés visuomotrices et la mémoire déclarative. Par contre, seules les données obtenues à l'aide des patients du groupe MP déments indiquent un déficit aux deux tâches d'apprentissage d'habiletés alors que la performance des patients parkinsoniens non-déments ne présente aucun déficit significatif à ces tâches. En plus de fournir des résultats fort pertinents, cette étude suggère que la sévérité de la maladie influence considérablement le patron des résultats obtenus à une épreuve mesurant l'acquisition d'habiletés.

Toujours dans le domaine des études cliniques, Harrington et ses collègues, en 1990, ont évalué un groupe de sujets normaux et un groupe de patients ayant la MP à l'aide d'un test de mémoire déclarative (le sous-test des mots pairés de l'échelle de mémoire de Wechsler [Wechsler, 1945]) et de deux tests évaluant la mémoire procédurale, l'un visuoperceptif (la lecture-miroir; Cohen & Squire, 1980), et l'autre visuomoteur (la poursuite rotative; Heindel et al., 1989). Comparativement aux sujets normaux, les patients du groupe MP ne montrent de déficit ni au test déclaratif ni à la lecture-miroir alors qu'ils réussissent significativement moins bien à la tâche de poursuite rotative. Des analyses subséquentes indiquent que seuls les patients montrant des symptômes plus sévères éprouvent des difficultés à l'épreuve visuomotrice, et que ce déficit n'est pas dû à un trouble moteur ou cognitif concomitant. À la lumière de ces résultats, les auteurs ont conclu que les noyaux gris centraux jouent un rôle majeur dans l'apprentissage d'une tâche procédurale visuomotrice, mais pas nécessairement dans l'acquisition d'une épreuve visuoperceptive. Il est à noter que deux autres études, celle

de Bondi et Kaszniak (1991) effectuée à l'aide de patients atteints de la MP et celle de Singh, Gabrieli, Willingham, Kirschner, Stebbins et Goetz (1992) chez les patients porteurs de la MH, n'ont pas démontré un tel déficit à l'aide de cette même tâche. Ces divergences de résultats peuvent cependant s'expliquer par plusieurs facteurs qui seront abordés plus loin dans le texte.

A nouveau dans le cadre d'études effectuées à l'aide de populations cliniques présentant une dysfonction striatale, Frith et ses collègues (1986) ont comparé la performance de patients parkinsoniens non-déments à celle d'un groupe contrôle dans l'exécution de tâches d'apprentissage manuel dans lesquelles les sujets devaient apprendre à poursuivre une cible en déplaçant un curseur sur un écran à l'aide d'une manette mobile. Chaque sujet fut testé lors de deux sessions de trois minutes séparées par une pause de 10 minutes. Afin de bien mesurer l'amélioration dans la performance de la première à la deuxième session, les auteurs ont divisé chacune des sessions en six essais de 30 secondes. Dans l'ensemble, les résultats indiquent que les patients ayant la MP passent moins de temps en contact avec la cible, mais qu'ils montrent des signes d'apprentissage puisque leur performance s'améliore significativement d'une session à l'autre. Les analyses statistiques indiquent, cependant, que les performances demeurent relativement stables à l'intérieur d'une session, ce qui serait principalement dû au manque d'amélioration à l'intérieur des deux premiers essais de 30 secondes au début de chaque session. À ce sujet, Flowers et Robertson (1985) mentionnent que l'amélioration inter-session reflète la capacité d'apprentissage permanent alors que l'amélioration intra-session est un indice de la capacité d'acquérir un mode d'habileté motrice («motor set») particulièrement adapté à la tâche. En se basant sur cette dernière proposition, Frith et al. (1986) suggèrent donc que la MP n'altère pas la composante permanente de l'apprentissage d'habiletés, mais qu'elle affecte plutôt la capacité d'acquérir un mode d'habileté motrice.

Les résultats obtenus dans le cadre d'études cliniques sont appuyés par quelques recherches dans lesquelles on a observé la présence d'activations au niveau du striatum à l'aide de la TEP en utilisant une séquence complexe de mouvements volontaires des doigts (ex., Friston, Frith, Passingham, Liddle & Frackowiak, 1992; Seitz & Roland,

1992; voir Doyon, 1997, pour une recension des écrits) ou encore à l'aide de la tâche de poursuite rotative (Grafton et al., 1992, 1994). Ainsi, Grafton et al. (1992), par exemple, ont rapporté une activation dans le flux sanguin au niveau du striatum lors de l'exécution de la tâche de poursuite rotative.

Récemment, un nombre grandissant de chercheurs ont étudié le rôle du striatum dans l'apprentissage d'habiletés à l'aide de versions adaptées de la tâche de séquence visuelle répétée (Nissen & Bullemer, 1987). Puisqu'il existe un nombre considérable de données obtenues à l'aide de ce paradigme expérimental, et que cette tâche est utilisée dans deux des trois expériences de cette thèse, la prochaine sous-section accorde une attention particulière aux résultats obtenus à l'aide de cette tâche.

Étude de la contribution striatale dans l'apprentissage visuomoteur à l'aide de la tâche de séquence visuelle répétée. Bien qu'il existe plusieurs versions de cette épreuve (ex., Doyon et al., 1997a, 1996; Nissen & Bullemer, 1987), de façon générale, elle comprend quatre boutons-réponses et quatre stimuli visuels disposés horizontalement, chacun de ces stimuli correspondant à l'un des boutons-réponses (voir Figure 5). Dans ce type de tâche, le sujet doit généralement appuyer sur la touche correspondant au stimulus visuel qui est présenté, le plus rapidement possible, tout en évitant les erreurs (voir Doyon et al., 1997a). Comme l'indique l'illustration, la boîte-réponse est reliée à un ordinateur IBM PC qui gère la présentation des stimuli de même que la compilation des variables dépendantes sélectionnées (temps de réponse et nombre d'erreurs). À l'insu du sujet, il est possible de programmer l'ordinateur de façon à ce que les stimuli soient administrés selon une séquence de «x» items qui revient continuellement à l'intérieur d'un bloc d'essais. Un des facteurs ayant contribué à l'utilisation de ce paradigme par plusieurs auteurs est sans doute le fait qu'il permet d'isoler la composante implicite de l'apprentissage puisque le sujet n'est pas informé de la présence d'une séquence pré-déterminée qui est répétée au fil des blocs d'essais (Adams, 1984; Cohen, Ivry & Keele, 1990; Howard, Mutter & Howard, 1992; Reed & Johnson, 1994; Wenger & Carlson, 1995; Willingham, Nissen & Bullemer, 1989).

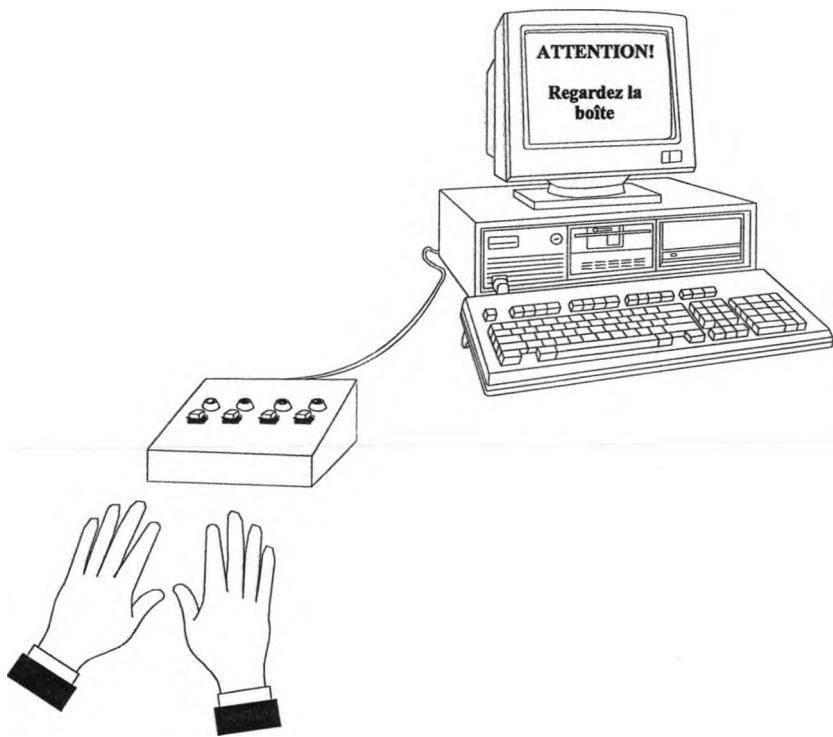


Figure 5. Représentation schématique de l'appareillage utilisé dans la tâche de séquence visuelle répétée adaptée de Nissen et Bullemer (1987).

Malgré certaines divergences entre les résultats obtenus jusqu'à maintenant à l'aide de cette tâche, plusieurs auteurs s'entendent pour dire que le striatum participe à l'apprentissage incrémentiel d'une séquence visuelle répétée (Doyon et al., 1997a; Ferraro et al., 1993; Jackson, Jackson, Harrison, Henderson & Kennard, 1995; Knopman, 1991; Knopman & Nissen, 1991; Nissen & Bullemer, 1987; Willingham & Koroshetz, 1993). Cependant, il est important de souligner que Corkin et al. (1992) n'ont pas observé de déficit chez les patients ayant la MP à cette même tâche. De plus, Rothlind, Bylsma et Brandt (1993) ne rapportent aucune différence dans l'amélioration de la performance entre un groupe de patients porteurs de la MH et des sujets contrôles. Ces résultats contradictoires peuvent toutefois s'expliquer par certaines variables qui sont discutées dans la prochaine sous-section.

Enfin, il est important de souligner que les résultats des études cliniques mentionnées plus haut, lesquelles corroborent le rôle du striatum dans l'apprentissage d'habiletés, sont également soutenus par des études d'imagerie cérébrale récentes réalisées à l'aide de l'épreuve de séquence visuelle répétée chez des sujets témoins (Doyon et al., 1996, 1997b; Grafton et al., 1995; Hazeltine et al., 1997; Metz et al., 1993; Rauch et al., 1995; voir Doyon, 1997, pour une recension des écrits). Dans chacune de ces recherches, il est possible de constater une activation au niveau du striatum lors de l'exécution de la tâche de séquence visuelle répétée.

Incohérences dans la littérature. Tel que mentionné tout au long du texte, la littérature traitant de la contribution du striatum dans l'apprentissage d'habiletés comporte certaines incohérences. Cependant, une lecture approfondie de l'ensemble de ces travaux permet d'identifier trois facteurs méthodologiques qui peuvent être à la source de ces divergences. Premièrement, certains résultats contradictoires peuvent s'expliquer par le fait que les auteurs n'utilisent pas les mêmes populations cliniques (ex., MP vs MH), connues pour différer en terme de changements pathophysiologiques. Dans le cas de la MP, par exemple, les travaux de Kish, Shannak et Hornykiewicz (1988) ont tenté de mesurer la réduction d'afférences dopaminergiques dans chacune des structures du striatum (noyau caudé et putamen). Les résultats de cette quantification ont permis

d'appuyer les données animales (Iversen, 1984) et humaines (Bernheimer, Birkmayer, Hornykiewicz, Jellinger et Seitelberger, 1973) qui suggèrent que les symptômes parkinsoniens ne se manifestent cliniquement que lorsque la réduction dopaminergique atteint 80% ou plus. De plus, les résultats de l'analyse histopathologique effectuée par Kish et ses collègues (1988) sur les tissus striataux de huit patients ont montré une diminution pratiquement complète dans le putamen (89 à 100%) et une diminution sévère (80% et moins) dans la partie dorso-rostrale du noyau caudé. En conséquence, ces auteurs mentionnent que les déficits moteurs fréquemment rapportés chez les patients ayant la MP seraient attribuables à la baisse dopaminergique quasi complète dans le putamen alors que la réduction caudale pourrait expliquer certains déficits obtenus lors des tests sollicitant les fonctions cognitives supérieures (voir Dubois, Boller, Pillon & Agid, 1991, pour une recension des écrits). À l'inverse, une recension des écrits effectuée par Brandt (1991) rapporte que la MH implique parfois le système limbique, le cortex frontal ou même le cervelet, en plus des changements neuropathologiques au niveau du striatum (Kuhl, Phelps & Markham, 1982; Leenders, Frackowiak, Quinn & Marsden, 1986). Considérant ces différences importantes entre les deux pathologies, il devient difficile de comparer directement les résultats obtenus chez les patients porteurs de la MH (Corkin et al., 1992; Knopman & Nissen, 1991; Willingham & Koroshetz, 1993) avec ceux recueillis à l'aide de groupes de sujets ayant la MP (Doyon et al., 1997a; Ferraro et al., 1993; Frith et al., 1986; Harrington et al., 1990; Pascual-Leone et al., 1993; Saint-Cyr et al., 1988). Ainsi, dans le domaine visuoperceptif, par exemple, l'étude de Martone et al. (1984) a fait ressortir un déficit chez les patients du groupe MH alors que celle de Harrington et al. (1990) n'a pu reproduire les mêmes résultats chez un groupe de patients parkinsoniens.

Deuxièmement, malgré le fait que certains auteurs aient proposé que la sévérité de la maladie est un facteur important à considérer dans les études comprenant des groupes de patients parkinsoniens (Mortimer, Pirozzolo, Hansch & Webster, 1982; Taylor, Saint-Cyr, Lang & Kenny, 1986; à ce sujet, voir aussi Doyon et al., 1997a; Harrington et al., 1990; Owen, Beksinska, James, Leigh, Summers & Marsden, 1993; Owen & Robbins, 1993, pour une recension des écrits), d'autres recherches n'ont pas tenu compte

de la progression dans la sévérité de la maladie (Bondi & Kaszniak, 1991; Heindel et al., 1989; Singh et al., 1992). En effet, dans ces travaux, les auteurs ont combiné les patients manifestant des symptômes unilatéraux (qui correspondent à une dégénérescence unilatérale significative [Stade 1 selon l'échelle de Hoehn & Yahr, 1967]) et ceux présentant des symptômes bilatéraux (lesquels sont révélateurs d'une dysfonction striatale bilatérale [Stades 2-3]) (voir aussi Hornykiewicz, 1993). Tel que l'indique Doyon et ses collègues (1997a), cette différence inhérente au type de patients utilisés peut être à la source de plusieurs divergences entre les études.

Finalement, le manque de cohérence entre les résultats peut aussi s'expliquer par la disparité qui existe d'une recherche à l'autre entre le nombre de sessions expérimentales et la durée des pauses entre les blocs d'essais. Par exemple, alors que Heindel et al. (1989) n'ont pas trouvé de déficit chez les patients du groupe MP à la poursuite rotative en employant trois blocs de huit essais chacun (20 secondes/essai; temps total de la tâche: huit minutes) administrés le même jour et avec des pauses inter-blocs de 30 minutes, Harrington et al. (1990) ont montré un déficit en utilisant trois blocs de six essais (30 secondes/essai) effectués chaque jour sur une période de trois jours (temps total de la tâche: 27 minutes). En ce sens, il est possible de soutenir que l'absence de déficit au niveau de la mémoire procédurale obtenue par Heindel et al. (1989) dans la tâche de poursuite rotative, ainsi que par certains auteurs utilisant d'autres types de tâches (Corkin et al., 1992; Rothlind et al., 1993), soit uniquement due au fait que ceux-ci ont testé les patients en début d'apprentissage seulement. Enfin, notons que cette divergence observée entre les résultats peut également être abordée sous un autre angle, c'est-à-dire celui de la puissance méthodologique inhérente à l'épreuve utilisée. Par exemple, il est possible que l'absence d'effet obtenu chez les patients du groupe MP non-démentés de Heindel et al. (1989) dans la tâche de poursuite rotative, par Harrington et al. (1990) à la lecture-miroir, ainsi que par Frith et al. (1986) aux tâches d'apprentissage manuel, reflète un manque de puissance méthodologique propre au type de tâche utilisée. D'autres recherches seront nécessaires afin d'éclaircir cette question méthodologique.

Résumé. Cette section permet d'apprécier le nombre considérable d'études portant sur le rôle du striatum dans l'apprentissage visuomoteur et plus particulièrement dans l'apprentissage d'une séquence visuelle répétée. Un examen approfondi des résultats obtenus dans ces recherches permet de croire que les incohérences observées entre les recherches s'expliquent par plusieurs variables telles que 1) les différences au niveau des changements pathophysiologiques observés dans les différentes populations cliniques utilisées, 2) le fait que certains auteurs ne considèrent pas la progression dans la sévérité de la maladie et 3) que ces travaux ne sont pas réalisés avec le même nombre de sessions expérimentales et emploient quelquefois des tâches pour lesquelles la validation ne repose que sur une simple étude pilote. Malgré cela, les résultats corroborant la participation du striatum dans l'acquisition d'habiletés implicites proviennent de plusieurs domaines spécialisés des neurosciences tels que la neurophysiologie cellulaire, la neurochimie, les études lésionnelles réalisées chez les rongeurs et les primates non-humains, la neuropsychologie expérimentale chez des populations de patients présentant une dysfonction striatale et, plus récemment, une vague de travaux effectués à l'aide de diverses techniques d'imagerie cérébrale chez les sujets normaux. En plus de son rôle dans l'apprentissage, certaines études suggèrent que le striatum pourrait être impliqué dans la phase d'automatisation des apprentissages (Brotchie et al., 1991a, 1991b; Marsden, 1982, 1987; Marsden & Obeso, 1994), dans l'apprentissage de type perceptivomoteur (Aosaki et al., 1994a, 1994b; Knowlton, Mangels & Squire, 1996; McDonald & White, 1993; Packard & White, 1990; Singh, Metz, Gabrieli, Willingham, Dooley, Jiang, Chen & Cooper, 1993; voir Graybiel, 1995; Graybiel & Kimura, 1995; White, 1989, 1997, pour une recension des écrits; voir aussi le Chapitre IV) ainsi que dans l'adaptation contextuelle (Graybiel & Kimura, 1995; Kimura, 1992; Marsden & Obeso, 1994; Wise & Houk, 1994). En plus du striatum, quelques travaux récents indiquent également que le cervelet est impliqué dans ce même type d'apprentissage. La prochaine section présente les études qui se sont particulièrement intéressées au rôle du cervelet dans l'apprentissage d'habiletés visuomotrices.

### Contribution du cervelet dans l'apprentissage d'habiletés

Tout comme pour le striatum, les connaissances acquises concernant l'implication du cervelet dans l'apprentissage d'habiletés proviennent d'études effectuées dans divers champs d'activité tels que la neurophysiologie (Albus, 1971; Cajal, 1911; Dow & Moruzzi, 1958; Gilbert, 1975; Gilbert & Thach, 1977; Ito, 1982, 1993; Marr, 1969; Mushiake & Strick, 1993; Thach et al., 1992; voir Bloedel, 1992; Thach, 1996, pour une recension des écrits), les études lésionnelles chez l'animal (Dahhaoui, Caston, Auvray & Reber, 1990; Guillaumin, Dahhaoui & Caston, 1991; Nixon & Passingham, 1996; Shimansky, Wang, Bloedel & Bracha, 1994; Shimansky, Wang, Bracha & Bloedel, 1995; voir Bloedel & Bracha, 1997; Bloedel et al., 1996, pour une recension des écrits), les études cliniques effectuées à l'aide de patients porteurs de lésions cérébelleuses (Daum, Ackermann, Schugens, Reimold, Dichgans & Birbaumer, 1993; Doyon et al., 1997a; Gauthier, Hofferer, Hoyt & Stark, 1979; Sanes, Dimitrov & Hallett, 1990; Weiner, Hallett & Funkenstein, 1983) ainsi que les études d'imagerie cérébrale chez des groupes de sujets sains (Doyon et al., 1997b, 1996; Flament, Ellermann, Kim, Ugurbil & Ebner, 1996; Friston et al., 1992; Rao et al., 1995; Seitz et al., 1994; voir Doyon, 1997, pour une recension des écrits).

Tout d'abord, au plan physiologique, Marr (1969) a été parmi les premiers à proposer un modèle fonctionnel du cervelet. Selon ce dernier, les deux afférences principales aux cellules de Purkinje du cervelet, soit les fibres grimpantes et moussues, envoient des signaux distincts permettant l'apprentissage et le maintien d'événements associatifs. Avec l'apprentissage, ces signaux agissent sur les synapses reliant les fibres parallèles aux cellules de Purkinje par un processus de modification hétérosynaptique qui surviendrait lorsque les activations des deux systèmes coïncident. Dans une version modifiée de la théorie de Marr (1969), Albus (1971) a suggéré que les afférences des fibres grimpantes vers les cellules de Purkinje, lesquelles originent de l'olive inférieure, fourniraient un signal contenant les renseignements élémentaires à propos du mouvement à exécuter. Les afférences des fibres moussues, qui proviennent des noyaux pédonculospontins, pourraient quant à elles contenir des informations contextuelles nécessaires à

l'exécution appropriée du mouvement. En 1977, Gilbert et Thach ont d'ailleurs fourni des données neurophysiologiques qui corroborent ce dernier modèle. En effet, ces auteurs ont montré que l'activité des cellules de Purkinje, produite par les fibres grimpantes au site d'afférence, est augmentée de façon transitoire dans certaines cellules lorsque les animaux doivent adapter un mouvement appris en raison d'une contrainte contextuelle (Gilbert, 1975). En se basant sur ces travaux, Gilbert et Thach (1977) ont suggéré que l'engramme de l'apprentissage se crée par l'activation congruente des fibres grimpantes et parallèles ainsi que par la participation du locus coeruleus.

De son côté, Ito (ex., 1982, 1989, 1993) s'est intéressé au rôle de la plasticité synaptique dans l'apprentissage moteur. Cet auteur a suggéré que les changements synaptiques observés dans le cervelet pourraient être à la base de l'apprentissage. Selon Ito, l'acquisition d'une habileté motrice produit une dépression à long terme (DLT) de l'activité neuronale au niveau des synapses entre les cellules de Purkinje et les fibres parallèles, lesquelles seraient influencées par l'activité des fibres grimpantes. En se basant sur l'organisation du système cérébelleux et les caractéristiques physiologiques des interactions neuronales qui surviennent dans le cortex cérébelleux, d'autres auteurs tels que Thach (Thach et al., 1992; voir Thach, 1996, pour une recension des écrits) ainsi que Bloedel (1992), ont aussi avancé un modèle du rôle du cervelet dans l'apprentissage moteur. Dans le premier cas, Thach et al. (1992) ont proposé que l'une des fonctions primaires du cervelet est de coordonner ensemble les mouvements simples dans le but de créer un mouvement général exécuté en douceur, et de façon continue. Par contre, Bloedel et ses collègues (Bloedel, 1992; Lou & Bloedel, 1988) stipulent que le cervelet, et plus particulièrement le cortex cérébelleux, est impliqué dans les opérations «en temps réel» requises pour le contrôle de l'activité motrice coordonnée.

Au niveau des études animales, plusieurs travaux portant sur la contribution du cervelet dans la plasticité du réflexe vestibulo-oculaire (Ito, 1982, 1989) ou encore sur l'acquisition et la rétention du conditionnement classique de la membrane nictitante chez le lapin (Krupa, Thompson & Thompson, 1993; McCormick & Thompson, 1984; Thompson, 1986, 1987, 1988, 1992; Yeo, Hardiman & Glickstein, 1985a, 1985b, 1985c; voir Bloedel & Bracha, 1997; Harvey & Welsh, 1996, pour une recension des écrits) ont

permis de montrer que le cervelet joue un rôle essentiel dans l'apprentissage associatif et qu'il possède donc une grande capacité d'adaptation. Toutefois, Bloedel et ses collègues (Bloedel et al., 1996) ont récemment mis en doute la pertinence des conclusions provenant des études effectuées à l'aide du conditionnement classique en soulignant que ce type d'apprentissage ne requiert pas de l'animal qu'il sélectionne une stratégie lui permettant de réaliser le mouvement appris de façon précise et bien coordonnée. Ainsi, basés sur les résultats obtenus à l'aide de diverses tâches d'apprentissage de mouvements volontaires complexes, Bloedel et al. (1996) proposent trois principes quant aux sites responsables de l'apprentissage moteur. Tout d'abord, les données indiquent que les circuits sollicités semblent spécifiques au type d'apprentissage en cause. Ensuite, dépendamment du mouvement requis, les résultats suggèrent qu'il existe plusieurs sites corticaux et sous-corticaux pouvant être impliqués dans cette forme d'apprentissage. Finalement, ces sites incluent souvent les noyaux qui reçoivent des projections convergentes de régions spécifiques du cervelet, en plus d'autres systèmes de fibres participant à l'acquisition d'un comportement moteur volontaire. En conclusion, ces auteurs proposent donc que les changements, qui surviennent dans la plasticité neuronale lors de l'apprentissage de mouvements volontaires complexes chez l'animal, font appel à un circuit distribué comprenant le cervelet et d'autres régions impliquées dans le contrôle du mouvement.

Quelques travaux réalisés chez des populations cliniques porteuses d'une dysfonction cérébelleuse corroborent également l'hypothèse selon laquelle le cervelet participe à l'apprentissage d'habiletés motrices (Daum et al., 1993; Doyon et al., 1997a; Gauthier et al., 1979; Sanes et al., 1990; Weiner et al., 1983). Sanes et al. (1990), par exemple, ont comparé la performance de sujets atteints de lésions cérébelleuses à celle de sujets témoins lors d'une épreuve d'apprentissage d'habiletés visuomotrices, soit la tâche de dessin-miroir. Leurs résultats ont montré que les patients porteurs d'une atrophie olivo-ponto-cérébelleuse n'affichent pas de façon significative le temps requis pour compléter la figure. De plus, leur taux de précision à cette tâche demeure relativement stable malgré un grand nombre d'essais, suggérant ainsi que le cervelet et les structures qui y projettent, participent à l'apprentissage d'habiletés visuomotrices.

Récemment, Doyon (1997) a présenté une excellente revue critique des études effectuées à l'aide de diverses techniques d'imagerie cérébrale telles que la TEP, l'IRMf, ou la tomographie par émission de photons simples (TEPS) chez des sujets normaux. Cette recension des écrits permet de réaliser qu'un nombre croissant d'auteurs ont observé des activations au niveau du cervelet en utilisant diverses tâches nécessitant, par exemple, la poursuite visuelle dans des conditions main-oeil inversés (Grafton et al., 1992, 1994) ou non (Flament et al., 1996; Lang, Lang, Podreka, Steiner, Uhl, Suess, Muller & Deecke, 1988), la réalisation de mouvements bidimensionnels de différentes amplitudes lors du traçage de stimuli simples ou complexes (Seitz et al., 1994), l'exécution séquentielle de mouvements des doigts (Friston et al., 1992; Seitz & Roland, 1992; Seitz et al., 1990), la réalisation d'une tâche de labyrinthe (Van Mier, Tempel, Perlmutter, Raichle & Petersen, submitted) ou encore l'exécution d'une tâche de séquence visuelle répétée (Doyon et al., 1996; Grafton et al., 1995; Hazeltine et al., 1997; Jenkins et al., 1994; Rao et al., 1995). Malgré le nombre considérable d'études ayant observé une activation au niveau du cervelet, il est important de souligner que quelques auteurs n'ont pas obtenu de tels résultats (Grafton et al., 1995, 1992; Rauch et al., 1995). Par exemple, Grafton et al. (1992) ont étudié le rôle du cervelet dans la phase initiale de l'apprentissage d'habiletés d'une tâche de poursuite visuelle. Contrairement à Seitz et al. (1990), ces auteurs ont montré que l'activation cérébelleuse était associée à l'exécution de la tâche et non pas à l'apprentissage de l'habileté visuomotrice comme telle. Toutefois, Grafton et ses collègues ont expliqué cette différence de résultats par le fait que leur étude n'utilisait pas un protocole qui permettait de mesurer les changements du flux sanguin lors de l'automatisation de l'habileté. Enfin, tel que l'indique Doyon (1997), dans deux des trois études mentionnées plus haut (Grafton et al., 1992; Rauch et al., 1995), il est possible que l'absence d'activation cérébelleuse soit aussi due au fait que le champ de vision de la caméra TEP utilisée dans ce genre d'étude ne permettait pas de visualiser des changements d'activation dans les portions ventrales et latérales du cervelet.

**Résumé.** Tout comme pour le striatum, les connaissances acquises concernant la participation du cervelet dans l'apprentissage d'habiletés proviennent de plusieurs

domaines comprenant les études chez l'animal et l'humain. Il est intéressant de noter que, dans le domaine des études cliniques, contrairement aux recherches réalisées à l'aide de populations souffrant d'une dysfonction striatale, il existe un bon consensus au niveau de la participation du cervelet dans cette forme d'apprentissage. En effet, l'ensemble des recherches portant sur l'apprentissage d'habiletés suggèrent que le cervelet participe à cette forme de mémoire, et ce, sans exception. En plus de son rôle dans l'apprentissage, certaines études récentes ont même proposé que le cervelet serait impliqué dans la phase d'automatisation des apprentissages (Doyon, Laforce, Bouchard, Gaudreau, Roy, Poirier, Bédard, Bédard & Bouchard, sous presse). Il semblerait également qu'un des mécanismes pouvant expliquer les déficits observés dans les tâches d'apprentissage serait la participation du cervelet dans la mise en séquence de mouvements (Hikosaka, Rand, Miyachi & Miyashita, 1995; Holmes, 1939; Inhoff et al., 1989; voir aussi Chapitre IV). Enfin, quelques auteurs ont aussi exploré la participation du striatum et du cervelet dans l'acquisition d'habiletés visuomotrices dans le cadre d'une même étude. La prochaine section présente ces travaux, après quoi une section spécialement réservée à la nature de la contribution spécifique de chaque structure suivra.

### Contribution du striatum et du cervelet dans l'apprentissage d'habiletés visuomotrices

Beaucoup moins d'études ont essayé de comparer directement la participation possible du striatum et du cervelet dans l'apprentissage d'habiletés visuomotrices. En fait, contrairement aux données présentées dans les sections précédentes, celles qui font état d'une telle approche comparative proviennent uniquement d'études effectuées en neuropsychologie expérimentale à l'aide de groupes de sujets porteurs d'une dysfonction striatale ou cérébelleuse (Doyon et al., 1997a; Pascual-Leone et al., 1993) ou encore de recherches effectuées à l'aide de la TEP chez des sujets normaux (ex., Doyon et al., 1996; Grafton et al., 1994; Jenkins et al., 1994; Passingham et al., 1995; Seitz et al., 1990).

En ce qui concerne les études cliniques, il est intéressant de constater que les deux seules recherches qui ont comparé le rôle du striatum et du cervelet dans l'apprentissage d'habiletés ont été réalisées en utilisant des versions adaptées de la tâche de séquence

visuelle répétée. Ainsi, en 1993, Pascual-Leone et ses collègues ont tenté d'approfondir le rôle de ces structures dans 1) l'apprentissage d'une séquence de mouvements, 2) le transfert d'une habileté procédurale à la mémoire déclarative et 3) la capacité à utiliser l'information déclarative dans le but d'améliorer sa performance aux tests d'apprentissage. En tout, 19 patients ayant la MP, 10 patients porteurs d'atrophies cérébelleuses, 5 patients avec des atrophies olivopontocérébelleuses et 30 sujets normaux ont participé à l'étude. Contrairement aux patients cérébelleux qui n'affichent aucune connaissance déclarative de la séquence implicite, les résultats indiquent que 25% des patients du groupe MP ont réussi à détecter une telle séquence. Aussi, à l'inverse des patients cérébelleux qui montrent un déficit d'apprentissage à la tâche de séquence visuelle répétée, la performance des patients parkinsoniens ne diffère pas significativement des sujets contrôles. Les résultats montrent également que seuls les patients du groupe MP étaient en mesure d'utiliser leurs connaissances déclaratives de la séquence pour améliorer leur niveau de performance. Basés sur ces résultats, les auteurs concluent que le striatum et le cervelet sont impliqués dans l'apprentissage d'habiletés visuomotrices. Toutefois, ils mentionnent que leurs rôles respectifs pourraient être différents. Selon eux, il est possible que le circuit striato-frontal permette l'accès à l'information déclarative afin de parvenir à un apprentissage de la séquence alors que l'intégrité du cervelet se révèle cruciale dans les fonctions cognitives impliquant une séquence. Il est important de souligner que les travaux de Pascual-Leone et al. (1993) sont en accord avec les résultats présentés précédemment dans la section portant sur le rôle du cervelet dans l'apprentissage d'habiletés visuomotrices. Toutefois, tout comme Corkin et al. (1992), ces auteurs ne rapportent aucune différence dans l'amélioration de la performance entre les patients du groupe MP et les sujets contrôles. Tel que mentionné précédemment, il est possible que ces divergences de résultats soient uniquement dues au fait que les auteurs ont testé ces patients au début de l'apprentissage seulement.

Toujours dans le cadre d'études effectuées avec des populations cliniques, Doyon et al. (1997a) ont trouvé un déficit dans l'apprentissage d'une tâche de séquence visuelle répétée chez des patients souffrant d'une dysfonction striatale bilatérale (Stades 2-3 de la maladie selon l'échelle de Hoehn & Yahr [1967]) et des patients porteurs d'une lésion

circonscrite au cervelet. En effet, dans le cadre de deux projets de maîtrise portant respectivement sur le rôle du striatum (Laforce, Gaudreau, Castonguay, Roy, Bédard & Doyon, 1993b) et du cervelet (Gaudreau, Laforce, Castonguay, Bouchard & Doyon, 1993) dans l'apprentissage d'habiletés visuomotrices, la performance de 15 sujets normaux a été comparée à celle de 15 patients parkinsoniens non-déments (Stade 1, n=8; Stades 2-3, n=7), et celle de 12 sujets témoins à la performance de 12 patients porteurs d'une lésion circonscrite au cervelet (CE). Tous les sujets ont été testés une fois par semaine pendant six semaines consécutives. Au total, chaque sujet a complété six sessions, comprenant chacune quatre blocs de 100 essais. À l'intérieur de chaque bloc de 100 essais, les sujets ont exécuté un total de 10 présentations d'une séquence de 10 items. Aussi, dans le but d'examiner la possibilité d'une dissociation entre la mémoire déclarative et la mémoire non-déclarative, l'étude a comporté une mesure de la mémoire déclarative développée à partir des mêmes stimuli que ceux utilisés dans la tâche d'apprentissage. Cette mesure fut administrée lors de la dernière session expérimentale afin d'évaluer les connaissances déclaratives des sujets en fin d'apprentissage. S'appuyant sur les résultats des recherches antérieures, il était prévu que les patients des groupes MP et CE démontreraient une difficulté d'apprentissage au test de mémoire procédurale et que ce trouble serait lié à la sévérité de la maladie dans le cas des patients MP. De plus, l'ensemble des recherches effectuées antérieurement permettait de prédire que la performance au test déclaratif ne serait pas différente de celle des sujets contrôles (Dubois et al., 1991; Appollonio, Grafman, Schwartz, Massaquoi & Hallett, 1993). Tel que prévu, les résultats ont montré que seuls les patients parkinsoniens de Stades 2-3 et les patients du groupe CE ont affiché un déficit d'apprentissage à la tâche de séquence visuelle répétée en fonction des sessions expérimentales. De plus, cette différence d'apprentissage entre les groupes fut obtenue même s'ils ont démontré une connaissance déclarative équivalente des stimuli, appuyant ainsi l'hypothèse d'une dissociation entre les deux systèmes de mémoire. Il est important de mentionner que, dans les deux cas, le déficit d'apprentissage d'habiletés fut significatif seulement lors des dernières phases de l'apprentissage, indiquant ainsi que le déficit était évident seulement lors des phases plus avancées de l'apprentissage, c'est-à-dire lorsque le processus devient de plus en plus automatique (Anderson, 1983a, 1990). Ainsi, ces

données suggèrent que le trouble d'apprentissage observé chez les patients MP de Stades 2-3 et les patients porteurs d'une lésion circonscrite au cervelet s'explique davantage par un déficit au niveau de la phase lente plutôt qu'un trouble au niveau de la phase rapide d'apprentissage (Karni, 1996; Karni et al., in press).

Quelques recherches effectuées à l'aide de la TEP chez des sujets normaux corroborent également la contribution conjointe de ces deux structures dans l'apprentissage d'habiletés visuomotrices. Dans ces études, les auteurs ont utilisé divers types de tâches nécessitant soit l'apprentissage d'une séquence de mouvements des doigts (Jenkins et al., 1994; Passingham et al., 1995; Seitz et al., 1990), soit la poursuite d'une cible en mouvement (Grafton et al., 1994), soit la réalisation d'une séquence visuelle répétée (Doyon et al., 1996). Par exemple, Seitz et al. (1990) ont rapporté une étude dans laquelle les sujets devaient réaliser une séquence de seize mouvements des doigts alors que les expérimentateurs mesuraient l'activité métabolique du cerveau durant les phases de repos, d'apprentissage initial, d'apprentissage avancé et durant la phase finale où les sujets maîtrisaient bien la série de mouvements. Au fil des phases d'apprentissage, les auteurs ont noté une diminution initiale, suivie d'une augmentation du flux sanguin cérébral régional (FSCR) au niveau du striatum. À l'inverse, ils ont observé une activité métabolique constante au niveau du cervelet durant toutes les phases d'apprentissage. Toujours à l'aide d'une tâche où les sujets devaient apprendre une séquence de mouvements des doigts, Jenkins et al. (1994) ont obtenu des résultats indiquant que le striatum et le cervelet sont actifs dès les premières phases de l'apprentissage d'une séquence de mouvements apprise par essais et erreurs. Contrairement aux résultats obtenus par Seitz et al. (1990) leur étude suggère que seul le cervelet participe aux phases plus avancées de l'apprentissage. Enfin, toujours dans le cadre de ce même paradigme, il est intéressant de noter que les résultats suggérant une participation active du striatum et du cervelet dans les premières phases de l'apprentissage d'habiletés ont récemment été appuyés par une série d'études réalisées par Passingham et al. (1995). Toutefois, comme il est possible de le constater, d'autres travaux seront nécessaires afin de mieux comprendre le véritable rôle de ces structures dans les diverses phases de l'acquisition d'une séquence de mouvements des doigts.

Poursuivant dans le domaine de l'apprentissage moteur, mais cette fois-ci dans le cadre d'une étude effectuée à l'aide d'une tâche de poursuite rotative, Grafton et al. (1994) ont observé que le cervelet ainsi que certaines régions corticales participent aux premières phases d'apprentissage alors que le striatum est davantage actif dans le cas de mouvements procéduralisés. Finalement, dans une étude visant spécifiquement à éliminer la possibilité que les activations obtenues à la TEP en situation d'apprentissage soient explicables par la seule activité motrice nécessaire pour exécuter la tâche, Doyon et al. (1996) ont obtenu des résultats suggérant que le striatum et le cervelet participent tous deux à l'apprentissage d'une séquence visuelle répétée. De plus, à l'aide d'un protocole permettant d'illustrer l'implication des structures en début et en fin d'apprentissage, ces auteurs ont montré que le striatum ventral et le noyau dentelé du cervelet entrent en jeu principalement lors des dernières phases de l'apprentissage. Les auteurs ont conclu que ces structures sont impliquées dans l'apprentissage d'habiletés par la pratique, possiblement dans les phases d'automatisation du processus d'acquisition.

**Résumé.** La section précédente recense les études s'étant intéressées au rôle du striatum et du cervelet dans le cadre d'une même étude, à l'aide de populations cliniques présentant de telles dysfonctions. De plus, elle relate les recherches dans lesquelles les auteurs ont observé des changements du flux sanguin, tant au niveau du striatum que du cervelet. Comme il est possible de le constater, les études cliniques corroborent la participation de ces structures dans l'apprentissage et fournissent même des pistes quant à la nature de leur contribution au niveau de cette forme d'apprentissage. Ainsi, tel que mentionné plus tôt dans le texte, il semble que le striatum et le cervelet puissent être impliqués au niveau des phases plus avancées de l'apprentissage. D'autre part, bien que les études d'imagerie corroborent la participation de ces deux structures dans l'apprentissage d'habiletés, elles présentent plusieurs divergences principalement au niveau de la phase précise d'apprentissage à laquelle le striatum ou le cervelet participent. Toutefois, ces différences de résultats peuvent s'expliquer par le fait qu'il existe une grande disparité entre le type de tâches utilisées, et le nombre d'essais employés par les auteurs. Plus encore, ces études diffèrent quant aux stades d'apprentissage durant lesquels

les images cérébrales sont prises, amenant ainsi une grande variabilité au niveau des sites d'activations selon les études. Toutes ces variables font en sorte qu'il devient difficile de comparer directement ces études entre elles. Quoiqu'il en soit, combinées aux éléments portant respectivement sur le rôle du striatum ou du cervelet dans l'apprentissage d'habiletés visuomotrices, les études décrites ci-dessus soulèvent des hypothèses fort intéressantes quant à la véritable nature de la contribution de chaque structure dans ce type d'apprentissage. La prochaine section tente d'approfondir plus particulièrement cette question.

#### Nature de la contribution du striatum et du cervelet dans l'apprentissage d'habiletés visuomotrices

Les trois sections précédentes permettent de constater qu'un nombre important de recherches corroborent la participation du striatum et du cervelet dans l'apprentissage d'habiletés visuomotrices. Considérant le fait que ces deux structures font partie de deux circuits neuroanatomiques distincts (voir Figure 4) (Asunama et al., 1983; Kemp & Powell, 1971; Leiner et al., 1986; Middleton & Strick, 1994; Percheron et al., 1993; Sakai et al., 1996; Yamamoto et al., 1992) et qu'elles diffèrent au plan neurophysiologique (ex., Graybiel & Kimura, 1995; Ito, 1982, 1993), il est certes étonnant que si peu d'auteurs aient tenté d'éclaircir la véritable nature de leur contribution dans ce type d'apprentissage (Burton, 1990; Houk & Wise, 1995; Jueptner et al., 1997; Pascual-Leone et al., 1993; Wise & Houk, 1994). Avant d'aborder les rares conceptualisations qui intègrent à la fois les fonctions du striatum et du cervelet, les prochaines sous-sections résument respectivement les modèles des fonctions du striatum et du cervelet qui pourraient contenir des pistes intéressantes quant à la nature distincte de leur contribution dans ce processus.

Modèles fonctionnels du striatum. Parmi les modèles fonctionnels du striatum (Flowers, 1978; Marsden, 1982, 1987; Marsden & Obeso, 1994; Robertson & Flowers, 1990; Schmidt, 1975; Willingham & Koroshetz, 1993), celui de Marsden et Obeso (1994)

représente l'intégration la plus complète des connaissances actuelles sur le rôle de cette structure dans les fonctions cognitives et d'apprentissage. De plus, deux des trois études réalisées dans cette thèse ont tenté de tester des hypothèses directement reliées avec les travaux de ces chercheurs. Par conséquent, une emphase particulière sera accordée à ce dernier modèle. Basé sur l'étude approfondie de l'organisation neuroanatomique du striatum suite à une thalamotomie ou à une pallidotomie (neurochirurgies qui consistent à procéder à l'ablation partielle d'une région du thalamus ou du pallidum), Marsden a proposé que cette structure gère deux aspects subtils du contrôle du mouvement soit 1) l'exécution automatique de séquences de mouvements, soit 2) la capacité d'interrompre le programme moteur en cours dans le but de l'adapter à un changement contextuel. Les deux prochaines parties présentent donc ces avenues de recherche en lien avec les autres modèles actuels sur les fonctions du striatum.

**L'exécution automatique de séquences de mouvements.** En 1982, basé sur des données neuroanatomiques et électrophysiologiques, Marsden a amené les premiers éléments d'une théorie selon laquelle le striatum serait impliqué dans l'aspect séquentiel du mouvement. Selon lui, le complexe striatal joue un rôle important au niveau de la structure du mouvement, notamment dans l'aspect séquentiel des programmes moteurs. Comme il le mentionne, tout mouvement implique une séquence d'événements, laquelle est élaborée à partir de programmes moteurs indépendants. À ce sujet, Marsden se réfère à la définition de Keele (1968), et Keele et Summers (1976), qui a proposé qu'un programme moteur constitue un patron de commandes musculaires structurées et prêtes à être exécutées avant même que ne débute la séquence motrice comme telle. Encore selon Marsden (1987), le striatum n'est pas nécessairement responsable de l'initiation du mouvement ou encore du moment précis (*«timing»*) où la contraction musculaire doit avoir lieu pour faire en sorte que le mouvement soit bien exécuté. Au contraire, sa théorie avance que l'exécution d'une action motrice (nommée *«plan moteur»*) requiert une série de programmes moteurs séquentiels que le striatum est capable d'organiser.

L'hypothèse de Marsden (1982; Marsden & Obeso, 1994) voulant que le striatum soit responsable de l'organisation des programmes moteurs est appuyée par de nombreux

travaux tant au niveau neurophysiologique (DeLong, Georgopoulos, Crutcher, Mitchell, Richardson & Alexander, 1984) que chez des populations cliniques présentant une dysfonction striatale (Benecke, Rothwell, Dick, Day & Marsden, 1987; Bradshaw, Phillips, Dennis, Mattingley, Andrewes, Chiu, Pierson & Bradshaw, 1992; Canavan, Passingham, Marsden, Quinn, Wyke & Polkey, 1989; Flowers, 1978; Georgiou, Bradshaw, Iansek, Phillips, Mattingley & Bradshaw, 1994; Georgiou, Bradshaw, Phillips, Bradshaw & Chiu, 1995; Georgiou, Iansek, Bradshaw, Phillips, Mattingley & Bradshaw, 1993; Inhoff & Bisiacchi, 1990; Jones, Phillips, Bradshaw, Iansek & Bradshaw, 1992; Kermadi & Joseph, 1995; Kermadi, Jurquet & Joseph, 1993; Roy et al., 1993; Stelmach, Worringham & Strand, 1987; Stern, Mayeux, Rosen & Ilson, 1983; Willingham & Koroshetz, 1993). Par exemple, en mesurant l'activité neuronale présente au niveau de diverses régions du striatum, DeLong et al. (1984) ont observé que les neurones des zones efférentes du striatum, particulièrement au niveau du globus pallidus médian et de la substance noire *pars reticulata*, s'activent de façon intense chez les primates entraînés à exécuter une séquence de mouvements des bras. Au plan clinique, Benecke et al. (1987) ont étudié la contribution du striatum dans l'aspect séquentiel à l'aide de tâches nécessitant certaines séquences de mouvements telles que la flexion du pouce et des doigts ou encore l'extension du coude gauche suivie d'une flexion de la main gauche. Ces auteurs ont obtenu des résultats qui suggèrent que le striatum favorise le passage d'un programme moteur à un autre tel qu'indiqué par une augmentation significative du temps total d'exécution des patients du groupe MP lorsqu'il leur est demandé d'enchaîner des programmes moteurs. Selon eux, ce trouble s'explique par le fait qu'une dysfonction striatale empêche la programmation d'actions séquentielles. De plus, il semble que le déficit observé ne puisse être attribuable à la composante temporelle (ou «timing») de la tâche comme telle puisque cet aspect de la mise en séquence semble préservé dans l'exécution globale des gestes.

Toujours dans le contexte d'études cliniques, Georgiou et al. (1993) ont obtenu des résultats permettant de mieux caractériser la nature du déficit séquentiel observé dans la MP, en se basant sur des résultats obtenus à l'aide d'une tâche où les sujets devaient réaliser une séquence prédéterminée en appuyant sur des touches lumineuses disposées

sur une plaque horizontale selon deux conditions (avec et sans indices). Tel qu'attendu, leurs données indiquent que la performance des sujets du groupe MP est grandement affectée par l'absence d'indices contextuels externes spécifiques (auditifs ou visuels). Par contre, les résultats montrent que dans le cas d'une séquence apprise de façon explicite, et en l'absence d'indices externes spécifiques (auditifs ou visuels), les indices internes non spécifiques tels qu'une série d'indices auditifs générés de façon périodique par un métronome sont suffisants pour augmenter, à eux seuls, la rapidité et la précision avec laquelle une séquence de mouvements est réalisée chez les patients du groupe MP. Ces auteurs ont donc proposé que les noyaux gris centraux génèrent un indice interne non spécifique qui permet de déclencher le mouvement et ils ont suggéré que la MP provoquait un déficit dans ce mécanisme. Enfin, tout comme l'avait fait Flowers en 1978, les auteurs concluent que l'absence d'indices internes pourrait expliquer le déficit au niveau de l'aspect séquentiel du mouvement rencontré chez cette population clinique. En ce sens, le striatum lésé ne fournirait pas les indices moteurs internes nécessaires à la mise en séquence de programmes moteurs, ce qui produirait une lenteur dans ce type d'action.

Plus récemment, les travaux de Brotchie et al. (1991a, 1991b), qui ont observé une population de cellules du pallidum qui affichaient une double activation durant les phases avancées de l'apprentissage d'une séquence de mouvements, ont permis à Marsden et Obeso (1994) d'appuyer l'hypothèse selon laquelle le striatum ne serait pas uniquement impliqué au niveau de l'organisation séquentielle des programmes moteurs, mais également dans l'exécution automatique des séquences de mouvements. Comme l'indiquent les résultats de Brotchie et ses collègues, la première activation des cellules du pallidum survient après le premier mouvement de la séquence tandis que la seconde précède le mouvement subséquent. Selon ces derniers, les doubles potentiels d'action reflètent la présence d'indices internes générés par le striatum dans le but d'exécuter correctement un mouvement en séquence. De plus, le fait que ces derniers n'aient été observés que dans un contexte où les singes avaient bien appris la tâche motrice, suggère que le striatum pourrait faciliter l'exécution automatique ou routinière de ces programmes, lorsque le mouvement est bien appris.

Finalement, parallèlement à ces recherches corroborant l'implication du striatum dans l'exécution automatique de séquences de mouvements, il existe certains travaux réalisés chez l'animal (Graybiel & Kimura, 1995; McDonald & White, 1993; Packard et al., 1989; Packard & White, 1990) et l'humain (Knowlton et al., 1996; Singh et al., 1993) qui proposent que le striatum possède des habiletés particulières au niveau de l'élaboration du programme moteur tel que défini par Keele (1968), et Keele et Summers (1976). Ainsi, à l'aide d'une tâche de conditionnement classique, Graybiel et Kimura (1995) ont démontré que le complexe striatal affiche une plasticité synaptique qui permet l'élaboration de programmes moteurs. Ces données sont d'ailleurs appuyées par les modèles animaux de l'apprentissage chez le rat où l'on indique qu'une lésion du noyau caudé prive systématiquement l'animal de l'acquisition d'une association S-R à une version adaptée du test du labyrinthe radial («win-stay») (McDonald & White, 1993; Packard et al., 1989; Packard & White, 1990; voir White, 1997, pour une recension des écrits). De façon générale, ces recherches suggèrent donc que le striatum fonctionnerait tel un système d'apprentissage associatif simple qui permet aux stimuli neutres de produire différentes réponses suite au renforcement répété d'une association entre un stimulus et une réponse. Aussi, il est intéressant de noter que ces données corroborent également des résultats préliminaires obtenus chez l'humain à l'aide de la mesure du FSCr. En effet, en demandant à des sujets de répondre à neuf blocs d'essais aléatoires de la tâche de séquence visuelle répétée (présentée sans séquence cette fois), Singh et al. (1993) ont observé une augmentation du flux sanguin au niveau du thalamus et des ganglions de la base. Finalement, en s'inspirant de l'ensemble des travaux rapportés dans cette partie, il est possible de poser l'hypothèse selon laquelle le striatum pourrait agir tel un module d'intégration sensori-motrice nécessaire à l'élaboration des programmes moteurs et surtout à l'automatisation de ces derniers, basés sur des associations S-R appropriées au contexte. La prochaine partie traite spécifiquement du rôle de cette structure dans l'adaptation aux changements contextuels.

**Influence du contexte et striatum.** Des études électrophysiologiques mesurant la performance d'un groupe de singes soumis à différentes tâches d'apprentissage ont montré

que les neurones du putamen sont très actifs lorsque l'animal est en mouvement. À l'inverse, les neurones des autres régions du striatum, particulièrement ceux de la portion antérieure, sont sensibles aux stimuli externes ou aux indices environnementaux impliqués dans la préparation du mouvement (Caan, Perrett & Rolls, 1984; Kimura, 1992; Kimura, Kato & Shimazaki, 1990; Nambu, Yoshida & Jinnai, 1988, 1990; Rolls, Thorpe & Maddison, 1983). De plus, les résultats de ces études suggèrent que les indices contextuels seraient intégrés dans le programme moteur régi par le striatum afin de produire des mouvements plus rapides et plus perfectionnés. Par exemple, à l'aide de stimuli externes visuels et auditifs servant à déclencher ou à faire cesser un mouvement, Kimura (1992) a montré une activation significative dans les neurones du striatum. Dans le même ordre d'idée, les travaux de Graybiel et Kimura (1995) mentionnés dans la sous-section précédente, ont suggéré que la plasticité synaptique du mécanisme d'apprentissage S-R de ce système permettrait la modification des programmes moteurs lorsque le contexte le nécessite.

Dans le cadre d'une série d'études cliniques réalisées avec des populations de patients souffrant d'une dysfonction striatale, Georgiou et al. (1994) se sont intéressés à l'importance des indices externes dans la capacité à réaliser des séquences de mouvements chez des groupes de patients MP. Afin d'y parvenir, ils ont utilisé une tâche où le sujet devait appuyer sur des stimuli lumineux disposés en deux rangées (une rangée au-dessus de l'autre), selon une séquence préalablement connue du sujet. Cette tâche a été effectuée sous deux conditions: une première condition «sans» indice lumineux et une deuxième condition «avec» indice lumineux simple ou double. Dans la condition «avec» indice, vraisemblablement utilisée afin de faciliter la réalisation de la séquence, les sujets pouvaient alors percevoir le prochain stimulus dans la séquence (indice simple) ou encore les deux prochains stimuli dans la séquence (indice double), au fur et à mesure qu'ils réalisaient le parcours lumineux. Les résultats ont démontré que les patients du groupe MP sont plus lents à commencer le mouvement sans indice contextuel externe. De plus, à l'inverse des sujets témoins, ils n'ont pas bénéficié autant des indices lumineux (simples ou doubles), tels qu'illustrés par des temps d'exécution similaires dans les conditions «avec» ou «sans» indice. Il est intéressant de souligner que ces résultats vont dans le

même sens que ceux de Jones et al. (1992) chez les patients ayant la MP ainsi que ceux de Bradshaw et al. (1992), qui ont testé un groupe de patients porteurs de la MH dans le cadre d'une tâche presque identique à celle employée par Georgiou et al. (1994, 1993).

En conclusion, cette sous-section sur les modèles fonctionnels du striatum et du cervelet permet de mieux cerner la nature de la contribution striatale au niveau de l'apprentissage moteur. Comme l'indique le modèle actuel le plus complet dans le domaine (Marsden & Obeso, 1994), il semble que le striatum gère deux aspects importants du mouvement soit l'exécution automatique de séquences de mouvement et l'adaptation à une nouveauté contextuelle. La prochaine sous-section aborde les modèles des fonctions cérébelleuses.

Modèles fonctionnels du cervelet. Autrefois identifié par plusieurs auteurs comme le berceau du contrôle moteur, et plus précisément de la coordination des mouvements (Albus, 1971; Boylls, 1980; Braitenberg, 1961, 1967; Braitenberg & Onesto, 1961; Eccles, 1969; Gilbert, 1975; Gilbert & Thach, 1977; Llinas, 1981; Marr, 1969; Pellionisz-Llinas, 1979, 1980), le cervelet fait l'objet d'un nombre croissant de recherches dans le domaine neuroanatomique (Cambier, Masson & Dehen, 1989; Carpenter & Sutin, 1983; Middleton & Strick, 1994; Schmahmann, 1996; Schmahmann & Pandya, 1989, 1991; voir Middleton & Strick, 1997, pour une recension des écrits), animal (Lalonde & Botez, 1990; voir Bloedel et al., 1996; Houk & Wise, 1995, pour une recension des écrits), clinique (Appollonio et al., 1993; Doyon et al., 1997a; Pascual-Leone et al., 1993; voir Botez, 1996; Fiez, 1996; Leiner, Leiner & Dow, 1987, 1989, 1991, 1993, 1995, pour une recension des écrits), ou encore de l'imagerie cérébrale (Decety, Sjoholm, Ryding, Stenberg & Ingvar, 1990; Metter, Kempler, Jackson, Hanson, Riege, Camras, Mazziotta & Phelps, 1987; Petersen, Fox, Posner, Mintum & Raichle, 1988; voir Doyon, 1997, pour une recension des écrits), qui permettent maintenant de dégager une nouvelle conceptualisation de ses fonctions (Inhoff et al., 1989; Inhoff & Rafal, 1990; Ito, 1993; Ivry & Keele, 1992; Paulin, 1993; Schmahmann, 1996; Thach et al., 1992; voir Bloedel, 1992; Bloedel & Bracha, 1997; Doyon, 1997; Thach, 1996, pour une recension des écrits). Cette sous-section traitera d'abord des modèles davantage orientés sur les fonctions

motrices du cervelet pour ensuite enchaîner sur les nouvelles théories du cervelet qui tiennent compte de son rôle au niveau de certaines fonctions cognitives.

Au niveau moteur, les positions théoriques peuvent se classifier en deux grandes approches distinctes (voir Llinas, 1981; Thompson, 1986, pour une recension des écrits). La première orientation confère au cervelet un rôle de régulateur central, gérant notamment la coordination motrice. Elle est soutenue par plusieurs chercheurs tels que Eccles, Breitenberg, Pellionisz, Llinas, ou Bloedel et suggère que le cervelet joue un rôle plutôt passif dans le contrôle du mouvement. Par contre, la deuxième approche est appuyée par de nombreux scientifiques tels que Marr, Albus, Ito, Gilbert, Thach, ou Thompson, lesquels entrevoient généralement le cervelet comme étant le siège de l'apprentissage moteur. Dans cette ligne de pensée, le cervelet joue un rôle actif au niveau des fonctions motrices.

Parmi les positions théoriques récentes les plus influentes, celles de Ito (1993), Thach et al. (1992; voir Thach, 1996, pour une recension des écrits), Bloedel (1992; voir Bloedel et al., 1996, pour une recension des écrits) ne sauraient être passées sous silence. Pour Ito (1993), par exemple, le mécanisme de plasticité synaptique, c'est-à-dire le phénomène de DLT propre aux cellules retrouvées dans le cervelet, pourrait être à la base du rôle de cette structure dans l'apprentissage moteur. Les travaux de Thach et al. (1992) ont suggéré, quant à eux, que le cervelet permettrait de coordonner les mouvements simples dans le but de créer un mouvement général exécuté avec grâce. Finalement, tout comme Babinski (1899, 1909), Bloedel (1992) a proposé que le cortex cérébelleux participe «en temps réel» aux opérations requises pour le contrôle de l'activité motrice coordonnée. Tel que mentionné précédemment dans ce chapitre, une recension récente effectuée par Bloedel et al. (1996) a suggéré également que les changements qui surviennent dans la plasticité neuronale lors de l'apprentissage de mouvements volontaires complexes chez l'animal font appel à un circuit distribué comprenant le cervelet et d'autres régions impliquées dans le contrôle du mouvement.

Au niveau cognitif, plusieurs recherches ont proposé que cette structure participe à des fonctions supérieures telles que la motivation et l'émotion (Watson, 1978), le fonctionnement intellectuel verbal et non verbal (Botez, Gravel, Attig & Vézina, 1985),

l'apprentissage verbal (Bracke-Tolkmitt, Linden, Canavan, Rockstroh, Scholz, Wessel & Diener, 1989) et sémantique (Fiez, Petersen, Cheney & Raichle, 1992; Petersen et al., 1988; Raichle, Fiez, Videen, MacLeod, Pardo, Fox & Petersen, 1994), l'organisation visuospatiale (Botez, Botez, Cardu et Léveillé, 1989; Botez et al., 1985; Leiner et al., 1986; Schmahmann, 1996; Steinmetz, Lavond & Thompson, 1989), la capacité de planification (Grafman, Litvan, Massaquoi, Stewart, Sirigu & Hallett, 1992; Kim, Ugurbil & Strick, 1994; Wallesch & Horn, 1990), les fonctions exécutives (Appollonio et al., 1993; Diener, Hore, Ivry & Dighans, 1993; Leiner et al., 1986, 1993, 1995; Schmahmann, 1996; Schmahmann & Pandya, 1991), la capacité à réorienter son attention rapidement dans le cadre d'une tâche d'attention sélective (Akshoomoff et al., 1992) et la détection d'erreurs (Fiez et al., 1992; Flament et al., 1996). Ces recherches sont d'ailleurs appuyées par des travaux récents (Middleton & Strick, 1994, 1997; Schmahmann, 1996) qui ont décrit le substrat neuroanatomique qui serait à la base de la participation du cervelet dans les fonctions cognitives supérieures.

L'une des hypothèses, qui rejoint à la fois la contribution motrice et non-motrice du cervelet, concerne son rôle possible au niveau des mécanismes permettant la coordination motrice des événements sensoriels et moteurs dans le domaine temporel (Braitenberg, 1961, 1967; Brooks & Thach, 1981). Par exemple, une série d'études effectuées entre autres par Ivry et ses collègues (Diener et al., 1993; Ivry, 1992; Ivry & Keele, 1992; Ivry, Keele & Diener, 1988; Jueptner, Rijntjes, Weiller, Faiss, Timmann, Mueller & Diener, 1995; Keele & Ivry, 1987, 1991; Nichelli, Alway & Grafman, 1996; voir Ivry, 1996, pour une recension des écrits) à l'aide de tâches où l'aspect temporel est explicitement manipulé, ont montré que les patients cérébelleux affichent un déficit, notamment lors d'épreuves de production d'intervalles temporels et de perception du temps. À ce sujet, Dichgans et Fetter (1993) ont rapporté que la composition temporelle de la séquence bien ordonnée dans le temps d'un programme moteur complexe est perturbée par une lésion du cervelet. Ces auteurs ont émis l'hypothèse que le cervelet aide à la coordination (ou au «timing»), non seulement «dans», mais aussi «entre» les composantes isolées de chaque sous-unité d'un mouvement complexe dans les trois plans

de l'espace. De plus, selon eux, le cervelet entrerait en jeu lorsqu'il faut graduer l'importance et la durée de chaque action musculaire impliquée dans un mouvement.

D'autre part, plusieurs études ont évalué le rôle du cervelet dans l'exécution de mouvements sériels (Diener et al., 1993; Inhoff et al., 1989; Inhoff & Rafal, 1990). Par exemple, dans une étude où les sujets devaient exécuter une séquence de mouvements en réponse à un signal sonore, Inhoff et al. (1989) ont obtenu des résultats qui sont en accord avec l'implication du cervelet dans la programmation motrice de la vitesse, la fluidité et la précision avec laquelle un mouvement séquentiel est exécuté. De leur côté, Diener et al. (1993) soulignent que le cervelet contribue à la synchronisation de chacune des composantes d'un mouvement en ajustant l'amplitude de l'action musculaire et en coordonnant la séquence de l'action des agonistes et des antagonistes lors du mouvement.

En conclusion, il est intéressant de voir à quel point les études récentes suggérant que le cervelet participe à plusieurs fonctions cognitives forcent les auteurs à redéfinir les conceptualisations strictement «motrices» de cette structure. Plus encore, l'implication du cervelet dans diverses fonctions cognitives pourrait être à la base d'une contribution possiblement distincte comparativement à celles du striatum dans l'apprentissage. Voyons maintenant les rares modèles théoriques qui ont tenté d'intégrer les fonctions de ces deux structures.

Modèles intégrateurs du striatum et du cervelet dans l'apprentissage. Bien qu'il soit possible de recenser quelques modèles théoriques portant sur la contribution spécifique du striatum et du cervelet dans l'apprentissage moteur (Akshoomoff et al., 1992; Burton, 1990; Houk & Wise, 1995; Jueptner et al., 1997; Pascual-Leone et al., 1993; Wise & Houk, 1994), il n'existe actuellement qu'une seule étude empirique qui ait suggéré que la nature de la participation de ces deux structures dans l'apprentissage d'habiletés soit dissociable (Pascual-Leone et al., 1993). D'abord, au niveau théorique, Wise et Houk (1994; Houk & Wise, 1995) ont présenté un modèle spéculatif des interactions entre le cortex moteur, le cervelet, les ganglions de la base et certaines autres structures associées au contrôle du mouvement. D'après ces auteurs, ce dernier se construit selon trois niveaux distincts d'organisation. Au premier niveau, on retrouve la

notion de «modules» qui représentent des circuits dynamiques reliant le cortex avec les ganglions de la base (cortico-striatal), le cervelet (cortico-cérébelleux), le thalamus (cortico-thalamique) et d'autres régions du cortex cérébral (cortico-cortical), en particulier du cortex pré moteur. Le deuxième niveau d'organisation comprend des «arrangements de modules» («modular array») qui consistent tout simplement en des regroupements de modules de la même sorte (par exemple, un arrangement de modules cortico-cérébelleux). Finalement, les auteurs proposent l'existence d'un troisième niveau appelé «système», qui contient plusieurs types d'arrangements de modules et qui opère de façon parallèle dans le contrôle du mouvement.

L'intérêt soulevé par le modèle de Wise et Houk (1994; Houk & Wise, 1995) provient du fait qu'il précise la nature spécifique du rôle des circuits cortico-striataux et cortico-cérébelleux. Alors que le circuit constitué d'arrangements de modules cortico-cérébelleux serait responsable des paramètres favorisant une exécution fluide et progressive des programmes moteurs (emmagasinage, récupération et exécution des programmes moteurs), celui constitué d'arrangements de modules cortico-striataux serait impliqué au niveau de la reconnaissance du contexte dans lequel un mouvement est exécuté. Ils ont décrit le contexte comme incluant des aspects tels que l'état de l'organisme (le plan moteur en cours), le désir de poser un geste, les actions à venir (les plans moteurs à venir), la position de la cible d'action et les inputs sensoriels qui sélectionnent et déclenchent les programmes moteurs (habileté à tenir compte de la nouveauté contextuelle). Cette spécification du rôle du circuit cortico-striatal rejoint celle proposée par Marsden et Obeso (1994) qui ont conféré un rôle dualiste au striatum à savoir celui de l'assemblage des plans moteurs et de l'ajustement de ces plans en fonction du contexte. Il est à noter que cette fonction donnée au striatum pourrait être à la source des symptômes d'akinésie rencontrés chez les parkinsoniens, lesquels s'expriment par une lenteur à initier ou à exécuter un mouvement. En effet, ces symptômes pourraient s'expliquer par une diminution de l'habileté à utiliser les informations contextuelles avant de poser un geste (Houk, 1992).

D'autres éléments théoriques appuyant les paradigmes présentés plus haut sur le rôle spécifique du striatum et du cervelet ont été apportés par Burton (1990). En effet,

tout comme Marsden (1982; Marsden & Obeso, 1994), Burton (1990) affirme que le circuit cortico-striatal est impliqué dans l'élaboration des programmes moteurs. Toutefois, ce dernier ajoute que le cervelet assurerait une transition fluide entre les composantes des programmes moteurs dans le mouvement. Les travaux de Akshoomoff et al. (1992) renforcent cette hypothèse en soulignant que le cervelet, en opérant de façon parallèle avec le cortex préfrontal, serait chargé d'optimiser le déroulement des plans moteurs élaborés par les ganglions de la base. Enfin, en se basant sur des données obtenues à l'aide de la TEP qui suggèrent que, contrairement au striatum, il existe une relation entre le degré d'activation à l'intérieur du cervelet et la vitesse (Jenkins et al., 1994) ou encore la force du mouvement (Dettmers, Fink, Lemon, Stephan, Passingham, Silbersweig, Holmes, Ridding, Brooks & Frackowiak, 1995), Jueptner et al. (1997) ont récemment proposé que le cervelet joue un rôle plus important que le striatum au niveau des paramètres responsables de l'exécution du mouvement. Cette suggestion a d'ailleurs été appuyée par le fait que, contrairement à une stimulation des territoires thalamiques du striatum, une microstimulation des territoires thalamiques du cervelet évoque un mouvement (Miall, Price, Passingham, Winter & Stein, 1993).

Les élaborations théoriques mentionnées ci-dessus sont appuyées par les travaux de Pascual-Leone et al. (1993). En effet, à l'aide d'une version adaptée de la tâche de séquence visuelle répétée, Pascual-Leone et ses collègues (1993) ont observé une divergence entre le profil des résultats chez les patients des groupes MP et CE. Alors qu'environ 25% des patients du groupe MP ont réussi à détecter une séquence, aucun patient du groupe CE n'affichait une connaissance déclarative de la séquence implicite. À l'inverse des patients porteurs d'une lésion cérébelleuse, qui montraient un déficit d'apprentissage procédural, la performance des patients ayant la MP ne différait pas significativement des sujets témoins à cette tâche. Aussi, les résultats ont montré que seuls les patients MP ont su utiliser leurs connaissances déclaratives de la séquence pour améliorer leur niveau de performance. Bien que les auteurs concluent que le striatum et le cervelet sont tous deux impliqués dans l'apprentissage d'habiletés visuomotrices, ils mentionnent que leurs rôles respectifs pourraient être différents. Selon eux, le circuit striato-frontal aurait pour fonction de faciliter l'accès à l'information déclarative afin de

parvenir à un apprentissage de la séquence alors que le circuit cérébelleux jouerait un rôle crucial dans les fonctions cognitives impliquant une séquence de mouvements.

**Résumé.** Un examen différentiel des modèles recensés plus haut permet d'identifier quatre dissociations possibles quant à la nature de la contribution possible du striatum et du cervelet dans l'apprentissage d'habiletés. Premièrement, les recherches de Marsden (1982, 1987; Marsden & Obeso, 1994) ont suggéré que le striatum n'est pas responsable du moment précis («timing») de la contraction musculaire lors du mouvement. Cependant, le cervelet pourrait jouer un rôle important dans ce type de fonctions (Dichgans & Fetter, 1993; Diener et al., 1993; Ivry, 1992; Ivry & Keele, 1992; Ivry et al., 1988; Jueptner et al., 1995; Keele & Ivry, 1987, 1991; Nichelli et al., 1996; voir Ivry, 1996, pour une recension des écrits). Deuxièmement, les travaux de Marsden ont suggéré que le striatum pourrait participer à l'organisation d'une série de programmes moteurs séquentiels alors que plusieurs études ont indiqué que le cervelet jouerait un rôle important dans la programmation motrice de «l'exécution» de mouvements sériels (Diener et al., 1993; Inhoff et al., 1989; Inhoff & Rafal, 1990). Dans cette dernière hypothèse, il semble que la différence se situe entre la capacité à organiser des programmes (striatum) et la capacité à les exécuter correctement de façon rapide, précise, fluide et gracieuse (cervelet). Troisièmement, plusieurs études ont avancé l'hypothèse selon laquelle le striatum posséderait la capacité à adapter le programme moteur en fonction d'une nouveauté contextuelle (Georgiou et al., 1994; Graybiel & Kimura, 1995; Kimura, 1992; Marsden & Obeso, 1994) alors que cette fonction ne semble pas vraisemblablement attribuable au cervelet. Finalement, contrairement aux recherches qui ont proposé que le striatum serait impliqué dans l'élaboration des programmes moteurs (Graybiel & Kimura, 1995; Knowlton et al., 1996; McDonald & White, 1993; Singh et al., 1993), plusieurs auteurs ont suggéré que le cervelet ne semble pas être le site de storage de l'engramme moteur (Dichgans & Fetter, 1993; Doyon et al., 1997b; Flament et al., 1996; voir Bloedel, 1992; Bloedel et al., 1996; Doyon, 1997, pour une recension des écrits). Enfin, quelques rares modèles qui ont intégré les fonctions du striatum et du cervelet ont été proposés. En accord avec les modèles fonctionnels du striatum et du cervelet, ces derniers indiquent

que le striatum serait impliqué au niveau de la reconnaissance du contexte dans lequel un mouvement est exécuté (Houk & Wise, 1995; Wise & Houk, 1994) et de l'élaboration des programmes moteurs (Burton, 1990). De son côté, le cervelet serait davantage impliqué au niveau des variables qui facilitent l'exécution des programmes moteurs (Burton, 1990; Houk & Wise, 1995; Wise & Houk, 1994). Finalement, les travaux de Akshoomoff et al. (1992) ont renforcé ces hypothèses en soulignant que le cervelet, en opération de façon parallèle avec le cortex préfrontal, serait chargé d'optimiser le déroulement des plans moteurs élaborés par les ganglions de la base.

### Conclusion

Après avoir présenté un résumé des conceptualisations contemporaines de la mémoire, de la contribution du striatum et/ou du cervelet dans l'apprentissage d'habiletés ainsi qu'une revue des modèles actuellement disponibles sur les fonctions de ces structures, ce chapitre laisse plusieurs questions en suspens quant à la nature de la contribution du striatum et du cervelet dans l'apprentissage d'habiletés visuomotrices. Toutefois, les trois prochains chapitres de cette thèse présentent des résultats empiriques qui permettent, d'une part, de mieux cerner la contribution de ces structures dans l'apprentissage d'habiletés et, d'autre part, de fournir des données qui appuient certains des modèles théoriques actuels. Ainsi, le prochain chapitre présente les résultats de travaux effectués dans le but de mieux comprendre le rôle du striatum dans l'automatisation d'un séquence visuelle répétée. Quant au Chapitre IV, il rapporte la première double dissociation fonctionnelle entre le striatum et le cervelet dans le domaine de l'apprentissage visuomoteur. Enfin, le Chapitre V dévoile les résultats d'une étude préliminaire visant à approfondir le rôle de ces structures dans l'adaptation à un changement contextuel.

### **CHAPITRE III**

#### **ROLE OF THE STRIATUM IN THE AUTOMATIZATION OF A VISUOMOTOR SEQUENCE USING A DUAL-TASK PARADIGM**

## Introduction

As described earlier in Chapter II, a large body of research has now demonstrated the existence of a functional dissociation between the declarative and the procedural memory systems (see Squire & Knowlton, 1995, for a review). Although the anatomical substrate involved in the procedural memory system still remains a source of debate, there is increasing evidence from both animal and human studies which suggest that the striatum and the cerebellum, in concert with their associated structures (e.g., motor cortical regions in the frontal cortex), participate in this type of memory (see Bloedel, 1992; Doyon, 1997; Graybiel, 1995; Graybiel & Kimura, 1995; Leiner et al., 1993; Moscovitch et al., 1993; Thach et al., 1992, for reviews). Recent investigations in humans have demonstrated that these two structures do not only play a critical role in the early learning stages of a visuomotor skill (Friston et al., 1992; Jenkins et al., 1994), but that they may also participate in the "automatization" phase of the acquisition process (Doyon et al., 1997a, 1996; Grafton et al., 1994; Jenkins et al., 1994; Rauch et al., 1995; Seitz et al., 1990; see also Doyon, 1997, for a review). Current theories suggest that in the latter learning phase, the execution of the task has become more automatic after extended practice, hence reducing the mental effort and attention required to perform the skill, as well as the load on the subject's working memory capacity (Anderson, 1990).

The present chapter focuses on the role of the striatum in the automatization of a visuomotor sequence using a dual-task paradigm. A literature review on the cognitive processes involved in the automatization of a skill is first presented, followed by a section on empirical work conducted using dual-task paradigms. Further subsections explore the data on the nature of interference as a function of the characteristic of the task, and the effect of practice on resource capacities. Finally, I conclude with the presentation of experimental data supporting the role of the striatum in the automatization process.

### The Process of Automatization

Automatization as a cognitive process during the learning of a skill has been investigated since the turn of the century. In 1896, Solomons and Stein defined automaticity as a process for which there is a rapid increase in the speed of performance, a significant reduction in the amount of effort and attention required to perform a task, and a lack of memory for the automatically processed events. Although a few additional characteristics have been added in recent years (e.g., resistance to intrusion, highly stereotypical, difficult to modify, activated without intention, etc.), the observations made at the time still provide the core set of attributes that typify automatic processing.

In an extensive series of studies, Schneider and Shiffrin (1977; see also Shiffrin & Schneider, 1977) have demonstrated that automatic processing for perceptual stimuli in normal control subjects, develops when they are required to respond in a consistent mapping condition in which the target stimuli are always selected from one set of items, and the distractors are selected from another. Based on such findings, these authors proposed a two-process theory to account for changes in performance with practice: 1) an automatic process, which appears as a result of extensive practice with consistent stimulus-response relations, and 2) a controlled process, which occurs in novel situations or in situations where stimulus-response relations are inconsistent over time. They characterized the first one as fast, parallel, and not limited by short-term memory capacity or attention, whereas the second was thought to be slow, serial, and capacity limited. Later, Schneider (1985) suggested a four-stage description of the changes that occur in performance with automatization. During the first phase, controlled processing predominates. With several repetitions, controlled and automatic processing co-occur and performance becomes a mixture of the two processing modes. The third phase is characterized by a lack of memory-load effect on performance (as revealed by dual-task experiments), even if subjects are still allocating attention to perform the task. Finally, performance obtained in the fourth phase expresses pure automatic processing. This conceptualization is in line with recent investigations (Cohen, Dunbar, McClelland, 1990; Logan, 1985; MacLeod & Dunbar, 1988), which suggest that automaticity may be better

characterized by a continuum rather than a dichotomy because the properties associated with the automatic processing appear to occur at different rates during learning.

Schneider and Shiffrin's (1977) description of the automatization process is somewhat similar to that of Anderson (1983a, 1990), who has distinguished three stages in the development of a cognitive skill: 1) a cognitive stage, in which a description of the procedure is learned, 2) an associative stage, in which a method for performing the skill is worked out, and 3) a proceduralization stage, in which the skill becomes more and more rapid and automatic. Although this author has identified a number of factors that can modulate the effect of practice (e.g., spacing of practice trials, method of learning a skill effectively, and variables that affect the rate of learning), his most significant contribution to our current understanding of the automatization process during cognitive skill learning, comes from his recent account of the Adaptive Character of Thought model (ACT) (Anderson, 1996). In a series of investigations, Anderson (1982, 1983b, 1987) described the acquisition and improvement of complex procedural skills, such as solving geometric problems, in terms of the ACT-production system theory. According to this framework, procedural skills are initially developed through the interpretation of declarative knowledge, similar to interpreting and executing the different steps of a new recipe. Executing procedures at this declarative stage typically requires effort, is slow, and error-prone. With continued interpretation of declarative knowledge as procedural actions, however, another memory representation is thought to appear in the form of productions. A production's action is immediately executed whenever necessary conditions are met. Finally, the establishment of direct condition-action associations, defined as proceduralization by Neves and Anderson (1981), is used to explain the improvement in performance after extended practice of a skill.

Neves and Anderson (1981), as well as Anderson (1982, 1983b) have also tried to explain the continued skill improvements with extended practice in terms of transformations or compilations of initial productions. Anderson described two major mechanisms named composition and strengthening. The former is a process that combines sequential productions into a single but more complex production, whereas the latter involves increasing the speed with which productions are executed. As Anderson

(1983b) pointed out, automaticity can be represented by the compilation and strengthening of productions. Automatic behaviors undergo compilation to such an extent that execution of these productions occurs without conscious control. In this view, the results of Woltz (1988), who made predictions concerning the distinct roles of working memory at different stages of skill acquisition using a procedural learning task, have important implications for the theories on automaticity. His results suggest that development of automatic skills after extended practice involves release from processing limits associated with controlled attention.

According to Logan (1988), automatization is defined as the acquisition of a domain-specific knowledge base, which is composed of representations ("instances") of each exposure to the task. Based on the Instance Theory (IT), practice and consistency of the stimuli are important factors that mediate the acquisition process. The IT of automaticity claims that people learn what they attend to, and express what they have learned, if they attend to the same things in the same way. This is in line with other authors who have argued that automatic processing occurs for task components rather than the tasks themselves (Jonides, Naveh-Benjamin & Palmer, 1985; Kramer & Strayer, 1988; see Jonides, 1981, for a review). In this framework, the distinction between encoding and retrieval is also important in understanding the acquisition and expression of automaticity because automatic performance emphasizes speed, and therefore may not be sensitive to stimuli that are retrieved slowly (Logan, Taylor & Etherton, 1996). Furthermore, considering that the IT assumes that automatic performance is based on retrieval of representations of past solutions from memory (what is also called a memory-based theory, see Logan, 1988, 1990, 1992), what "gets into" those representations during learning, and what is "taken out" of them during automatic performance, are key questions. An application of this was used in a study conducted by Strayer and Kramer (1994a, 1994b), where the contribution of strategic and data-driven factors to skilled performance was evaluated by manipulating the predictability of the class of stimuli used in a memory search task. Overall, they found that skilled performance can be conceptualized as an interaction between enhanced evidence accumulation and strategies in setting of response criteria. Finally, the proponents of the IT are also interested in the

processes involved in the automatization of skills. For example, in a recent study, Logan and Etherton (1994) examined the role of attention in automatization via seven experiments in which subjects searched 2-word displays for members of a target category in divided-attention, focused-attention, and dual-task conditions. Their results stressed the important role of attention in automatization as it appears to be capital for performance assessed under divided-attention and dual-tasks conditions (Neely, 1977).

### Dual-task Paradigms as Means to Examine the Process of Automatization

According to several investigators (Bahrick & Shelly, 1958; Bornemann, 1942a, 1942b; Brown & Poulton, 1961; Mohnkopf, 1933), the most important operational criterion used for automaticity, is the reduction of dual-task performance decrements. An extensive review of the litterature indicates that dual-task performance has not only been an object of study by itself, but has also been widely used as a tool for the assessment of automaticity and mental load (Heuer, 1996; Neumann, 1984; Nicolson & Fawcett, 1990; Singer, Lidor & Cauraugh, 1993; Yap & van der Leij, 1994). For example, Bahrick and Shelly (1958) found that the performance of their subjects on a reaction time task did not differ between a random condition, and another condition comprising a predictable sequence of stimuli. However, performance on a secondary task (e.g., a task completed concomittently with their reaction time task), discriminated the two conditions as their results revealed that with practice, the repeated sequence condition required fewer cognitive resources. The authors suggested that dual-task paradigms were sensitive to differences in automation.

An obvious reason why researchers have used the dual-task methodology to examine the level of automatization of a skill, lies in the fact that it allows to test for the attentional resources that can be devoted to a second cognitive task as subjects are becoming more efficient at performing a learned behavior (Baddeley, 1992; Brown & Carr, 1989; Brown & Marsden, 1991; Grafton et al., 1995; Hazeltine et al., 1997; MacLoed & Dunbar, 1988). Another reason suggested by Wickens (1984) pertains to the fact that the dual-task paradigm presents a high degree of face validity. In fact, it is very

difficult to investigate the automatization hypothesis with a single task since researchers cannot manipulate the actual primary task the subjects are performing. For example, Bahrick, Noble and Fitts (1954) used a secondary task to investigate the differences in learning of a perceptual-motor primary task that were not revealed by the primary-task performance. They used a secondary task as a means to assess mental workload. The difference between conditions was better revealed by relying on secondary-task rather than upon a primary-task performance alone.

Also, the growing interest of the applied community in the concept of mental workload raised interesting questions that are still examined today such as: "How busy is my operator?" "Can he/she handle any additional tasks?" A direct consequence of this interest was a massive increase in the number of studies aimed at better understanding the specific cognitive processes involved in performing dual-tasks. In 1984, Wickens adopted the resource metaphor to account for the role of attention in time-sharing between tasks. This concept emphasized the divisibility of attention: two activities will demand more resources than a single activity, and so there will be a greater deficiency between supply and demand in the former case. The resource metaphor also proposed that some operations might require different resources. An example of separate resources is provided in terms of the distinction between verbal and spatial slave systems in Baddeley and Hitch's working memory model (1974). According to this model, working memory provides a work-space and temporary storage function for use in on-line cognition (or information processing) via a modular structure of at least three functional subsystems (Baddeley, 1986, 1990; Baddeley & Hitch, 1974; Baddeley & Lieberman, 1980). Verbal speech-based information is dealt with by the articulatory loop, a slave system thought to act as a subvocal rehearsal buffer (Baddeley, Thomson & Buchanan, 1975; Vallar & Baddeley, 1982), while the visuospatial sketch pad (VSSP) has been associated with a mechanism specialized in short-term storage of visuospatial material (Baddeley, Grant, Wight & Thomson, 1975; Baddeley & Lieberman, 1980; Jonides, Smith, Koeppen, Awh, Minoshima & Mintun, 1993; Logie, 1986; Logie, Zucco & Baddeley, 1990). These two slave systems are believed to be deployed and supervised by a limited capacity central executive, supposedly involved in reasoning and decision making.

Much empirical evidence supporting the existence of sub-components in the working memory system (Farmer, Berman & Fletcher, 1986; Logie et al., 1990; Salway & Logie, 1995; Smyth & Pelky, 1992; Toms, Morris & Foley, 1994) has stemmed from the work of Wickens (1984). This author relied on the hypothesis of multiple resources theory, which suggests that instead of one central "pool" of resources with satellite structures, humans possess several different capacities with resource properties. According to this researcher, cognitive resources may be defined by three dichotomous dimensions: early vs late processes, auditory vs visual encoding, and spatial vs verbal modalities. Two direct consequences of this proposition is that, the more resources tasks share, the more they should interfere, and that practice should modify the resource capacities. The next subsections respectively addresses these issues.

Strength of Interference as a Function of the Task Characteristics. Much work has been done to better understand the conditions under which certain tasks will and will not compete for resources. In everyday life, we find it more difficult to read two messages at once than to read one while listening to the other. Within this framework, the competition between two tasks of similar structure is said to produce greater interference. In 1980, Baddeley and Lieberman investigated whether the subsystem of working memory responsible for imagery was visual or spatial in nature. They found that a spatial tracking task with no visual component (pointing to a moving sound source) had an effect similar to that of visual pursuit tracking on performance of Brooks' memory tests (1967). However, a visual task with no spatial component (brightness judgments) had no specific effect on imagery. These findings suggested a subsystem based primarily upon spatial coding. Toms and colleagues (1994) also reported two experiments using the dual-task methodology, which showed that exposure to irrelevant visual input during encoding selectively disrupted performance on a spatial task (the Brooks spatial matrix task), but not on a verbal version of the task. The extent of the disruption was shown to be independent of the visual complexity of the material, its similarity with the to-be-remembered information, or a change in the matrix patterns. Along the same line, Logie (1986) reported the results of four experiments conducted to develop a simple technique

for the study of visuospatial processing within the working memory framework suggesting that unattended visual material has privileged access to the mechanism(s) involved in short-term visuospatial processing and storage.

More recently, Logie and colleagues (1990) reported two experiments in which they examined selective interference in short-term visual memory. In the second of two experiments, the authors combined two span tasks (visual matrix patterns and visually presented letter sequences) with the matrix and verbal versions of Brooks tasks (1967). The results suggested that there was a substantially larger disruption of the span for the matrix patterns when a visuospatial, and not a verbal, task was used. The converse was true for letter span. The data also indicated that the selective interference due to the mode of processing has a stronger effect than the non-selective interference. This was consistent with the notion of a specialized visuospatial mechanism in working memory. Very recently, Salway and Logie (1995) showed that, whether or not performance on a visuospatial or verbal paradigm is disrupted by a secondary task, depends on the nature of the task with which it is combined. Using dual-task methodology, their study demonstrated that the matrix and verbal versions of Brooks tasks (1967) do indeed rely on separate, specialized cognitive resources. However, as they pointed out, when the secondary task is very demanding in terms of general purpose cognitive resources, both the matrix and verbal tasks were performed poorly, suggesting that each of these tasks draw heavily on a common, general purpose resource, as well as on their respective specialist resources.

Effect of Practice on Resource Capacities. Because the strength of interference in a slave system of the working memory model seems to be function of the characteristics of the tasks that are used in dual-task paradigms, some investigators have examined the effect of practice on resource capacities (Moray, 1967). Heuer (1988, 1996) suggested that practice is assumed to modify the performance-resource functions (Norman & Bobrow, 1975), such that the capacity needed for any particular level of performance declines over the course of practice. In other words, practice implies an upward shift of the performance-resource functions, and leaves spare resources to execute another task.

From the simple capacity account of automatization, it follows that the dual-task performance decrement after extensive practice is less than after little practice. This is consistent with Shiffrin and Schneider (1977), who stated that as expertise is gained, some of the processes become relatively automatic, and therefore demand less of the available resources. In the same line of thinking, Wickens (1984) proposed that a task that is more automatic will simply be performed at a level with more "spare capacity". Hence an easy and/or automatic task will be less disrupted by diverting resources from its performance than a task that is difficult and/or unpracticed. Further evidence supporting this phenomenon is provided by Brown and Carr (1989), who investigated the mechanisms that mediate changes in the dual-task interference using a speeded keypressing task. Among other conditions that were investigated, the changes in the amount of interference were examined in relation to the frequency of practice for specific sequences. The results showed that practice reduced the extent of dual-task interference. The authors interpreted these results in light of the formulations of intratask automaticity in which chunking and progressive information encapsulation underlie the formation of an integrated motor program. They proposed that, because working memory is no longer occupied by the sequential control structures of the keypressing task, its storage and rehearsal capabilities become more available to the secondary digit span task, hence reducing the dual-task interference. These results are similar to Schneider and Detweiler's (1988) who demonstrated that dual-task interference and performance on a skill is function of the amount of practice.

### Summary

According to several authors, automaticity refers to the ability to perform a learned task quickly and accurately with little conscious effort or attention. The major experimental evidence for effortless automatic processing comes from dual-task experiments which show that subjects in a practiced condition suffer less interference from a concurrent task compared to others in an unpracticed condition. The usual interpretation is that a practiced task requires fewer cognitive resources than an

unpracticed task. Also, some authors have suggested that dual-task interference could be due to competition for central processing resources in the form of either a single channel, or independent specialized processors. In the latter model, investigators have repetitively demonstrated that the strength of interference is modulated by the characteristics of the task, and that practice can reduce the need for processing resources. The next section describes a study that has specifically addressed these questions in order to better characterize the nature of the contribution of the striatum in incremental skill learning.

### Striatal Contribution to the Automatization of a Visuomotor Skill

In accordance with evidence of a striatal contribution in incremental learning (Apicella et al., 1992; Brotchie et al., 1991a, 1991b; Ferraro et al., 1993; Harrington et al., 1990; Heindel et al., 1988, 1989; Knopman & Nissen, 1991; McDonald & White, 1993; Phillips et al., 1988; Saint-Cyr et al., 1988; Seitz et al., 1990; Wang et al., 1990; Willingham & Koroshetz, 1993; see Butters et al., 1994; Moscovitch et al., 1993; Salmon & Butters, 1995; White, 1997, for reviews), Laforce et al. (1993b; see Doyon et al., 1997a) compared the performance of patients with Parkinson's disease (PD) with that of aged normal controls (ANC) on a version of the Repeated Sequence Test which was developed by Nissen and Bullemer (1987). The latter consists of a visual reaction-time task with a fixed embedded sequence of finger movements. The subjects received four blocks of trials (i.e., 40 presentations of a 10-item sequence) per day over six training sessions, which took place once a week during six consecutive weeks. The results of this study revealed that PD patients with a bilateral striatal dysfunction (i.e., Stages 2-3 of the disease according to Hoehn and Yahr's scale [1967]) failed to improve as much as their matched control subjects, especially in the last three training sessions (see Figure 1). Further analyses, excluding subjects who had acquired full explicit knowledge of the sequence (as measured by their ability to recall perfectly the 10-item sequence), revealed that the impairment was implicit in nature. Moreover, correlational analyses showed that the learning deficit was not related to a cognitive deterioration, mood disturbance, or to a motor deficit *per se*. By contrast, no significant difference between the clinical and

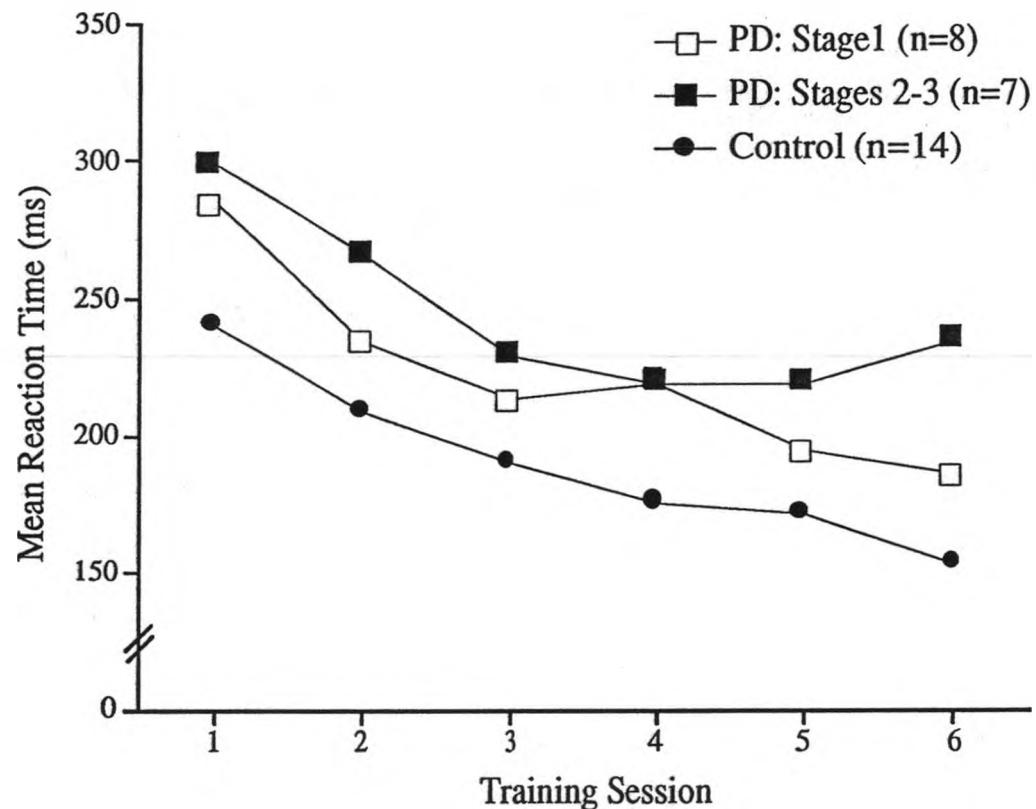


Figure 1. Repeated Sequence Test: Geometric mean reaction times of the six training sessions for both subgroups of PD patients and the group of Control subjects.

control groups was seen with respect to the level of declarative knowledge attained. Based on these findings, Laforce and colleagues (1993b; see Doyon et al., 1997a) proposed that, unlike declarative memory, the incremental acquisition of a visuomotor skill depends upon the integrity of the striatum. Furthermore, because the impairment was observed in the second half of the training sessions, this suggested that this structure was particularly important in the advanced learning stages of a visuomotor sequence, possibly in the "automatization" phase, during which the formation of a non-conscious pattern of response is consolidated (Anderson, 1990, 1996).

Although results of studies from our laboratory (Laforce et al., 1993b; see Doyon et al., 1997a) suggest that the striatum is involved in automaticity, the study described below tested experimentally if the learning deficit observed in patients with a bilateral striatal dysfunction was due to a lack of automatization of the sequence of finger movements using a dual-task paradigm. As mentioned earlier in this chapter, current theories on the automatization process suggest that this learning phase constitutes a step during which an implicit and fluid pattern of responses is being consolidated, and that the processing resources necessary to execute other cognitive tasks become increasingly available with practice (Anderson, 1990; Bahrick & Shelly, 1958; Brown & Carr, 1989; Heuer, 1996; Norman & Bobrow, 1975; Wickens, 1984). Consequently, it was predicted that, if the learning impairment observed in late phases of the learning process of the subgroup of PD patients in Stages 2-3 of the disease in Laforce and colleagues' study (1993b; see Doyon et al., 1997a) is attributable to a problem in the automatization of the visuomotor sequence, only this subgroup should fail to demonstrate a significant improvement in performance on the dual task across the six training sessions, when the first and last sessions of testing with the dual task are compared. In this view, an impairment in the last testing session of the matrices would reflect a reduced level of cognitive resources available to perform the secondary task because of a lack of automatization of the sequence of movements required by the primary task.

## Method

### Subjects

Two groups of PD patients and one group of normal control subjects participated in this study (see Table 1). All PD patients were recruited via the Department of Neurological Sciences at the Hôpital de l'Enfant-Jésus, Québec City (Québec), Canada. They were screened using a basic neuropsychological evaluation in order to exclude those showing signs of depression or dementia. ANC subjects were either acquaintances of the experimenters or volunteers from the community. None of the controls had any positive history of a psychiatric or neurological disorder. Each subject gave informed written consent for their participation in the study, which was approved by the Review Ethics Board of the Hôpital de l'Enfant-Jésus.

#### Parkinson's Disease Group (PD)

This group was composed of 11 patients who received a diagnosis of idiopathic Parkinson's disease. They were divided into two subgroups based on the severity of the disease using the Hoehn and Yahr's (1967) scale: Stage 1 (n=6); Stages 2-3 (n=5). When prescribed, patients were taking optimal levels of levodopa medication at the time of testing. Furthermore, there was no clinical evidence of motor deterioration during testing sessions. Patients with drug-induced parkinsonism, multiple system atrophy, cerebro-vascular disease, epilepsy, history of alcoholism, head injury or tumor, cerebellar disturbances, or disproportionate oculomotor and autonomic dysfunction, were excluded from the study.

Table 1. Subjects' Characteristics.

Variable/Group:	PD: Stage 1* (n=6)	PD: Stages 2-3* (n=5)	ANC (n=9)	
Age (years): Mean (SD)	54.5 (7.0)	55.2 (6.1)	53.7 (4.7)	
Education (years): Mean (SD)	13.5 (6.3)	12.4 (3.6)	13.7 (2.9)	
Sex (Female/Male)	4/2	2/3	4/5	
Diagnostic	Akineto-rigid: Tremor: Mixed:	2 3 1	Akineto-rigid: Tremor: Mixed:	1 1 3
Duration of the disease	0-5 years: 6-10 years: 11-30 years:	6 0 0	0-5 years: 6-10 years: 11-30 years:	0 2 3
Lateralization	Left: Right: Bilateral:	3 3 0	Left: Right: Bilateral:	0 0 5
Medication	L-Dopa:  Anticholinergics Artane: Cogentin: Parsitan:	6  2 0 1	L-Dopa:  Anticholinergics Artane: Cogentin: Parsitan:	5  1 1 2

\*Note. Hoehn & Yahr's Scale (1967).

### Aged Normal Control Group (ANC)

A group of nine normal control subjects was included to match the clinical subgroups with respect to sex distribution, mean age and mean level of education (see Table 1). All of them gave written consent for their participation in the experiment.

### Material and Procedure

#### Primary Task

The primary task consisted of a shortened version of the same repeated sequence test used by Laforce and colleagues (1993b; see Doyon et al., 1997a). This test was administered using a response box that had four identical lights (stimuli) and four buttons, one below (1.75 cm) each light. The lights and buttons were arranged horizontally and equidistant from one another. This box was connected to an IBM PC computer that controlled stimulus presentation and recorded the subject's reaction time and accuracy on each trial (see Figure 2). The subjects were instructed to use the middle and index fingers of each hand, and to keep one finger on each of the four keys. They were asked to press the button corresponding to the light that was illuminated as quickly as possible, while making as few errors as possible. The stimuli remained displayed until the subject made a response. After responding, the light went off, and was followed, 500 ms later, by the display of another stimulus. The order of the stimuli was programmed in a specific sequence of 10 positions. Hence, if one were to designate the four possible locations as 1, 2, 3, and 4 from left to right, the sequence was the following: 4-2-3-1-3-2-4-3-2-1. In this experiment, each block of trials was composed of three continuous repetitions of this 10-position sequence with no pause between them, so that each block appeared as a continuous series of 30 trials. The subjects were not informed of the repeated sequence, nor did they receive feedback concerning the speed and/or accuracy of their responses.

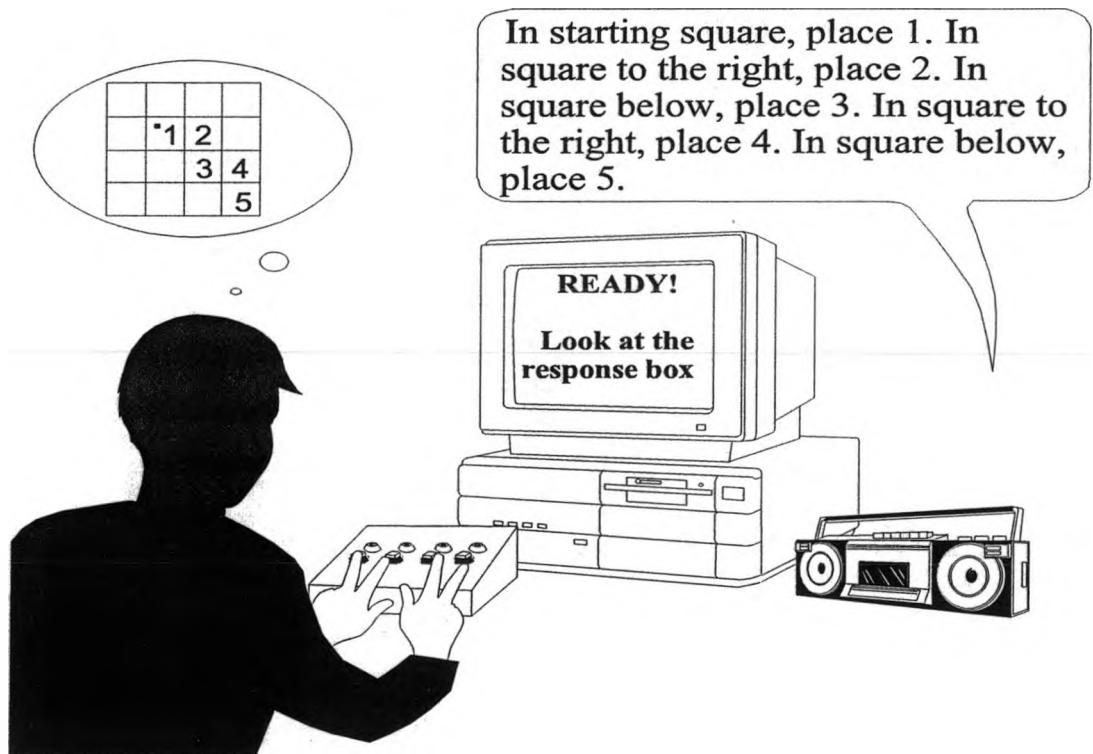


Figure 2. Diagram illustrating the materials used and a representative experimental trial in the dual-task performance situation.

### Secondary Task

This task consisted of the Brooks' visuospatial task originally described by Brooks (1967). As mentioned by Logie et al. (1990), the widespread use of the matrices in the working memory literature has given this task the status of an almost definitive paradigm for studying visuospatial functions (Baddeley & Lieberman, 1980; Logie, Baddeley, Mané, Donchin & Sheptak, 1989; Logie et al., 1990; Quinn, 1994; Quinn & Ralston, 1986). It is also worth noting that, in accordance with current notions of automaticity (Anderson, 1990; Heuer, 1996; Logan, 1992), resource (Wickens, 1980, 1984), and interference (Baddeley & Lieberman, 1980; Logie et al., 1990; Toms et al., 1994), this task was specifically chosen to interfere with the visuospatial processing elicited while executing the repeating visuomotor sequence (Doyon et al., 1996). In this task, subjects were required to keep in mind a visuospatial pattern made of five digits in a 4 x 4 matrix, the location of each digit being dependent upon oral instructions that were communicated to them via an audio cassette player (see Figure 2). They were always asked to place the first digit in the same "Starting" square (2nd row, 2nd column of the matrix), and to position the remaining four digits in separate, but connecting squares. Following completion of the auditory instructions, subjects were given a template on which a matrix was presented, and were then required to indicate the location of the five digits from memory. A different set of instructions representing a unique visuospatial pattern of digits was administered on each experimental trial. A total of 16 different sets of instructions were previously recorded, and divided into two groups of eight sets each (A and B), which were administered during the first and second dual-task sessions.

Before the first dual-task session began, subjects were given appropriate instructions and a number of practice trials to familiarize themselves with the visuospatial secondary task. First, two trials were given where a template of the matrix was placed in view of the subjects, and where they were required to write down immediately the digits in the appropriate squares as they were hearing the instructions. Second, two other practice trials were administered in which a template was again placed in view of the subjects, but this time were asked to wait until the end of the auditory instructions before

writing down the digits in the appropriate squares on the template. Finally, five additional trials were given where the subjects were again required to wait until the end of the auditory instructions before writing down the digits in the squares, but this time, the template was hidden from the subjects' view during the instructions. Performance in this practice condition was used as a control measure of the subjects' ability to perform the Brooks' visuospatial task (1967) alone. The dependent measure of interest was the mean number of directional movements correctly reproduced within a matrix, as originally described by Brooks (1967).

### Experimental Design

This experiment was conducted concomitantly with the study by Laforce et al. (1993b; see Doyon et al., 1997a) described above. In fact, both the primary and the secondary tasks were given concurrently twice in separate testing sessions, which were held after the subjects had received either 40 or 240 presentations of the 10-item repeated sequence, in other words, after Sessions 1 and 6 in Laforce et al.'s study (1993b; see Doyon et al., 1997a). On each experimental trial, they were asked to execute a block of 30 trials of the repeated sequence task, while listening to the auditory presentation of the Brooks visuospatial task. On most trials, the end of the presentation of the visual stimuli in the Repeated Sequence Test (primary task) corresponded with the end of the auditory instructions of the matrix (secondary task). A single trial ended only after the subjects had written down the digits in the appropriate squares of a matrix pattern, that is, after the end of both the auditory instructions of the matrix and the block of trials of the repeated sequence. A total of eight experimental trials were administered in each of the two testing sessions. Finally, the order of presentation of the two groups of instructions (A and B) was counterbalanced within each group of subjects.

## Results

### Primary Task

Results of accuracy obtained in the primary skill learning task showed that subjects in the clinical and control groups were very accurate on this task, the mean number of correct responses per sequence (max = 10) ranging from 8.89 to 9.90. The results of a repeated measures ANOVA also revealed that PD patients made significantly more errors than the subjects in the ANC group,  $F(2,17) = 4.72$ ,  $p<0.05$ . Although there was a main effect of Group, the results of the *post hoc* comparisons did not reach significance, hence suggesting that the two subgroups of patients and the control subjects did not differ in their pattern of performance using this measure.

Figure 3 illustrates the geometric mean reaction times (RT) for the two experimental conditions (single vs dual tasks) in Sessions 1 and 6. An average of the RT for each trial within a sequence was computed, and these RT measures were then averaged within blocks of sequences. In the single task condition, the dependent measure consisted of the average of four blocks of sequences, each block comprising 10 presentations of the 10-item sequence. By contrast, in the dual task condition, the mean RT corresponded to the average of three presentations of the 10-item sequence. The RT of all subjects were transformed to logarithms to reduce skewness in the distribution, and subsequent ANOVA's were performed using this transformation. The results are reported as geometric mean reaction times; this measure corresponds to the mean logarithmic score of each group reconverted to msec. These analyses revealed no main effect of Group. Highly significant effects of practice and of experimental condition were obtained, however, as all subjects were faster on Session 6 than on Session 1, while being slower in the dual- than in the single-task condition (Session:  $F(1,17) = 68.8$ ,  $p<0.0001$ ; Condition:  $F(1,17) = 100.97$ ,  $p<0.0001$ ). None of the double or triple interactions approached significance. These results suggest that, in general, the groups were similarly affected by the dual-task condition in both testing sessions.

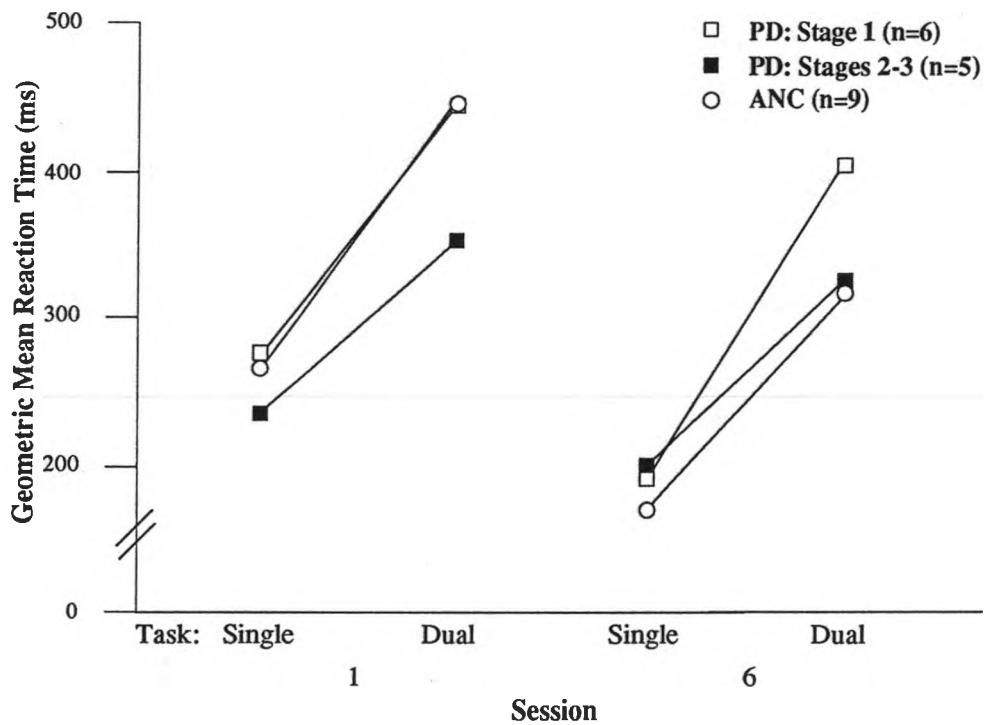


Figure 3. Primary task: Geometric mean reaction times obtained in single- and dual-task conditions for the two sessions of dual-task testing in the two subgroups of PD patients and the group of ANC subjects.

### Secondary Task

The results of the secondary task were analyzed using the mean number of directional movements correctly reproduced by the subjects when performing the Brooks visuospatial task concomittently with the Repeated Sequence Test (see Figure 4). The results of separate ANOVA's for repeated measures revealed that PD patients produced significantly more errors on this test than their controls,  $F(2,17) = 3.8$ ,  $p<0.05$ . In addition, a significant main effect of Session,  $F(1,17) = 5.74$ ,  $p<0.05$ , was observed, indicating that, overall, subjects improved their performance from Session 1 to Session 6. More importantly, and as predicted, a significant Group  $\times$  Session interaction was obtained,  $F(2,17) = 5.72$ ,  $p<0.02$ . Simple main effects were carried out to decompose this interaction and to provide a better understanding of the subjects' performances on each of the training session. The results revealed no significant difference between the three groups in the first session of dual-task testing, hence suggesting that all the groups had the same level of cognitive resources available to complete the matrices at the beginning of the study. On the other hand, the analysis performed on the number of directional movements correctly reproduced in Session 6 yielded a significant difference between the three groups,  $F(2,24) = 7.60$ ,  $p<0.05$ . Further analyses revealed that PD patients in Stages 2-3 obtained significantly lower completion scores on the matrices (Mean: 14.4, SD: 4.10) than subjects in the ANC group (Mean: 25.89, SD: 2.57),  $q = 11.5$ ,  $p<0.05$ , and those in the subgroup of PD patients in Stage 1 (Mean: 24.33, SD: 5.11),  $q = 9.9$ ,  $p<0.05$ . Finally, subsequent analyses revealed that the deficit observed in the PD Stages 2-3 subgroup on this secondary task could not be due to an inability to perform the Brooks' visuospatial task *per se*. This result is supported by the fact that no significant difference in performance between these patients, and their respective ANC subjects, was found with respect to the number of directional movements reproduced in the five matrices that were used in the introduction session to control for the subjects's ability to perform the Brooks's Matrices Test when administered alone.

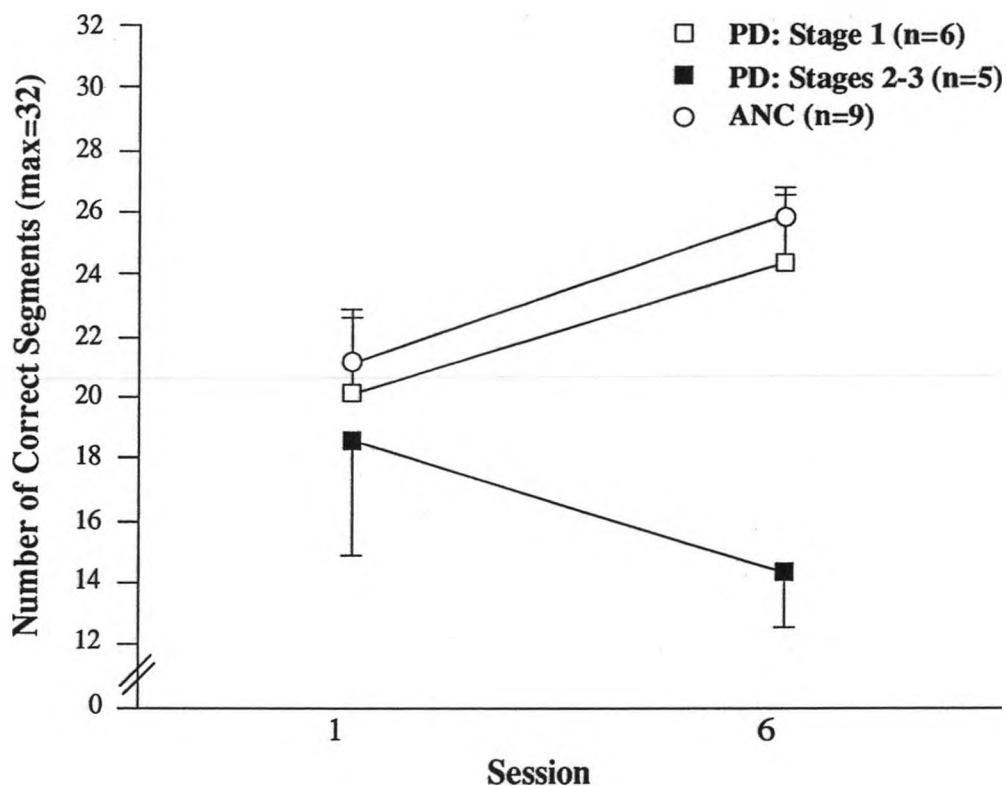


Figure 4. Brooks' visuospatial task: Number of segments correctly reproduced in the two dual-task sessions for both subgroups of PD patients and the group of ANC subjects.

## Discussion

The subjects' level of cognitive resources while executing a visuomotor sequence at different stages of the learning process, was measured using a dual-task paradigm with the Repeated Sequence Test as the primary task, and the Brooks Matrices Test (Brooks, 1967) as the secondary task. The results of the clinical groups on the primary task indicated that, overall, patients did not differ from the control subjects in their ability to execute the repeated sequence when another visuospatial task was introduced. All of the groups showed a significant effect of condition, as they were much slower to respond in the dual-task than in the single-task condition. In addition, the dual-task interference was still evident in Session 6. This suggests that, even after 240 presentations of the 10-item embedded sequence, the patients and control subjects had not achieved complete automatization of the sequence of movements, and thus that they were still in the proceduralization process (see Anderson, 1990). Such a finding is consistent with Karni et al. (1995), who have shown that healthy control subjects could only reach asymptotic performance of a simple 5-item sequence of finger movements (a task much simpler than the one used in this experiment) after 4-5 weeks of daily practice (15-20 minutes/day). More importantly, however, is the fact that the dual-task condition affected the performance of all groups in a similar fashion, suggesting that the results on the secondary task could not be due to a difference in the way subjects were doing the repeated sequence task.

By contrast, the results of the present study demonstrate that, as predicted, patients in Stages 2-3 of PD, were impaired on the Brook's matrices (1967). In fact, only this subgroup failed to demonstrate a significant improvement in performance, when compared on the two sessions of testing of the Brooks's visuospatial task. Further analyses showed that this deficit was not due to an inability to perform the matrices *per se*, because the performance of the patients did not differ from that of the control subjects when this task was administered alone in the practice session, and when it was first given in a dual-task condition (i.e., Session 1). Finally, contrary to recent proposals, such impairment could not be explained by a difficulty in attentional set shifting (Wise, 1996), or a depletion in central processing resources associated with the disease (Brown & Marsden, 1991; Malapani, Pillon, Dubois & Agid, 1994; Schwab, Chafetz & Walker, 1954), because the performance of the clinical and control groups

on Brooks' task did not differ on Session 1. Had this been the case following a striatal dysfunction, significant difficulties in the completion of the secondary task should have been readily observed in the first session of testing. Instead, the fact that only PD patients in Stages 2-3 did not show an improvement from Session 1 to Session 6 on the Brooks visuospatial task, suggests that they did not have the same residual level of cognitive resources to devote to performing the matrices. It is important to note that this impairment was observed in the same group of patients who showed, in our parallel study (Laforce et al., 1993b; see Doyon et al., 1997a), a learning impairment in the late phases of the acquisition process of the repeating visuomotor sequence. Thus, taken together, these results support the hypothesis that the impairment reported by Laforce and colleagues (1993b; see Doyon et al., 1997a) in acquiring such a visuomotor skill after damage to the striatum was due to a lack of automatization of the repeated sequence of movements.

The notion that the striatum is involved in the automatization phase of a visuomotor skill is in accordance with single-cell recording studies (Brotchie et al., 1991a, 1991b; Graybiel et al., 1994; see Graybiel & Kimura, 1995; Schultz et al., 1995a, 1995b, for reviews), which have demonstrated the existence of highly specific firing patterns during the learning of a motor skill. This is also consistent with several imaging studies with PET and fMRI, in which a signal change in blood flow in the basal ganglia has been associated with the learning of a repeating sequence of movements using very similar paradigms (Friston et al., 1992; Jenkins et al., 1994; see Doyon, 1997, for a review). More specifically, this is in accordance with recent PET imaging studies in which peaks of cerebral blood flow (CBF) activity were observed in the ventral striatum when the motor task was well learned (Doyon et al., 1997b, 1996; Grafton et al., 1994; Rauch et al., 1995, 1997; Seitz et al., 1990).

Although the results showing that PD patients with a bilateral dysfunction of the striatum showed no improvement on the Brooks matrices from Session 1 to Session 6 are in line with current evidence mentioned earlier, one specific issue needs to be addressed in order to fully understand the results of the present study. This question pertains to the strength of interference of the secondary task used in this paradigm. In this study, one may ask how efficient the visuospatial matrix interference was in Session 2 of dual-task testing, in interfering with the visuospatial aspects involved in performing the repeating embedded sequence test. First, as mentioned above, the results showed that none of the subjects reached

complete automatization of the primary task, and it is therefore possible that the amount of interference in the last testing session was comparable to the interference in the first session. Although the exact strength of the visuospatial interference in the last dual-task session is unknown, the deficit found in the PD group in Stages 2-3 can shed some light on this issue. In fact, if the secondary task had had no interference power on the primary task, particularly in the last dual-task session, we should not have observed a suppression effect on the matrices performance in any of the groups, since all of them showed similar resource capacities on the secondary task at the first testing session. Consequently, we believe that, as the skills required to execute the Repeated Sequence Test became well learned, PD Stage 1 and ANC subjects were left with more "spare capacity" to realize the matrices, compared to PD patients in Stages 2-3. This explains why performance on the secondary task was less disrupted by diverting resources at the sixth session than at the first session. The results of Laforce and colleagues (1993b; see Doyon et al., 1997a) may therefore be interpreted as a deficit in the automatization process. They can also be understood in light of both the working memory model (Baddeley & Hitch, 1974), and theories on the effect of practice on resource capacities (Heuer, 1996), where it is suggested that practice alters performance-resource functions (Norman & Bobrow, 1975), in that the capacity needed for any particular level of performance declines over the course of practice. These results also concur with Brown and Carr (1989), who suggested that, because working memory is no longer occupied by a primary task, its storage and rehearsal capacities become more available to execute a secondary task.

As proposed by Kahneman (1973), the ideal secondary-task technique is one that uses a battery of secondary-task measures sensitive to different resources in the system. The various secondary-task workload measures may, of course, be evaluated in terms of their likelihood of intrusion. Although this study was conducted with only one type of interfering task, further research addressing this specific issue would be helpful in fully understanding the intrusive power of the task employed. Finally, in a methodological assessment and evaluation of dual-task paradigms, Fisk, Derrick and Schneider (1987) outlined three incorrect assumptions, often implicitly made about dual-task experiments to assess mnemonic processes, and established three criteria for dual-task experiments that draw inferences from secondary-task decrement. First, these authors suggested that researchers pay attention to resource trade-offs between tasks. Second, the resource demands of both tasks needed to be evaluated before

the study, and third, the need to evaluate the resource sensitivity of the secondary task. Future research taking these three factors into consideration should contribute significantly to investigations on automaticity in clinical populations.

#### Final Comment

It is important to mention that the results presented in this chapter are part of a larger study (Doyon et al., *in press*), which not only investigated the effects of PD, but of lesions to the cerebellum and the frontal lobes on the automatization of a visuomotor skill as well. In the latter experiment, Doyon and colleagues (*in press*) reported similar impairment in patients with cerebellar damage, but not in those with frontal-lobe lesions. The results also showed that, compared to ANC subjects, PD patients who converted from Stage 1 to Stage 2 (PD-CS) of the disease (hence suggesting further striatal degeneration), as well as those with damage to the cerebellum, did not show as much retention of the ability to produce the repeating visuomotor sequence, approximately one year after they had been exposed to extensive training of this skill (Doyon et al., 1997a). Thus, in accordance with the results presented in this chapter, such a retention impairment was only observed in groups of patients who had previously demonstrated a learning impairment in the late phases of the acquisition process (Doyon et al., 1997a), due to a possible lack of automatization of the sequence of movements.

To our knowledge, the latter investigations constitute the first demonstration in clinical populations, that an impairment in the incremental learning of a visuomotor skill following a dysfunction in the striatum may be due to a difficulty in the automatization process of a skill. Together with findings from previous investigations that demonstrated an impairment in the early stages of skill acquisition on a variety of skill learning tasks following damage to the striatum or the cerebellum (e.g., Ferraro et al., 1993; Saint-Cyr et al., 1988), these results suggest that both structures are involved in all stages of the learning process, including the automatization phase. Further research will be needed, however, to better elucidate the nature of their contribution in the automatization of a repeating visuomotor sequence, as well as other types of skills.

## CHAPITRE IV

### DISTINCT FUNCTIONAL CONTRIBUTION OF THE STRIATUM AND THE CEREBELLUM TO VISUOMOTOR SKILL LEARNING

**Distinct Functional Contribution of the Striatum and the Cerebellum to Visuomotor  
Skill Learning**

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**Running title: Striatum vs Cerebellum in Skill Learning.**

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#### Author's Note

This work served as partial fulfillment of the requirements for a doctoral degree at the Department of Psychology, Laval University, Québec City (Québec), Canada. It was supported in part by a scholarship from "La Fondation de l'Université Laval" to Robert Laforce, Jr., and by a grant from the Natural Sciences and Engineering Council of Canada (OPGIN-012) to Dr. Julien Doyon. We are grateful to the patients and control subjects who participated in the present study. Also, we would like to address special thanks to Joanne Roy for her help in various aspects of this research. Thanks are also addressed to Rhonda Amsel for her statistical advice, and to all the members of the Groupe de recherche en réadaptation physique, IRDPQ, site François-Charon, Québec City (Québec), Canada, for their support.

### Abstract

The aim of this study was to examine the distinct contribution of the striatum and the cerebellum in visuomotor skill learning. The performance of patients in early (Stage 1) or advanced stages (Stages 2-3) of Parkinson's disease (PD), and of a group of patients with damage to the cerebellum (CE) was compared, respectively, to that of a group of aged (ANC) and young (YNC) matched normal controls on a random version of the Serial Reaction Time task (SRT), as well as on an adapted version of the Mirror-Tracing Test. In the former task, subjects were asked to press a button located to the right of the stimulus that was illuminated whereas, in the latter, they were required to trace a series of complex figures which consisted of the juxtaposition of three simple figures that they had either practiced prior to testing (Practiced condition), or had never traced individually before (Unpracticed condition). The results revealed no significant difference between the CE and the YNC groups on the random version of the SRT task, whereas both groups of PD patients were impaired on this task when compared to the ANC group. By contrast, only patients in the CE group failed to show a facilitation effect when tracing the figures in the practiced vs unpracticed conditions. For the first time, these findings provide behavioral evidence of a double functional dissociation between the striatum and the cerebellum in acquiring visuomotor skilled behaviors. In accordance with existing theoretical models, these results therefore suggest that the striatum plays a critical role in perceptivomotor learning mechanisms based on stimulus-response types of associations, whereas the cerebellum is preferentially involved in the ability to integrate separate learned movements into a fluid sequence.

## Introduction

A considerable number of investigations in both animals and humans have demonstrated that the striatum and the cerebellum play an important role in the ability to acquire skilled behaviors through practice (see Bloedel, 1992; Graybiel, 1995; Graybiel & Kimura, 1995; Leiner, Leiner & Dow, 1993; Moscovitch, Vriezen & Goshen-Gottstein, 1993; Thach, Goodkin & Keating, 1992, for reviews). In humans, pathological degenerative processes affecting the striatum (as in Parkinson's [PD] or Huntington's [HD] diseases), or circumscribed damage to the cerebellum, have been shown to produce an impairment on a variety of skill learning tasks, especially in the visuomotor modality (Bylsma, Brandt & Strauss, 1990; Corkin, Growdon & Koroshetz, 1992; Doyon, Gaudreau, Laforce, Castonguay, Bédard, Bédard & Bouchard, 1997a; Doyon, Laforce, Bouchard, Gaudreau, Roy, Poirier, Bédard, Bédard & Bouchard, in press; Ferraro, Balota & Connor, 1993; Harrington, York Haaland, Yeo & Marder, 1990; Heindel, Butters & Salmon, 1988; Heindel, Salmon, Shults, Walicke & Butters, 1989; Knopman & Nissen, 1991; Pascual-Leone, Grafman, Clark, Stewart, Massaquoi, Lou & Hallett, 1993; Roy, Saint-Cyr, Taylor & Lang, 1993; Saint-Cyr & Taylor, 1992; Saint-Cyr, Taylor & Lang, 1988; Sanes, Dimitrov & Hallett, 1990; Singh, Metz, Gabrieli, Willingham, Dooley, Jiang, Chen & Cooper, 1993; Willingham & Koroshetz, 1993; see Butters, Salmon & Heindel, 1994; Salmon & Butters, 1995, for reviews). These clinical findings have also been supported in several studies with healthy control subjects using modern brain imaging techniques such as positron emission tomography (PET) or functional magnetic resonance imaging (fMRI), in which hemodynamic changes have been observed in the striatum and/or the cerebellum during the incremental acquisition of visuomotor skills (Doyon, Karni, Song, Adams, Maisog, Ungerleider, 1997b; Doyon, Owen, Petrides, Sziklas & Evans, 1996; Flament, Ellermann, Kim, Ugurbil & Ebner, 1996; Grafton, Mazziotta, Presty, Friston, Frackowiak & Phelps, 1992; Grafton, Woods & Mike, 1994; Jenkins, Brooks, Nixon, Frackowiak & Passingham, 1994; Passingham, Jueptner, Frith, Brooks & Frackowiak, 1995; Rao, Harrington, Haaland, Bobholz, Binder, Hammeken, Frost, Myklebust, Jacobson, Bandettini & Hyde, 1995; Rauch, Savage, Brown, Curran, Alpert,

Kendrick, Fischman & Kosslyn, 1995; Rauch, Whalen, Savage, Curran, Kendrick, Brown, Bush, Breiter & Rosen, 1997; Van Mier, Tempel, Perlmutter, Raichle & Petersen, submitted; see Doyon, 1997, for a review). Despite these findings, however, there is evidence that these two structures might contribute differently to the learning of skills, as they are part of two distinct cortico-subcortical circuits (Asunama, Thach & Jones, 1983; Middleton & Strick, 1994; Percheron, François, Yelnik, Fénelon & Talbi, 1993; Sakai, Inase & Tanji, 1996; Yamamoto, Yoshida, Yoshikawa, Kishimoto & Oka, 1992), and that they differ with respect to their physiological properties (e.g., Graybiel & Kimura, 1995; Ito, 1982, 1993).

In accordance with the notion of a possible functional dissociation between the striatum and the cerebellum, several models have recently been proposed in which a critical role for the incremental acquisition of skills has been allocated separately to the basal ganglia (Graybiel, 1995; Graybiel & Kimura; 1995; Knowlton, Mangels & Squire, 1996; Marsden, 1987; Marsden & Obeso, 1994; McDonald & White, 1993; Saint-Cyr & Taylor, 1992; Singh et al., 1993; White, 1997), and to the cerebellum (Albus, 1971; Bloedel, 1992; Boylls, 1980; Braitenberg, 1967; Eccles, 1969; Gilbert & Thach, 1977; Ito, 1993; Marr, 1969; Pellionisz-Llinas, 1980; Thach et al., 1992; Thompson, 1992). Furthermore, recent attempts at delineating the role of each structure in an integrated model of motor learning have also been put forward (Burton, 1990; Houk & Wise, 1995; Jueptner, Frith, Brooks, Frackowiak & Passingham, 1997; Pascual-Leone et al., 1993; Wise & Houk, 1994). Yet, very little behavioral evidence supporting such dissociation of function has been gathered to date (see Pascual-Leone et al., 1993, for an exception). The goal of the present study was thus to investigate the possible distinct contribution of the striatum and the cerebellum to the learning of visuomotor skills using two current models which suggest that the striatum would be involved in the elaboration of perceptivomotor programs based on stimulus-response (S-R) types of associations that are reminiscent of those examined in animal research (Graybiel & Kimura, 1995; Knowlton et al., 1996; Marsden & Obeso, 1994; McDonald & White, 1993; Singh et al., 1993; see White, 1997, for a review), while the cerebellum would play a preponderant role in the

sequencing of learned movements (Bloedel 1992; Inhoff, Diener, Rafal & Ivry, 1989; Inhoff & Rafal, 1990; Ito, 1993; Thach et al., 1992).

Evidence supporting the role of the striatum in perceptivomotor learning comes from physiological and behavioral studies in animals (see Graybiel & Kimura, 1995; Marsden & Obeso, 1994; see White, 1989, 1997, for reviews). For example, Graybiel and Kimura (1995) have demonstrated that the striatum contains tonically active neurons (TANs) which undergo electrophysiological changes in responsiveness as non-human primates are learning to associate a response to the presentation of a conditioning stimulus. Using a "win-stay" version of the 8-arm radial maze, White and his collaborators have also shown that the dorsal striatum mediates the generation of reinforced S-R associations (McDonald & White, 1993; Packard, Hirsh & White, 1989; Packard & White, 1990; see White, 1997, for a review). Further evidence that the striatum contributes to this type of learning comes from two studies in humans (Knowlton et al., 1996; Singh et al., 1993). First, Knowlton et al. (1996) showed that patients with PD failed to learn a probabilistic classification task, in which they were required to predict which of two outcomes would occur on each trial based on a particular combination of cues presented. They concluded that the striatum plays a critical role in the ability to acquire non-motor dispositions that depend on new stimulus-response associations. Second, in a brain imaging study with PET, Singh and his colleagues (1993) have reported increased activity in the striatum and thalamus while normal control subjects were executing blocks of trials in a random condition of the SRT task (Nissen & Bullemer, 1987), and thus suggested that simple sensori-motor associations may depend on the integrity of a striato-thalamic circuit.

Likewise, evidence in favour of the cerebellar participation in the sequencing of learned movements is based on the study of cell physiology, which has demonstrated that this structure is involved in linking together the constituent, simpler movements that make up volitional compound motor actions (Thach et al., 1992), and in providing an on-line modification of activity in the central motor pathways that are required for optimal coordination of movements (Bloedel, 1992; Ito, 1982, 1993). This notion is also in accordance with a series of studies which have demonstrated that a lesion to the

cerebellum impairs the ability to translate a programmed sequence into action before the onset of movement (Inhoff & Bisiacchi, 1990; Inhoff et al., 1989; Inhoff & Rafal, 1990). It should be noted that some researchers (Benecke, Rothwell, Dick, Day & Marsden, 1987; Bradshaw, Phillips, Dennis, Mattingley, Andrewes, Chiu, Pierson & Bradshaw, 1992; Canavan, Passingham, Marsden, Quinn, Wyke & Polkey, 1989; Georgiou, Bradshaw, Iansek, Phillips, Mattingley & Bradshaw, 1994; Georgiou, Bradshaw, Phillips, Bradshaw & Chiu, 1995; Georgiou, Iansek, Bradshaw, Phillips, Mattingley & Bradshaw, 1993; Harrington & Haaland, 1991; Jones, Phillips, Bradshaw, Iansek & Bradshaw, 1992; Roy et al., 1993; Stelmach, Worringham & Strand, 1986, 1987; Stern, Mayeux, Rosen & Ilson, 1983; Weiss, Stelmach & Hefter, 1997; see Dominey & Jeannerod, 1997, for a review) have previously investigated the role of the striatum in the sequencing of movements, by examining the performance of patients with PD who were required to switch between two completely different types of motions such as elbow extention and hand squeeze (Benecke et al., 1987), or were asked to shift from one step in the sequence to the next by changing hand postures (Harrington & Haaland, 1991), in situations where patients had explicit knowledge of the sequence of movements they had to perform. By contrast, in this experiment, the notion first proposed by Flourens (1824), Babinski (1899) and Holmes (1939) that damage to the cerebellum produces a "decomposition of movements", was further investigated using a new sequencing task that did not require switching between separate movements, but instead measured the patients ability to perform a fluid sequence of movements in an implicit fashion.

The present study therefore explored the possible distinct contribution of the striatum and the cerebellum in the two types of skilled behaviors described above by comparing the performance of patients in early (Stage 1) or advanced stages (Stages 2-3) of Parkinson's disease (PD), and of a group of patients with damage to the cerebellum (CE), to that of a group of aged (ANC) or young (YNC) matched normal controls, respectively, on two visuomotor skill learning tasks. Their ability to make stimulus-response associations was first examined using a version of the SRT task in which stimuli were presented at random, and the subjects had to respond by pressing a button located to the right of the stimulus that was displayed. Second, implicit sequencing of learned

movements was tested with an adapted version of the Mirror-Tracing Test, in which subjects were required to trace a series of complex figures which, unbeknown to the subjects, consisted of the juxtaposition of three simple figures that they had either practiced prior to testing (Practiced condition), or had never traced individually before (Unpracticed condition). In accordance with the models mentioned above (Inhoff et al., 1989; Ito, 1982, 1993; Thach et al., 1992; see Bloedel, 1992; Graybiel & Kimura, 1995; Marsden & Obeso, 1994, for reviews), it was predicted that, compared to the ANC group, patients in the PD groups would show a deficit in acquiring perceptivomotor associations as reflected by a smaller reduction in reaction time across sessions, whereas the performance of patients in the CE group would not differ significantly from that of the YNC group on this task. Based on the results of our previous laboratory studies (Doyon et al., 1997a, 1997b, in press, 1996), we hypothesized that this impairment should be more evident in late (slow) phase as opposed to early (fast) phase of learning, and in patients with a bilateral striatal dysfunction (i.e., patients in stages 2-3 of PD according to the Hoehn & Yahr scale, 1967). By contrast, it was expected that, compared to their respective control groups, patients in the CE group, but not those in the PD groups, would fail to show a facilitation effect when tracing triads that were composed of practiced simple figures versus those that were made up of unpracticed figures.

### Method

#### Subjects

Five groups of subjects participated in this study. All of the patients were recruited via the Department of Neurological Sciences and Neuroradiology at the Hôpital de l'Enfant-Jésus, Québec City (Québec), Canada, whereas aged and young normal control subjects were either acquaintances of the experimenters or volunteers from the community. None of the controls had a positive history of a psychiatric or neurological disorder. Each subject gave informed written consent for their participation in the study, which was approved by the Review Ethics Board of the Hôpital de l'Enfant-Jésus.

### Parkinson's Disease Groups (PD)

Two groups of patients with a diagnosis of idiopathic Parkinson's disease (PD) were included in the present experiment. The first group was composed of 15 patients (5 female, 10 male) in Stage 1 of the disease as assessed by an experienced neurologist (Dr. P.J. Bédard, Hôpital de l'Enfant-Jésus) using Hoehn and Yahr's scale (1967). On average, these patients were 58.7 (SD: 9.5) years old, and had 12.8 (SD: 4.5) years of education (see Table 1). The second group consisted of 15 patients (7 female, 8 male) who were in Stages 2-3 of the disease, and who were, on average, 59.3 (SD: 6.3) years old, and had 13.5 (SD: 4.2) years of education. All of these patients were taking optimal levels of levodopa medication at the time of testing. Patients with drug-induced parkinsonism, multiple system atrophy, cerebro-vascular disease, epilepsy, history of alcoholism, head injury or tumor, cerebellar disturbances, or disproportionate oculomotor and autonomic dysfunction were excluded from this study.

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Insert Table 1 about here

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### Cerebellar Group (CE)

A heterogeneous group of 15 patients (mean age [years]: 40.7, SD: 11.8; mean level of education [years]: 11.9, SD: 3.0) with a radiologically-documented lesion to the cerebellum was also tested (see Table 1). Twelve of these had pure cerebellar atrophy (PCA), whilst the last three had lesions extending into the brainstem or spinal cord. All of these patients showed signs of dysarthria, ataxia, and/or dysmetria, although the severity of these cerebellar symptoms differed between patients. Because two patients with PCA were able to complete testing on only half of the skill learning tasks (i.e., the Mirror-Tracing task or the random version of the SRT task), two other patients with PCA were included into the study to complete the data acquisition on the remaining task. It is important to note that the latter patients were well matched to the original group of

patients so that there was still no significant difference when compared to the control subjects with respect to their mean age and mean level of education, as well as to the sex distribution. In addition, these new patients showed a pattern of results on the basic neuropsychological assessment that was similar to the overall group of patients in the CE group.

### Normal Control Groups

Two separate groups of normal control subjects were selected to match the clinical groups with respect to mean age, mean level of education, and sex distribution (see Table 1). They were composed of a group of 15 aged-normal subjects (ANC), and of a group of 15 young-normal subjects (YNC) that were tested, respectively, as controls for the PD and cerebellar groups. Again, because a few control subjects ( $n=4$ ) were only available to complete half the testing, other subjects were recruited to replace them in order to bring the sample size up to 15 subjects in each group. These subjects were selected to match the overall groups' characteristics with regards to age, education, and sex distribution.

### Basic Neuropsychological Assessment

A short battery of neuropsychological tests was administered to the patients in the three clinical groups in order to eliminate those showing signs of dementia and/or depression. This assessment consisted of the Mini-Mental State Examination (Folstein, 1983), the "Vocabulary", "Digit Span", "Picture Arrangement", and "Block Design" subtests of the WAIS-R (Wechsler, 1987), as well as the French version of the Beck Depression Inventory-Revised (BDI; Bourque & Beaudette, 1982). A home-made General Health Status scale, in which patients had to provide their own subjective estimate of their motor condition (1- Worse than usual, 2- Same as usual, and 3- Better than usual) before testing began, was also completed. This measure allowed to determine that their physical state at the beginning of testing did not differ from their overall general health status.

Furthermore, there was no clinical evidence of motor deterioration during testing sessions. It should be noted that PD patients in Stage 1 of the disease showed, on average, a score of 11.5 (SD: 9.1) on the BDI, which reflects signs of a mild level of depression in this group. However, these patients were not excluded because: 1) Taylor, Saint-Cyr, Lang & Kenny (1986) have demonstrated that such mild depressive states do not interfere significantly with patients' performance on cognitive tasks, and 2) consistent with this notion, the results of the present neuropsychological assessment revealed that these patients did not suffer from an overall deterioration in their level of cognitive functioning. Finally, except for the three clinical groups who showed an impairment on the Purdue Pegboard task, hence reflecting a deficit in fine motor coordination, the results of the patients on the remaining tests of the basic neuropsychological evaluation reveal that they did not show any significant cognitive deterioration (see Table 2).

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Insert Table 2 about here

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### Material and Procedure

#### Random Version of the SRT Task: Perceptivomotor Skill Learning

The subject's ability to acquire perceptivomotor associations was measured with a random version of the original SRT task. This test was administered using a response box that had four identical lights (stimuli) and four buttons, one below (1.75 cm) each light. The lights and buttons were arranged horizontally and equidistant from one another. This box was connected to an IBM PC computer that controlled stimulus presentation and recorded the subject's reaction time (RT) and accuracy on each trial (see Figure 1).

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Insert Figure 1 about here

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Contrary to the original SRT task, in which each block of trials was composed of a repeated 10-item sequence (Doyon et al., 1997a), this version used a completely random presentation of the stimuli. The subjects were instructed to use the middle and index fingers of each hand, and to keep one finger on each of the four keys. Furthermore, they were asked to press as quickly as possible the button corresponding to the right of the one under which the visual stimulus (light) appeared, while trying to make as few errors as possible. When the stimulus to the far right was displayed, the subjects were instructed to press the button to the far left. This experimental manipulation was used to increase the level of difficulty of the task, hence reducing the possibility of obtaining floor effects within the six training sessions. The stimulus remained displayed until the subject responded. After the subject's response, the light went off, and was followed 500 ms later by the display of another stimulus. Each subject completed 6 sessions of 4 blocks, each block comprising 100 random trials (total = 2400 trials). The sessions were separated by pauses varying between 10 and 20 minutes, while the blocks of trials within a session were administered 90 seconds apart.

#### Mirror-Tracing Task: Sequencing of Practiced Movements

Sequencing of practiced movements was measured with a new visuomotor skill learning task that was developed in our laboratory and was based on the original Mirror-Tracing Test. In this task, the subjects were required to learn to trace figures of different shapes while viewing their hand and figures through the reflection of a mirror. The apparatus consisted of a wooden baseboard (30cm X 30cm) with a rear vertical panel (30cm X 30cm), on which a mirror (23cm X 23cm) was fixed (see Figure 2). Perpendicular to this panel, a metal plate was mounted 15cm above the baseboard to prevent the subject's direct view of the hand and figures. This metal plate could be fixed on either side of the board to allow right- or left-handed subjects to complete the task adequately using their dominant hand.

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Insert Figure 2 about here

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In this experiment, the subjects were asked to trace two different types of drawings including simple figures and complex triads. The simple figures (Figure 3a) consisted of curved or angled designs, whereas the triads (Figure 3b) were comprised of the consecutive juxtaposition of three of these simple figures. All of these figures were originally created using the software Autocad (Version 12, Autodesk Inc.).

Paper sheets on which the different simple figures or triads were illustrated were placed directly on the baseboard at the beginning of each trial. Using a pencil, the subjects were asked to trace the figures as quickly as possible, while avoiding to touch the edges. They were also required to follow as accurately as possible the overall shape of the figures. Each trial began by asking the subjects to place their pencil at the starting point displayed on the figure, and to start tracing at the "Go" signal. Two dependent measures were recorded: The completion time (CT) (i.e., the amount of time in seconds required to complete each figure from the beginning to the finishing line), and the number of errors (i.e. the number of times a subject crossed the borders of a figure).

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Insert Figure 3 about here

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Each subject completed four phases of testing. In Phase I, the subjects were asked to trace 12 simple figures in order to familiarize themselves with the mirror-tracing task. In Phase II, the subjects were then required to trace each of the 12 triads once. These were later divided into two sets, and were used in both the Practiced and Unpracticed conditions of Phase IV. The reasons for this testing phase were two-fold: First, it allowed to familiarize again the subjects with the task using complex instead of simple figures. Second, although the results of a pilot study (described below) revealed that the triads used in both Practiced and Unpracticed conditions did not differ in terms of their physical characteristics and their level of difficulty, this phase was administered to ensure that this was the case in the present experiment. In Phase III (called "Learning of simple

figures"), the subjects were given 10 blocks of practice in which they had to trace 18 new simple figures that were repeatedly presented at random within each block. The aim of this phase was to have the subjects learn a series of simple movements by repeatedly tracing the same simple figures. Finally, Phase IV (named "Sequencing of practiced movements"), consisted of three testing blocks of trials, each block comprising six triads in a Practiced condition and six triads in an Unpracticed condition. In the Practiced condition, the triads were composed of the consecutive juxtaposition of three simple figures that were previously practiced in Phase III of testing, while the triads in the Unpracticed condition were made up of three simple figures that subjects had never traced individually before. This phase was administered to explore the ability of the subjects to integrate learned simple movements into a fluid sequence by comparing the performance of the triads in the Practiced vs Unpracticed conditions.

It is important to note that the level of difficulty of the different sets of simple figures that were used in the familiarization and learning phases, as well as for designing the triads of the Practiced and Unpracticed conditions of Phase IV, was controlled based on the results of two pilot studies. The first pilot experiment was carried out with 20 control subjects (mean age [years]: 25.8, SD: 7.2; mean level of education [years]: 14.3, SD: 5.6) to determine the mean completion time and the number of errors that were made while tracing once the 48 simple figures. On average, these figures were 10.4 cm (SD: 2.6) long; the subjects took 6.91 sec. (SD: 9.87) and committed .73 (SD: 1.16) errors per figure. Twelve of these figures were selected to be used in Phase I of the new Mirror-Tracing task discussed above, whereas the remaining 36 simple figures were then divided randomly into two subsets of 18 figures, which were used to create the triads in the Practiced and Unpracticed conditions.

The second pilot experiment was conducted to ensure that the triads used in the Practiced condition were equivalent to those in the Unpracticed condition with respect to their physical characteristics and level of difficulty (i.e., accuracy and completion time). As expected, the results of a one-way analysis of variance conducted on the performance of a group of 20 new normal control subjects (mean age [years]: 26.3, SD: 11.2; mean level of education [years]: 13.4, SD: 9.7) yielded no significant difference between these

two types of complex figures. On average, the triads in the Practiced condition had a total length of 33.9 cm (SD: 1.6), whereas the triads in the Unpracticed condition were 34.4 cm (SD: .47) long. Furthermore, the triads in the Practiced condition took a mean time of 15.7 sec. (SD: 12.6) to complete, whereas 16.5 sec. (SD: 11.1) were required for the triads in the Unpracticed condition. Finally, there was no significant difference in the mean number of errors committed when tracing both types of triads (Practiced: 2.06, SD: 2.69; Unpracticed: 2.27, SD: 3.04).

### Experimental Design

This study was conducted on two separate days of testing. The subjects were first asked to complete a short neuropsychological assessment. They were then required to execute either the random version of the SRT test or the mirror-tracing task on the first of these two days; the order of administration of these two visuomotor skill learning tasks being counterbalanced within each group.

### Results

Patients in both PD groups and the CE group were well matched to their respective normal control subjects as separate one-way analyses of variance (ANOVA's) revealed no significant difference with respect to either age or level of education. Also, there was no significant difference in sex distribution of the subjects in both clinical and control groups as measured with the  $\chi^2$ .

In the random version of the SRT task, the dependent measures of interest were a) the number of correct responses, and b) the mean RT in milliseconds. For each training session, the mean RT of each block of trials for the correct responses only were transformed into logarithms to reduce skewness in the distribution. Subsequent ANOVA's for repeated measures with trend analyses were all performed using this transformation. Therefore, the results in Figures 4 and 5, and in the text below, are reported as geometric mean RT corresponding to the mean logarithmic scores reconverted

into milliseconds. In the adapted version of the Mirror-Tracing Test, the dependent measures of interest were a) the number of errors, and b) the mean CT in seconds. Finally, separate statistical analyses were conducted comparing the PD and CE groups with their respective control groups. When significant, interactions were decomposed using simple main effects followed by post-hoc pairwise tests using the Newman-Keuls procedure.

#### Random Version of the Serial Reaction Time Task: Perceptivomotor Skill Learning

##### Accuracy

Overall, PD and ANC groups were very accurate on this test. The mean percentage of correct responses was 90.2% (SD: 1.35) for the ANC group, 91.6% (SD: 1.23) for PD patients in Stage 1, and 87.4% (SD: .8) for PD patients in Stages 2-3. An ANOVA for repeated measures with Group and Session as between- and within-subjects factors, respectively, was conducted to compare the performance of the groups of PD patients to that of the ANC subjects. This analysis yielded a main effect of Session,  $F(5,210) = 2.79$ ,  $p < .05$ , suggesting that the groups improved in performance from Session 1 to Session 6. However, the Group effect and the Group  $\times$  Session interaction were not significant, indicating that the number of correct responses did not differ between the three groups across training sessions.

A similar pattern of results was found for the CE and the YNC groups. The repeated-measures ANOVA on the percentage of good responses yielded no significant difference between groups (CE: 86.2%, SD: 9.1; YNC: 90.3%, SD: 4.7). There was a significant effect of Session,  $F(5,140) = 3.80$ ,  $p < 0.001$ , but the Group  $\times$  Session interaction did not reach significance, again suggesting that the profile of correct responses across sessions did not differ significantly between the two groups.

### Reaction Time

A one-way ANOVA was first conducted in order to determine whether the PD groups differed from the ANC group with respect to the mean RT on the very first practice session. This analysis yielded no main effect of Group, hence suggesting that the subjects' ability to perform the random version of the SRT task was equivalent at the beginning of the training sessions.

A repeated-measures ANOVA on the RT data of Session 1 to Session 6 was then conducted (see Figure 4). The results revealed a main effect of Group,  $F(2,42) = 8.53$ ,  $p < 0.001$ , PD patients in Stages 2-3 of the disease being overall significantly slower to respond (484.55 ms, SD: 1.27) to the stimuli than the two other groups (ANC: 367.14 ms, SD: 1.17; PD Stage 1: 414.44 ms, SD: 1.21). There was a main effect of Session,  $F(5,210) = 104.68$ ,  $p < 0.0001$ , but most importantly, and consistent with our hypothesis, the Group x Session interaction was significant,  $F(10,210) = 3.01$ ,  $p < 0.001$ , hence suggesting that the three groups differed in their learning ability on this version of the SRT task.

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Insert Figure 4 about here

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Simple main effects were carried out to decompose the Group x Session interaction described above and to provide a better understanding of the subjects' performance across training sessions. Significant group differences were found at each session except on Session 1 (Session 2:  $F(2,61) = 46.7$ ,  $p < 0.05$ ; Session 3:  $F(2,61) = 59.2$ ,  $p < 0.05$ ; Session 4:  $F(2,61) = 59.9$ ,  $p < 0.05$ ; Session 5:  $F(2,61) = 10.5$ ,  $p < 0.05$ ; Session 6:  $F(2,61) = 12.6$ ,  $p < 0.05$ ). Post-hoc pairwise tests using Newman-Keuls procedure were then used to identify the groups that differed significantly from each other on the different practice sessions. The results showed that PD patients in Stages 2-3 were consistently slower to complete the random version of the SRT task than ANC subjects from Session 2 to Session 6 (Session 2:  $q = 4.30$ ,  $p < 0.05$ ; Session 3:  $q = 5.34$ ,  $p < 0.05$ ; Session 4:  $q = 6.05$ ,  $p < 0.05$ ; Session 5:  $q = 6.01$ ,  $p < 0.05$ ; Session 6:  $q = 7.21$ ,  $p < 0.05$ ). By contrast,

patients with a unilateral dysfunction to the striatum (PD Stage 1) only differed significantly from ANC at the very last training session, Session 6:  $q = 3.63$ ,  $p < 0.05$ . Finally, the performance of PD patients in Stages 2-3 of the disease differed significantly from that of the PD patients in Stage 1 on two occasions, that is on Session 3,  $q = 3.53$ ,  $p < 0.05$ , and on Session 6,  $q = 3.58$ ,  $p < 0.05$ . Altogether, these results suggest that a unilateral dysfunction is sufficient to elicit a slowing of response in late phase of learning compared to controls, whereas a lack of improvement in speed of response was readily noticeable on Session 2 in PD patients with a clinically significant bilateral striatal degeneration.

More importantly, each group separately showed a significant reduction in reaction times across the six training sessions as revealed by tests of simple main effects (ANC:  $F(5,210) = 78.26$ ,  $p < 0.01$ ; PD Stage 1:  $F(5,210) = 30.43$ ,  $p < 0.01$ ; PD Stage 2-3:  $F(5,210) = 21.74$ ,  $p < 0.01$ ). However, between-sessions improvement in performance revealed a different pattern of learning among groups. Indeed, all subject groups showed a significant decrease in reaction time between Sessions 1 and 2 (ANC:  $q = 11.28$ ,  $p < 0.05$ ; PD Stage 1:  $q = 9.32$ ,  $p < 0.05$ ; PD Stage 2-3:  $q = 9.03$ ,  $p < 0.05$ ). Such an improvement was seen up to Session 3 in the PD Stage 1 group (Sessions 2-3:  $q = 3.34$ ,  $p < 0.05$ ), and to Session 4 in the ANC group (Sessions 2-3:  $q = 3.38$ ,  $p < 0.05$ ; Sessions 3-4:  $q = 3.27$ ,  $p < 0.05$ ). Taken together, these results suggest that the performance of both groups of PD patients did not improve across training sessions as much as the control subjects after Session 1. This suggests that the striatum plays a critical role in the ability to acquire perceptivomotor associations, possibly in the automatization phase of learning. Furthermore, these findings are consistent with the notion that the severity of the deficit in this type of learning mechanism is dependent upon the extent of striatal dysfunction, as patients in the PD Stages 2-3 stopped improving after fewer practice trials than patients in the PD Stage 1 group.

Figure 5 shows the geometric mean RT data for both the CE and YNC groups on the six training sessions. A one-way ANOVA conducted on the results of Session 1 only revealed a significant effect of Group,  $F(1,28) = 20.95$ ,  $p < 0.0001$ , suggesting that contrary to the PD groups, the patients with a lesion to the cerebellum were significantly slower

than their matched normal controls at the beginning of testing. An ANOVA for repeated measures using the mean RT of Sessions 1 to 6 showed that the CE group (599.24 ms, SD: 1.34) was also significantly slower to respond,  $F(1,28) = 37.53$ ,  $p < 0.0001$ , than subjects in the YNC group (327.95 ms, SD: 1.3). There was also a main effect of Session,  $F(5,140) = 64.44$ ,  $p < 0.0001$ , indicating that the RT of the two groups decreased from Session 1 to Session 6. Contrary to the results of both PD groups, the Group  $\times$  Session interaction was not significant, thereby suggesting that both the CE and the YNC groups did not differ in their ability to acquire perceptivomotor associations.

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Insert Figure 5 about here

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**Correlation Analyses.** To determine whether the deficit in visuomotor skill learning observed in both PD groups could be attributed to a cognitive dysfunction, a mood disturbance, or to the severity of motor symptoms, separate Pearson's product-moment correlations were carried out between the patients' level of learning (as measured by subtracting the mean RT of Session 6 from that of Session 1), and several neuropsychological measures such as the Mini-Mental State Examination, the General Health Status scale, the Beck Depression Inventory, the Purdue Pegboard and the results obtained with the different subtests from the WAIS-R ("Vocabulary", "Digit Span", "Picture Arrangement", and "Block Design"; Wechsler, 1987) gathered before testing began. None of the correlations was significant, hence suggesting that the perceptivomotor learning deficit in both PD groups could not be attributed to those variables.

Finally, further correlation analyses were conducted in which the relation between the RT and the number of correct responses across the six sessions of training on the SRT task was examined individually in all the groups. The results showed a significant negative correlation for the ANC group only ( $r = -.86$ ,  $p < 0.05$ ), revealing that, as the subjects in this group were improving their performance on the SRT task, they were also making a greater number of errors. However, a subsequent analysis of covariance

(ANCOVA) on the RT data for the two PD groups and the ANC group was carried out using the percentage of correct responses as a covariate. This analysis revealed a pattern of results that was similar to the one observed without the covariate, hence suggesting that the results obtained in the two PD groups and their matched controls could not be explained by a speed-accuracy trade-off *per se*.

### Mirror-Tracing Task: Sequencing of Practiced Movements

#### Phase I: Familiarization to the Tracing of Simple Figures

Accuracy. A one-way ANOVA conducted on the mean number of errors made by the two PD groups and their matched control subjects while they were tracing simple figures for the first time, yielded a significant effect of Group,  $F(2,42) = 3.71$ ,  $p < 0.05$ . This difference was due to the PD patients in Stage 1 who produced, on average, fewer tracing errors (.39, SD: .97) than the two other groups (ANC: 1.07, SD: 1.43; PD Stages 2-3: 1.0, SD: 1.47). By contrast, a separate one-way ANOVA comparing the performance of CE and YNC subjects revealed no significant difference between these groups with respect to the number of errors per figure (CE: .79, SD: 1.36; YNC: .74, SD: 1.18).

Completion Time. The results of the mean time in seconds to complete each simple figure yielded no significant difference between the PD groups and their controls (ANC: 8.49, SD: 6.67; PD Stage 1: 6.95, SD: 5.14; PD Stages 2-3: 9.17, SD: 7.57). The same pattern of results was observed for the YNC and the CE groups as they showed no significant difference on this measure (CE: 8.59, SD: 10.33; YNC: 6.51, SD: 8.87). This suggests that the clinical groups did not differ from their respective control groups in terms of the mean time to complete the simple figures on Phase I.

## Phase II: Familiarization to the Tracing of Complex Triads

Accuracy. A two-way repeated measures ANOVA was conducted comparing the performance of the PD and ANC groups on the tracing of triads that would later be used in the Practiced and Unpracticed conditions in Phase IV of testing. This analysis yielded a significant Group difference,  $F(2,42) = 3.84$ ,  $p < 0.05$ , because PD patients in Stage 1 were again producing fewer errors (1.13, SD: 1.6) than the two other groups (ANC: 3.17, SD: 4.05; PD Stages 2-3: 3.22, SD: 3.7). There was also a main effect of Condition,  $F(1,42) = 4.74$ ,  $p < 0.05$ , as the triads in the Practiced condition were traced with fewer errors (2.24, SD: 2.97) than those in the Unpracticed condition (2.77, SD: 3.27). However, the Group x Condition interaction did not reach significance, suggesting that the triads in both conditions were equivalent in difficulty between the groups with regards to the mean number of errors made while tracing them. The analysis conducted on the CE and YNC groups revealed no main effect of Group (CE: 2.24, SD: 2.73; YNC: 1.76, SD: 2.13), Condition (Practiced: 2.02, SD: 2.59; Unpracticed: 1.98, SD: 2.26), and the Group x Condition interaction was not significant.

Completion Time. Although the results of the pilot study showed no significant difference in the mean time in seconds required to trace the triads used in both Practiced and Unpracticed conditions in Phase IV, a two-way repeated measures ANOVA was nevertheless carried out separately for the PD and CE groups in order to verify that this was indeed the case in the present experiment. The results showed that the PD patients in Stages 2-3 (36.52, SD: 30.79) were slower to trace complex figures than the two other groups (ANC: 24.75, SD: 18.80; PD Stage 1: 23.92, SD: 13.42),  $F(2,42) = 4.19$ ,  $p < 0.05$ , but that the CE patients (22.64, SD: 16.66) were not significantly slower to complete the figures than the YNC subjects (14.99, SD: 9.56). There was a main effect of Condition between CE patients and the YNC subjects only, as Practiced (18.14, SD: 13.82) triads were traced significantly faster than Unpracticed triads (19.49, SD: 12.40),  $F(2,42) = 4.19$ ,  $p < 0.05$ . However, the Group x Condition interactions were not significant in neither

comparisons, suggesting that the triads used in both conditions did not differ in difficulty between the groups, as reflected by the mean time the subjects needed to complete the figures.

### Phase III: Learning of Simple Figures

**Accuracy.** An ANOVA for repeated measures with Group and Block as between-and within-subjects factors respectively, was conducted to compare the performance of the two groups of PD patients to that of the ANC subjects on the 10 Blocks of training trials with the simple figures. The results showed a Group effect,  $F(2,42) = 16.02$ ,  $p < 0.0001$ , PD patients in Stage 1 making fewer errors (.03, SD: .005) than the ANC group (.12, SD: .01), and the PD group in Stages 2-3 (.25, SD: .03). In addition, there was a main effect of Block,  $F(9,378) = 13.78$ ,  $p < 0.0001$ , and the Group  $\times$  Block interaction,  $F(18,378) = 1.75$ ,  $p < 0.0001$ , was also significant. Simple main effects and post-hoc pairwise tests revealed, however, that this interaction was only due to the fact that the performance of PD patients in Stage 1 (.009, SD: .002) was significantly better than that of the PD patients in Stages 2-3 (.34, SD: .04) on Block 3,  $q = .27$ ,  $p < 0.05$ .

The analysis comparing the CE and YNC groups yielded a significant effect of Group,  $F(1,28) = 6.50$ ,  $p < 0.05$ , as YNC subjects made fewer errors (.19, SD: .35) than the CE group (.32, SD: .57) when tracing the simple figures. Contrary to the PD patients, the main effect of Block did not reach significance, indicating that subjects in the CE group did not significantly reduce their number of errors across training Blocks. However, the Group  $\times$  Block interaction was not significant, hence suggesting that both the CE and the YNC groups did not differ in their number of errors across blocks. Finally, it is important to note that all of the subjects who completed this Phase made very few errors (i.e., less than one per figure on average) while tracing the simple figures.

**Completion Time.** The mean CT in seconds required to trace the simple figures for the PD and ANC groups across the 10 training Blocks of trials are shown in Figure 6. Again, a repeated-measures ANOVA yielded a Group effect,  $F(2,42) = 15.68$ ,

$p<0.0001$ , as PD patients in Stages 2-3 were slower to trace the simple figures (4.11, SD: .15) than the other groups (ANC: 2.25, SD: .07; PD Stage 1: 3.83, SD: .10). The results also showed a main effect of Block,  $F(9,378) = 29.23$ ,  $p<0.0001$ , as all groups improved their performance across training trials. Finally, there was no significant Group x Block interaction, hence suggesting that both PD groups and the ANC group showed a similar amount of learning to trace the simple figures.

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Insert Figure 6 about here

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Figure 7 shows the mean CT required to trace the simple figures for the CE and YNC groups across the 10 training Blocks of trials. The repeated-measures ANOVA revealed a Group effect,  $F(1,28) = 29.68$ ,  $p<0.0001$ , the YNC subjects being faster to trace the simple figures (2.12, SD: .91) than the CE group (4.44, SD: 2.77). The results also showed a main effect of Block,  $F(9,252) = 9.95$ ,  $p<0.0001$ , because both groups improved their performance across training trials. By contrast, there was no significant Group x Block interaction, suggesting that these two groups did not differ in their learning ability to trace simple figures.

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Insert Figure 7 about here

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#### Phase IV: Sequencing of Practiced Movements

Accuracy. The data obtained in Phase IV were analyzed using a three-way ANOVA for repeated-measures (with Group being the between-subjects factor, and Condition and Block as within-subjects factors) to compare the precision of the subject groups on the three Blocks of trials in tracing the complex figures. The results revealed a main effect of Group,  $F(2,42) = 4.26$ ,  $p<0.05$ , where PD patients in Stages 2-3 produced significantly more errors (1.79, SD: 2.18) than the ANC group (.86, SD: 1.32) and the PD group in Stage 1 (.73, SD: 1.11). There was also a main effect of Condition,  $F(1,42) =$

18.45,  $p<0.0001$ , as the triads in the Practiced condition were traced with fewer errors (.95, SD: 1.35) than those in the Unpracticed condition (1.31, SD: 1.72), and a main effect of Block,  $F(2,84) = 7.33$ ,  $p<0.005$ , as all groups improved their performance across the three Blocks of trials. More importantly, however, no significant Group x Condition interaction was noted, hence suggesting that the three groups showed the same level of precision in tracing the triads in both conditions. None of the other double (Group x Block; Condition x Block) interactions reached significance. Finally, there was a Group x Condition x Block interaction,  $F(2,84) = 2.74$ ,  $p<0.05$ , as subjects in the ANC group showed a smaller reduction in their number of errors across Blocks, particularly for the triads in the Unpracticed conditions. This interaction can be explained by the fact that subjects in the ANC group made fewer errors on the first Block of trials to begin with, and therefore had less room to improve across the three Blocks.

The performance of YNC and CE groups was compared using the same statistical procedure described above for the PD and ANC groups. The results of this analysis yielded no main effect of Group, although CE patients produced more errors (2.0, SD: 2.27) than the YNC group (1.02, SD: 1.48). There was no effect of Condition, but here again, the results showed a main effect of Block,  $F(2,56) = 4.65$ ,  $p<0.05$ . Finally, the Group x Condition interaction, as well as the other double and the triple interactions were not significant, hence suggesting that the two groups showed the same level of precision in tracing the complex figures in both the Practiced and Unpracticed conditions.

Completion Time. The results of a three-way repeated measures ANOVA conducted on the mean CT in seconds of the three Blocks of trials for the two PD and the ANC groups are presented in Figure 8. The results showed a main effect of Group,  $F(2,42) = 4.72$ ,  $p<0.05$ , as the ANC subjects were significantly faster (8.38, SD: 4.76) than the two PD groups (PD Stage 1: 12.13, SD: 11.73; PD Stages 2-3: 12.6, SD: 7.48). There was a main effect of Condition,  $F(1,42) = 79.65$ ,  $p<0.0001$ , the triads in the Practiced condition being traced significantly faster (9.76, SD: 4.79) than the triads in the Unpracticed condition (12.32, SD: 7.28). The results also showed a learning effect in tracing the complex figures from Block 1 to Block 3,  $F(2,84) = 13.78$ ,  $p<0.0001$ . More

importantly however, the Group x Condition interaction did not reach significance, suggesting that the three groups showed a similar facilitation effect in the tracing of triads in both Practiced and Unpracticed conditions. Interestingly, subsequent analyses conducted on the first Block of trials did not yield any significant difference between the three groups in tracing the triads, thus providing further evidence that PD patients showed the same facilitation effect than ANC subjects in tracing the complex figures in both Practiced vs Unpracticed conditions, even when first exposed to the two types of triads. The other double (Group x Block; Condition x Block), and the triple (Group x Condition x Block) interactions did not reach significance.

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Insert Figure 8 about here

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Figure 9 shows the performance of YNC and CE groups in Phase IV of testing. There was a main effect of Group,  $F(1,28) = 12.32$ ,  $p < 0.005$ , with the YNC subjects being considerably faster to trace the complex figures (7.48, SD: 3.88) than the CE group (14.69, SD: 8.9). There was also a main effect of Condition,  $F(1,28) = 10.42$ ,  $p < 0.005$ , as the triads in the Practiced condition were traced significantly faster (10.36, SD: 6.2) than those in the Unpracticed condition (11.81, SD: 6.57), and of Block,  $F(2,56) = 4.61$ ,  $p < 0.05$ , where all groups improved their performance across the three Blocks of trials. Again, the other double (Group x Block; Condition x Block) and the triple (Group x Condition x Block) interactions did not reach significance. However, as predicted and contrary to the profile of the PD patients, this analysis revealed a significant Group x Condition interaction,  $F(1,28) = 9.05$ ,  $p < 0.01$ . This suggests that the CE group did not show the same level of facilitation in tracing the triads in both Practiced and Unpracticed conditions. Such an impairment is particularly revealing as both groups had shown evidence of a similar degree of learning to trace the simple figures in Phase III of testing. Moreover, subsequent analyses conducted on the first Block of trials yielded a similar Group x Condition interaction,  $F(1,28) = 7.24$ ,  $p < 0.05$ , suggesting that the difference in performance between Practiced and Unpracticed conditions could also be seen at the beginning of testing when subjects were first exposed to the complex figures. Considered

together, these results suggest that, compared to the PD patients, those with damage to the cerebellum showed an impairment in the sequencing of learned simple figures.

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Insert Figure 9 about here

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In order to eliminate the possibility that the impairment in the tracing of triads in both Practiced and Unpracticed conditions found in the cerebellar group was due to the presence of additional extracerebellar damage, further analyses were carried out comparing the performance of the control group to that of a subgroup of patients ( $n=12$ ) in which the lesions were circumscribed to the cerebellum. Interestingly, these analyses revealed a very similar pattern of findings to that of the group as a whole. Indeed, the results showed a significant effect of Group,  $F(1,25) = 8.50$ ,  $p<0.01$ , Condition,  $F(1,25) = 14.15$ ,  $p<0.005$ , and again, the Group x Condition interaction reached significance,  $F(1,25) = 5.46$ ,  $p<0.05$ . Thus, as for the results of the whole group of patients with damage to the cerebellum, these findings indicate that patients with lesions restricted to the cerebellum also show a lack of facilitation effect in tracing complex triads of figures in the Practiced condition.

**Correlation Analyses.** To determine whether the impairment in the sequencing of learned movements found in the CE group could be due to cognitive or mood defects, separate Pearson's product-moment correlations were carried out between the patients' level of learning (as measured by subtracting the mean CT of the three Blocks of triads in the Practiced condition from that of the three Blocks of triads in the Unpracticed condition), and the dependent measures that were gathered during the basic neuropsychological evaluation. Because the importance of assessing the severity of the cerebellar dysfunction has been stressed in previous studies (e.g., Inhoff et al., 1989; Kish, El-Awar, Stuss, Nobrega, Currier, Aita, Schut, Zoghbi & Freedman, 1994), a rating of the motor signs in the upper limbs based on adiadokokinesia, dysmetria, and intention tremors was included in the present analysis. The latter rating was performed by an experienced neurologist, using scores between 0 and 5, where 0 indicates a relatively normal level of

functioning and 5 indicates a severe dysfunction (Inhoff et al., 1989). The results of these analyses revealed no significant correlation, therefore suggesting that the deficit in the sequencing of practiced movements observed in the CE group could not be attributed to a cognitive dysfunction, a mood disturbance, nor to the severity of the motor symptoms.

### Discussion

The goal of this study was to examine the distinct contribution of the striatum and the cerebellum in visuomotor skill learning. More specifically, this investigation aimed to explore the effects of damage to these structures on two different learning mechanisms which have been proposed as functional models for the striatum (Graybiel, 1995; Graybiel & Kimura; 1995; Knowlton et al., 1996; Marsden, 1987; Marsden & Obeso, 1994; McDonald & White, 1993; Saint-Cyr & Taylor, 1992; Singh et al., 1993; see White, 1997, for a review), or the cerebellum (Albus, 1971; Bloedel, 1992; Boylls, 1980; Braitenberg, 1967; Eccles, 1969; Gilbert & Thach, 1977; Ito, 1993; Marr, 1969; Pellionisz-Llinas, 1980; Thach et al., 1992; Thompson, 1992). The results showed that both PD groups were impaired in the learning of a random version of the SRT task when compared to the ANC group, whereas no significant difference was found between the performance of the CE and the YNC groups. By contrast, patients in the CE group, but not in the PD groups, failed to show a facilitation effect when tracing triads of figures in the Practiced vs Unpracticed conditions of the mirror-tracing task. Further correlational analyses revealed that the respective impairments in both skill acquisition tests were not related to a general decline in cognitive functioning, to mood disturbances, or to a motor limitation *per se*. For the first time, these findings provide behavioral evidence of a double functional dissociation between the striatum and the cerebellum in the incremental acquisition of visuomotor skilled behaviors.

Random Version of the SRT Task: Perceptivomotor Skill Learning

As predicted, the results show that, compared to controls, patients with PD, but not those with damage to the cerebellum, were impaired on a random version of the SRT task, as reflected by an earlier flattening of their reduction in reaction time across the six sessions of testing. One possible interpretation of these results, is that this deficit might be attributed to difficulties in ancillary cognitive processes and not to a learning impairment *per se*. Indeed, given that the SRT task requires both attentional and visuospatial processing abilities, and that deficits in each of these functions have been reported in patients with a striatal dysfunction (Boller, Passafiume, Keefe, Rogers, Morrow & Kim, 1984; Doyon, Bourgeois & Bédard, 1996; Owen, Roberts, Hodges, Summers, Polkey & Robbins, 1993; Sprengelmeyer, Canavan, Lange & Homberg, 1995; see Brown & Marsden, 1990; Dubois, Boller, Pillon & Agid, 1991; Ogden, 1990; Wise, 1996, for reviews), one could argue that the impairment observed in both PD groups results from a deficit in these processes. However, the results of the present study suggest that this is not the case because, if a problem in attentional and/or visuospatial functions was the source of the impairment, group differences would have been readily observed on the first session of training. The fact that no difference in performance was noted at the beginning of testing is thus inconsistent with such an interpretation. Furthermore, although a negative correlation between the mean reaction time data and the percentage of correct responses was found for the ANC group, the results of the ANCOVA revealed that a speed-accuracy trade-off could not account for the significant pattern of results observed in both PD groups, as a similar impairment was found when adjusting for the number of errors. Instead, we propose that the dissociation in performance between the PD groups and the CE group on this version of the SRT task suggests that the striatum plays a critical role in the ability to acquire perceptivomotor types of associations. Also, we conjecture that this impairment may be due to a difficulty in the automatization of the S-R associations acquired with practice, as all groups showed a significant increase in performance from Session 1 to Session 2, but PD groups stopped improving earlier than controls on this simple skill learning task. Thus, consistent with

other studies, these findings would suggest that a striatal dysfunction does not affect the learning of an incremental perceptivomotor skill at the very beginning (i.e., Session 1, fast learning stage), but does so in the later (i.e., slow learning phase) stages of the acquisition process (Doyon et al., 1997a, 1997b, *in press*, 1996; Karni, 1996; Karni, Meyer, Rey-Hipolito, Jezzard, Adams, Turner & Ungerleider, *in press*).

This impairment in perceptivomotor learning following a striatal dysfunction due to a degeneration in the nigro-striatal dopaminergic system, is consistent with much evidence from physiological and behavioral studies in animals (Aosaki et al., 1994a, 1994b; McDonald & White, 1993; Packard et al., 1989; Packard & White, 1990; see Graybiel, 1995; Graybiel & Kimura, 1995; Marsden & Obeso, 1994; White, 1989, 1997, for reviews), which have demonstrated that the striatum contributes to sensorimotor types of learning. Obviously, the task used in this study differs from the ones used with animals, where learning mechanisms are examined in the context of reward learning. However, the results are nevertheless reminiscent of those of Graybiel and her associates (1995) who have demonstrated that tonically active neurons undergo physiological changes in responsiveness as monkeys perform an associative conditioning task. They are also in accordance with the notion proposed by Schultz and colleagues, suggesting that learning-associated changes in the striatum are dopamine dependent (Gerfen, 1984; Schultz, 1986; Schultz, Apicella & Ljundberg, 1993; Schultz & Romo, 1990). The latter is supported by studies which have shown that the dopaminergic neurons may favor reinforcement-related inputs to influence sensorimotor processing (see Schultz, Romo, Ljungberg, Mirenowicz, Hollerman & Dickinson, 1995, for a review), and that TANs responses are affected following dopaminergic denervations (Graybiel, Aosaki, Flaherty & Kimura, 1994; see Graybiel & Kimura, 1995, for a review). Finally, the present findings are consistent with elegant behavioral studies by White and colleagues (McDonald & White, 1993; Packard et al., 1989; Packard & White, 1990; see White, 1997, for a review) who have reported that rats with lesions to the dorsal striatum are impaired on the "win-stay" task. This paradigm has originally been thought to measure the animal's ability to build S-R associations, but has also recently been interpreted as a stimulus-reward type of task (Petrides, 1987, 1996; Sziklas & Doyon, 1997).

The present deficit in perceptivomotor learning is also consistent with evidence from a clinical study conducted by Knowlton et al. (1996) in which PD patients were impaired in the learning of simple S-R associations, and with the results of a single brain imaging study with PET, in which significant changes in blood flow in both the thalamus and basal ganglia of normal control subjects were reported while they executed blocks of trials in a random condition of the SRT task (Singh et al., 1993). Taken together, these results suggest that simple sensori-motor associations may depend, at the very least, on the integrity of the striatum. Finally, although the present results may apparently disagree with the data reported by Willingham and Koroshetz (1993), who have shown that patients with Huntington's disease can learn at a normal rate a similar adapted random version of the SRT task than the one used in the present experiment, this discrepancy may be due to the fact that both studies differ in terms of the learning stage that the subjects reached during practice. In fact, when the data gathered on the mean RT of the first three blocks of trials of Session 1 (i.e., after subjects had completed the same number of trials [i.e., 300] and therefore achieved the same level of learning than those who participated in Willingham and Koroshetz [1993]) were reanalyzed, no significant difference was found between patients in both PD groups and the ANC subjects. Thus, these findings are consistent with other studies which suggest that a striatal dysfunction does not affect performance in the early (fast) learning stage but does so in the late (slow) learning stage of the acquisition process of a skill (Doyon et al., 1997a, 1997b, in press, 1996; Karni, 1996; Karni et al., in press).

The fact that the deficit in acquiring the perceptivomotor skill appeared earlier in the PD Stages 2-3 than in the PD Stage 1 group, is consistent with the notion that the severity of the basal ganglia disease is an important factor to consider when investigating skill learning abilities (Doyon et al., 1997a; Harrington et al., 1990; Mortimer, Pirozzolo, Hansch & Webster, 1982; Owen et al., 1993; Owen & Robbins, 1993; Taylor et al., 1986). Also, this would suggest that the ability to learn perceptivomotor associations may be one of the primary function of the striatum. The fact that patients in the PD Stage 1 group are impaired on this task (albeit later than patients with a bilateral striatal dysfunction) but not when they are required to learn a repeating sequence of movements

implicitly with the SRT task (Doyon et al., 1997a), reinforces the idea that the striatum plays a critical role in such a basic learning mechanism. Because acquiring a motor skill often depends heavily on this type of stimulus-response associations, this could explain, in part, the deficits that have been reported in clinical studies using a variety of visuomotor skill learning paradigms (Bylsma et al., 1990; Corkin et al., 1992; Doyon et al., 1997a; Ferraro et al., 1993; Harrington et al., 1990; Heindel et al., 1988; Heindel et al., 1989; Knopman & Nissen, 1991; Roy et al., 1993; Saint-Cyr & Taylor, 1992; Saint-Cyr et al., 1988; see Butters et al., 1994; Moscovitch et al., 1993; Salmon & Butters, 1995, for reviews). This learning mechanism could also account for the changes in blood flow in the striatum reported using similar tasks with PET and fMRI (Doyon et al., 1997b, 1996; Grafton et al., 1992, 1994; Jenkins et al., 1994; Passingham et al., 1995; Rauch et al., 1995, 1997).

Taken together, the present data suggest that the striatum could contribute to the programming and implementation of actions through a simple associative S-R type of learning system. Unlike the cerebellum, this structure could act as a sensori-motor integrative module necessary to the elaboration of motor programs based on S-R types of associations that are reminiscent of those examined in animal studies. An interesting parallel can be made with Marsden and Obeso's theory (1994), suggesting that the role of the basal ganglia lies in the automatic sequencing of motor plans. Although Marsden (1987) suggested that motor plans are not stored in the basal ganglia, it does not exclude the possibility that simple motor programs, which are the essential components of motor plans, could be elaborated in the basal ganglia based on such a mechanism.

#### Mirror-Tracing Task: Sequencing of Practiced Movements

Consistent with our predictions, the results reveal that patients with damage to the cerebellum, but not those with PD, are impaired on the mirror-tracing task as they did not show any facilitation effect when tracing the triad figures in the Practiced compared to the Unpracticed conditions. It is important to note that this lack of facilitation effect was observed even though the triads used in the Practiced and Unpracticed conditions did not

differ in level of complexity, and that patients in the CE group showed evidence of learning in tracing the simple figures in Phase III of testing. These results imply that patients in the CE group failed to benefit from earlier practice in tracing the individual simple figures before they were juxtaposed to produce the complex designs, hence suggesting that, contrary to patients with a striatal dysfunction, those with a cerebellar lesion are impaired in the sequencing of learned simple movements.

The present findings are in agreement with several neurophysiological investigations which showed that the cerebellum is involved in linking together the constituent, simpler movements that make up volitional compound motor actions (Hikosaka, Rand, Miyachi & Miyashita, 1995; Ito, 1982, 1993; Thach et al., 1992; see Bloedel 1992; Thach, 1996, for a review). They are also consistent with behavioral evidence in animals which demonstrates that this structure is involved in providing an on-line modification of activity in the central motor pathways that are required for the optimal coordination of movements (e.g., Gilbert & Thach, 1977; see Bloedel 1992; Harvey & Welsh, 1996; Thach, 1996, for reviews). In addition, they agree with the results of a series of clinical studies which reveal that damage to the cerebellum produces an impairment in the execution of programmed manual sequences before the onset of movement (Inhoff & Bisiacchi, 1990; Inhoff et al., 1989; Inhoff & Rafal, 1990). Finally, because the acquisition of a visuomotor skill usually results in an increase of both accuracy and speed with which movements can be harmonized into a fluid sequence of actions, the difficulty observed in the CE group in combining learned movements together could explain, in part, the deficits that have been reported in patients with cerebellar lesions using a variety of skill learning paradigms (Doyon et al., 1997a; Pascual-Leone et al., 1993; Sanes et al., 1990). Such a mechanism could also account for the changes in blood flow in the cerebellum that have been reported using similar tasks with PET and fMRI (Doyon et al., 1997b, 1996; Friston, Frith, Passingham, Liddle & Frackowiak, 1992; Grafton et al., 1994; Jenkins et al., 1994; Passingham et al., 1995; Seitz, Canavan, Yaguez, Herzog, Tellmann, Knorr, Huang & Homberg, 1994; Seitz, Roland, Bohm, Greitz & Stone-Elander, 1990).

The fact that patients with PD showed a significant facilitation effect, hence suggesting a preserved ability in combining acquired movements into a flowing action, may appear to be at variance with the results of recent clinical studies which suggest that PD impairs the smooth transition between two successive movements (Benecke et al., 1987; Canavan et al., 1989; Georgiou et al., 1994, 1995, 1993; Harrington & Haaland, 1991; Roy et al., 1993; Stern et al., 1983; Weiss et al., 1997; see Dominey & Jeannerod, 1997, for a review). Several reasons may explain this apparent divergence of findings. First, the difference could be related to the type of movements that were required. Indeed, in previous studies, a deficit in patients with PD was observed, for example, when they were asked to switch between two completely different types of movements such as elbow extention and hand squeeze (Benecke et al., 1987), or when transitions from one step in the sequence to the next required changes in hand posture (Harrington & Haaland, 1991). By contrast, no clear demarcation between the movements to perform while tracing the three juxtaposed simple figures in a triad was required, and thus our task did not elicit as much of the patients' capacity to switch from one motor program (which was learned in Phase III of testing) to another.

Second, the inconsistency may be due to the explicit vs implicit nature of the sequencing of movements that the patients had to execute. In the other studies, patients with PD acquired declarative knowledge of the sequence of movements they had to perform because 1) they were either asked to memorize the sequence (Rafal, Inhoff, Friedman & Bernstein, 1987; Stelmach et al., 1987) or to practice it before the experimental testing began (Benecke et al., 1987; Georgiou et al., 1994, 1995, 1993; Jones et al., 1992; Rafal et al., 1987), or 2) they were allowed to refer to a written version of the sequence they had to produce at all times during the experiment (Harrington & Haaland, 1991). In this study, however, the subjects were unaware that the triads in the Practiced condition were made of the consecutive juxtaposition of the simple figures they had practiced in Phase III, nor that the triads in the Unpracticed condition were composed of novel simple figures that they had never traced individually before. Therefore, it is possible that the difference between our results and those from earlier studies is due to

the fact that the patients' ability to combine learned movements into a sequence was measured in an implicit instead of an explicit fashion.

Third, evidence from animal (Brotchie, Iansek & Horne, 1991a, 1991b), clinical (Doyon et al., 1997a; Doyon et al., *in press*; Georgiou et al., 1994, 1995, 1993), and neuroimaging investigations (Doyon et al., 1997b, 1996; Grafton et al., 1994; Jenkins et al., 1994; Seitz et al., 1990), have demonstrated that the striatum is critically involved in the late phases of learning where automatization of a skill is thought to occur. Consistent with such a notion is the absence of deficit observed in both PD groups that may result from the fact that, in the present study, subjects had not achieved automatization of the task. It is thus possible that, if a greater number of trials had been given until subjects achieved asymptotic performance, a deficit following striatal dysfunctions could have been elicited as well. Finally, from a more methodological point of view, the normal performance of the PD groups could also be explained by the procedure that was used in our study. Contrary to the original version of this task (Blakemore, 1977) in which subjects started to trace directly between the contours of the figure (i.e., star), our version of this task always comprised a constant gap of 1 cm between the starting point and the beginning of the simple and complex figures. Given that the patient's performance was not recorded before he/she crossed this entry line, it is possible that such a gap helped by allowing them to set their motor program before they started to trace the figures. However, this seems highly unlikely because the distance of the gap was the same for all of the simple and complex figures, and also because trials in which subjects were seen to move around and to take an unusually long time before beginning the trial were very rarely encountered during the experiment.

Thus, together with the results of Inhoff and colleagues (1989), our findings suggest that the cerebellum is not only involved in the translation of a motor program into action before the onset of a movement, but that it plays an important role in combining the movements during the execution of a sequence of actions as well. They are also consistent with the classic view that the main symptom associated with cerebellar lesions is the decomposition of movements (Holmes, 1939).

### Final Comment

In recent years, several functional models have been proposed to account for the role of the striatum (Flowers, 1978; Marsden, 1982, 1987; Marsden & Obeso, 1994; Robertson & Flowers, 1990; Schmidt, 1975; Willingham & Koroshetz, 1993; see White, 1997, for a review), or the cerebellum (Inhoff & Rafal, 1990; Ito, 1993; Ivry & Keele, 1992; Paulin, 1993; Rispal-Padel, 1993; Thach et al., 1992; see Bloedel, 1992; Bloedel, Bracha, Shimansky & Milak, 1996; Ivry, 1996, for reviews), in motor skill learning. Other models that have tried to integrate the functions of both of these structures have also been put forth (Burton, 1990; Houk & wise, 1995; Jueptner et al., 1997; Wise & Houk, 1994). Very little evidence has been gathered, however, indicating that the contribution of the striatum and the cerebellum to the acquisition of skills could be dissociable (Doyon et al., 1997b; Grafton et al., 1994; Pascual-Leone et al., 1993). The findings of the present study constitute the first demonstration of a double functional dissociation between the striatum and the cerebellum in acquiring visuomotor skilled behaviors. In accordance with existing theoretical models (Bloedel, 1992; Bloedel et al., 1996; Burton, 1990; Graybiel & Kimura; 1995; Ito, 1993; Houk & Wise, 1995; Jueptner et al., 1997; Marsden & Obeso, 1994; Pascual-Leone et al., 1993; Thach, 1996; Thach et al., 1992; Wise & Houk, 1994), the results thus suggest that the striatum plays a critical role in perceptivomotor learning mechanisms based on S-R types of associations, whereas the cerebellum is preferentially involved in the ability to integrate separate learned movements implicitly into a fluid sequence. Considering the multitude of functions that have been assigned to each of these structures (e.g., Houk & Wise, 1995; White, 1997), it is expected that other dissociation in functions will soon be unveiled in future studies.

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Table 1. Subjects' Characteristics.

Variable/Group:	PD: Stage 1* (n=15)	PD: Stages 2-3* (n=15)	ANC (n=15)	Cerebellar (n=15)	YNC (n=15)
Age (years): Mean (SD)	58.7 (9.5)	59.3 (6.3)	53.0 (9.6)	40.7 (11.8)	42.5 (9.4)
Education (years): Mean (SD)	12.8 (4.5)	13.5 (4.2)	13.4 (4.0)	11.9 (3.00)	14.1 (3.3)
Sex (Female/Male)	5/10	7/8	9/6	8/7	5/10
Diagnostic	Akineto-rigid: 2 Tremor: 2 Mixed: 11	Akineto-rigid: 8 Tremor: 1 Mixed: 6	VCA: 4 OPCA: 1 CA: 8 SP: 2		
Duration of the disease	0-5 years: 11 6-10 years: 4 11-30 years: 0	0-5 years: 3 6-10 years: 6 11-30 years: 6	0-5 years: 4 6-10 years: 5 11-30 years: 6		
Lateralization	Left: 7 Right: 8 Bilateral: 0	Left: 0 Right: 0 Bilateral: 15	Left: 7 Right: 2 Bilateral: 6		
Medication	L-Dopa: 15  Anticholinergics Artane: 2 Parsitan: 0	L-Dopa: 15  Anticholinergics Artane: 4 Parsitan: 1			

\* Hoehn & Yahr's Scale (1967).

Legend: VCA: Vascular cerebral accident; OPCA: Olivo-ponto-cerebellar atrophy; CA: Cerebellar atrophy; SP: Spinocerebellar atrophy.

Table 2. Results of the Basic Neuropsychological Assessment for the Clinical Groups.

Test/Group	PD: Stage 1 (n=15) Mean (SD)	PD: Stages 2-3 (n=15) Mean (SD)	Cerebellar (n=15) Mean (SD)	Normative Data
Mini-Mental State Examination	28.90 (1.0)	28.30 (1.4)	27.30 (1.8)	Cutoff: < 27 <sup>1</sup>
General Health Status	2.13 (.35)	2.13 (.35)	2.20 (.56)	Cutoff: < 2
Beck Depression Inventory	11.50 (9.1)*	9.27 (5.1)	7.47 (5.9)	Cutoff: > 9
Purdue Pegboard (Both Hands)	9.13 (1.9)*	8.33 (1.5)*	7.13 (2.8)*	13.1 (1.3) <sup>2</sup>
WAIS-R: Mean Scaled Scores (SD)				
Digit Span	10.50 (3.0)	9.33 (2.7)	8.13 (2.1)	10 (3) <sup>3</sup>
Vocabulary	10.90 (2.8)	11.40 (1.8)	9.40 (1.9)	10 (3) <sup>3</sup>
Picture Arrangement	9.40 (3.3)	9.93 (3.0)	7.73 (2.7)	10 (3) <sup>3</sup>
Block Design	11.50 (3.3)	12.00 (3.9)	9.73 (3.0)	10 (3) <sup>3</sup>

\* Differs significantly from normative data.

Reference: <sup>1</sup> Folstein, 1983; <sup>2</sup> Spreen & Strauss, 1991; <sup>3</sup> Wechsler, 1987.

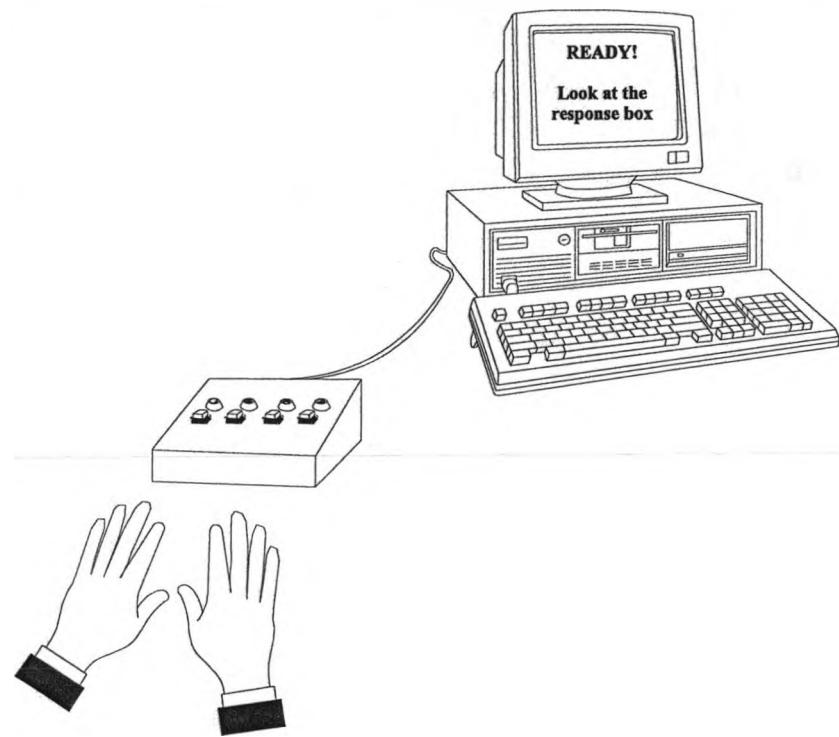


Figure 1. Diagram illustrating the response box used in the random version of the Serial Reaction Time task.

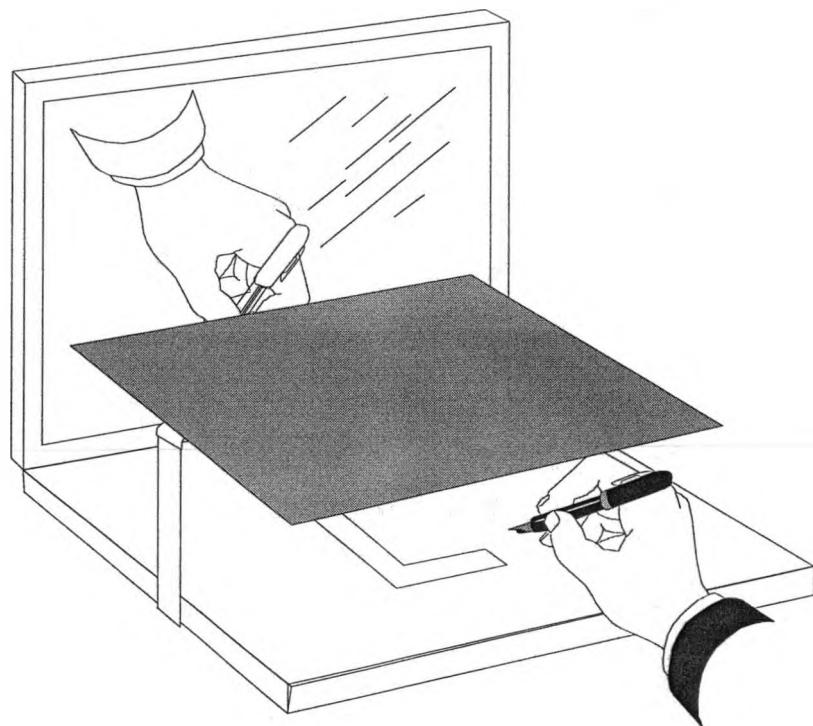


Figure 2. Diagram illustrating the mirror-tracing apparatus.

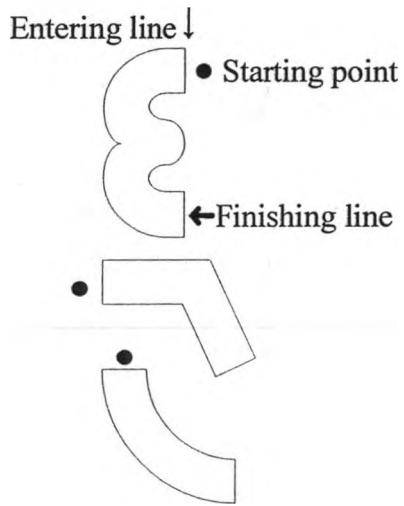
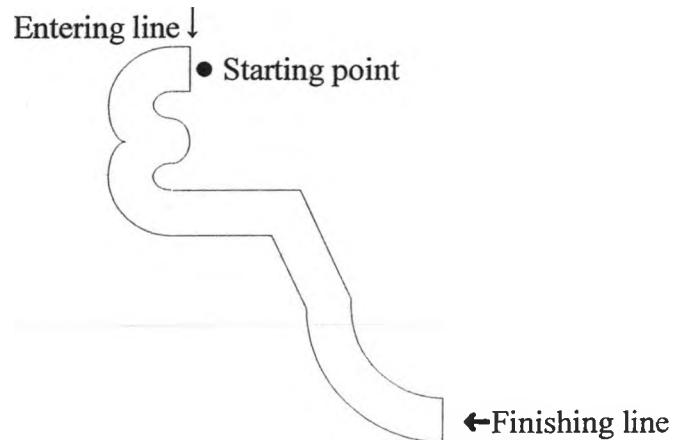
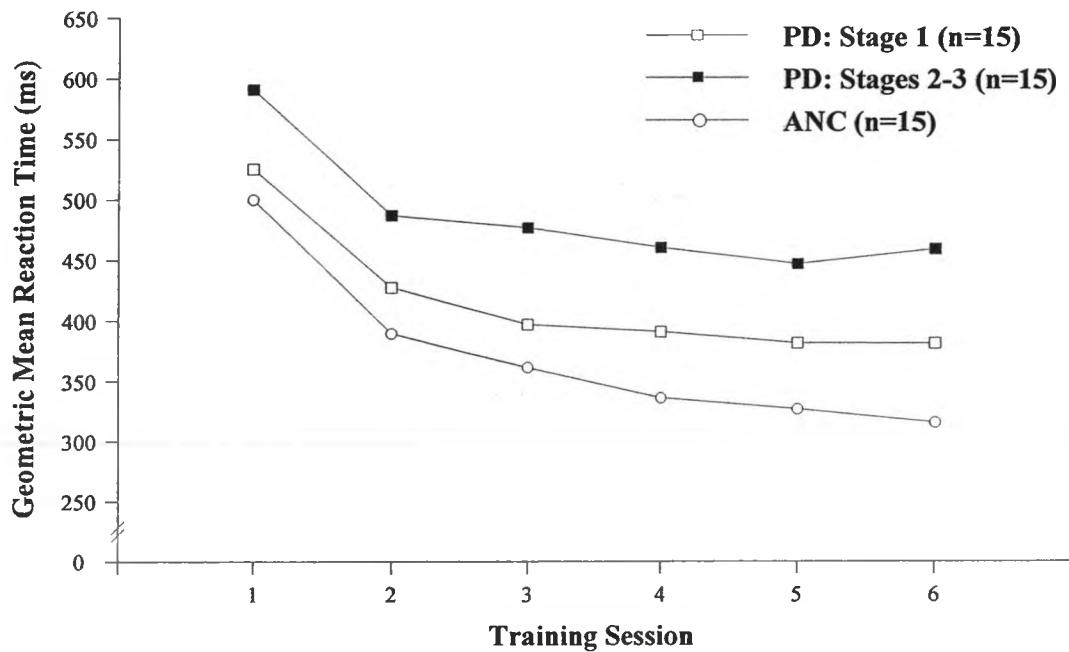
**A. Simple Figures****B. Triad of Simple Figures**

Figure 3. Examples of the a) simple figures, and b) complex triads used in the new adapted version of the Mirror-Tracing Test. In this task, subjects were asked to trace the figures through the reflection of a mirror as quickly as possible, while avoiding to touch the contours. The simple figures consisted of curved or angled designs, whereas the complex triads were composed of the consecutive juxtaposition of three simple figures.



**Figure 4.** Random Version of the Serial Reaction Time Task: Perceptivomotor Skill Learning. Geometric mean reaction times of the six training sessions for both groups of Parkinson's disease (PD) patients and the group of aged normal control subjects (ANC). Because the variance was almost nonexistent after a logarithmic transformation was applied to the RT data, no standard error bar is presented here.

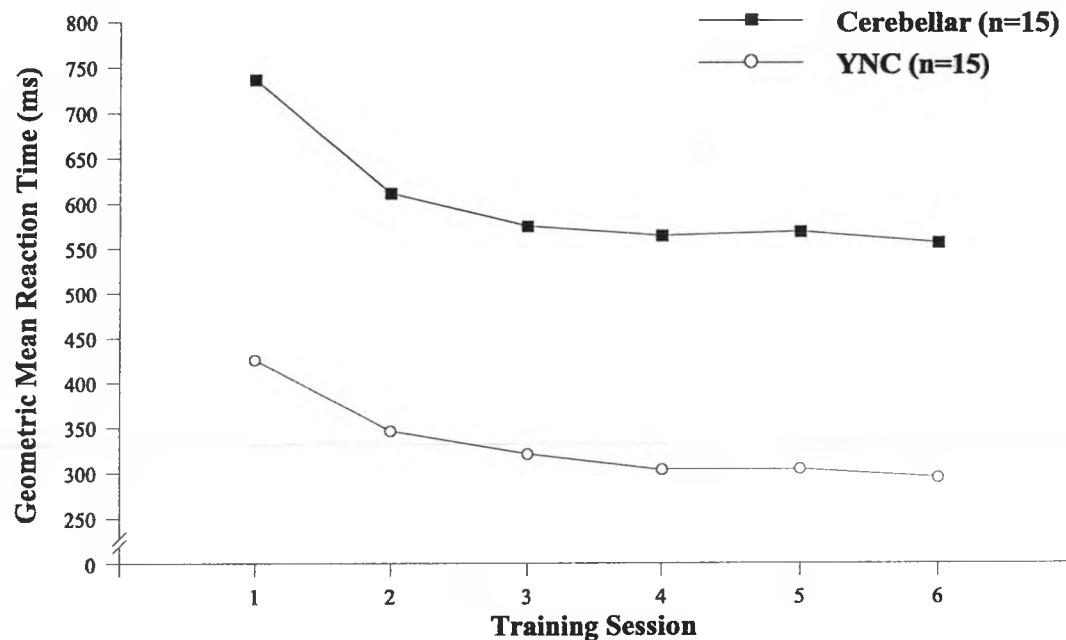
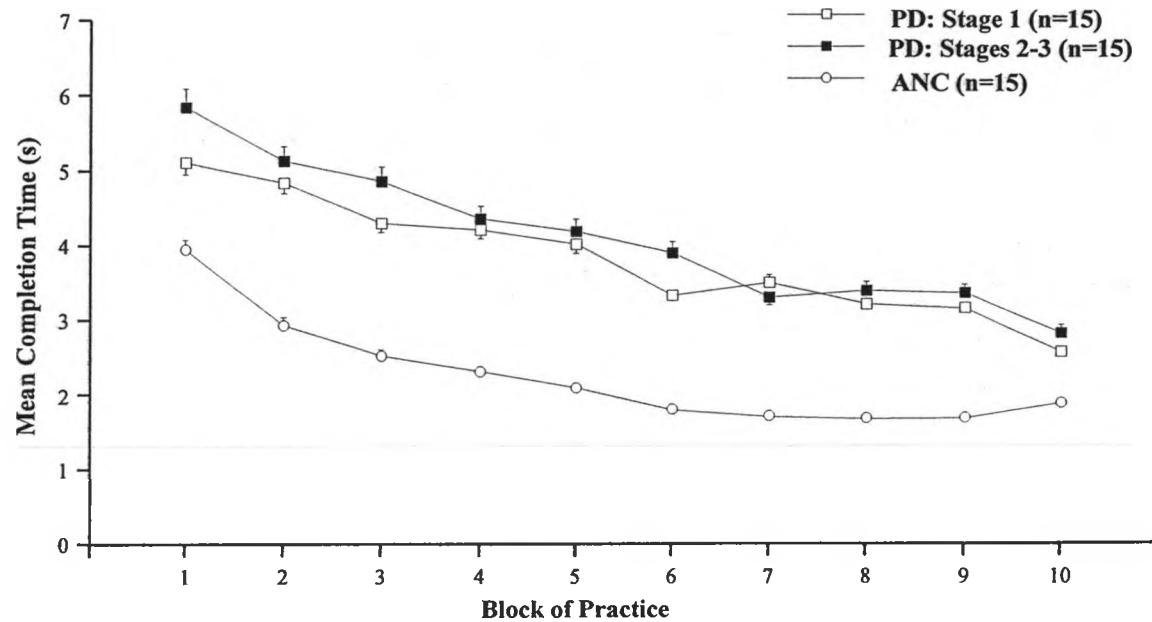
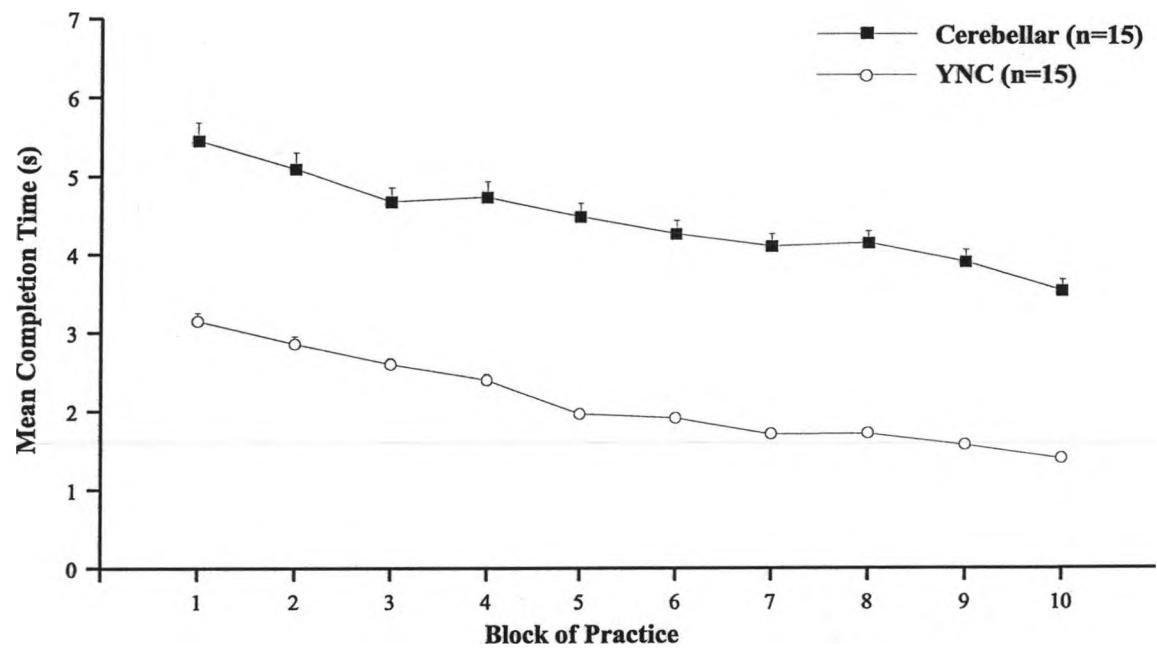


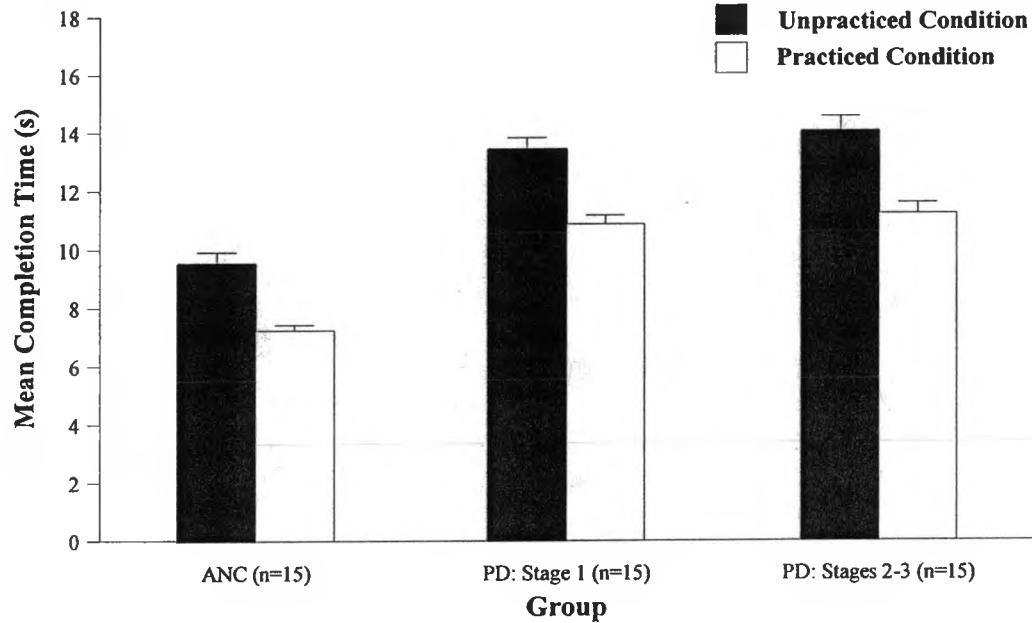
Figure 5. Random Version of the Serial Reaction Time Task: Perceptivomotor Skill Learning. Geometric mean reaction times of the six training sessions for the group of patients with damage to the cerebellum and the group of young normal control subjects (YNC). As for Figure 4, no standard error bar is presented because of the very small variance following the logarithmic transformation.



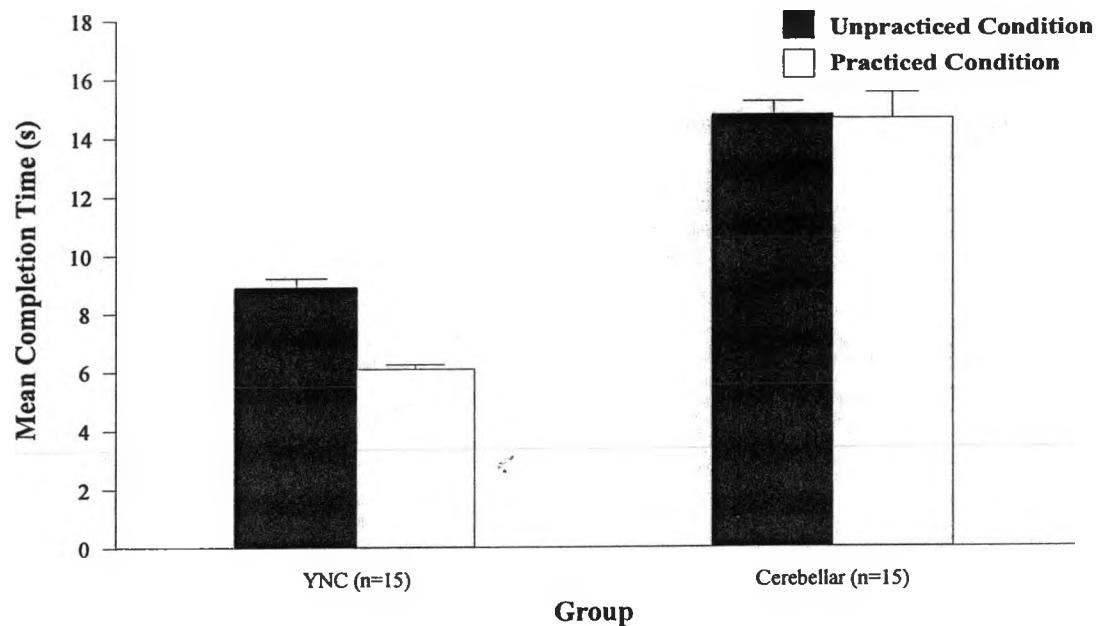
**Figure 6.** Mirror-Tracing Task: Learning of Simple Figures. Mean completion times for both PD groups and the ANC group.



**Figure 7.** Mirror-Tracing Task: Learning of Simple Figures. Mean completion times for the CE and YNC groups.



**Figure 8.** Mirror-Tracing Task: Sequencing of Practiced Movements. Mean completion times of the three sessions of triads in Practiced and Unpracticed conditions for both PD groups and the group of ANC subjects.



**Figure 9.** Mirror-Tracing Task: Sequencing of Practiced Movements. Mean completion times of the three sessions of triads in Practiced and Unpracticed conditions for the CE and YNC groups.

## CHAPITRE V

### ROLE OF THE STRIATUM AND THE CEREBELLUM IN THE ADAPTATION TO CONTEXTUAL CHANGE EXAMINED USING A VISUOMOTOR SKILL LEARNING PARADIGM

**Role of the Striatum and the Cerebellum in the Adaptation to Contextual Change  
Examined Using a Visuomotor Skill Learning Paradigm**

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**Running title: Striatum vs Cerebellum in the Adaptation to Contextual Change.**

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#### Author's Note

This work served as partial fulfillment of the requirements for a doctoral degree at the Department of Psychology, Laval University, Québec City (Québec), Canada. It was supported in part by a scholarship from "La Fondation de l'Université Laval" to Robert Laforce, Jr., and by a grant from the Natural Sciences and Engineering Council of Canada (OPGIN-012) to Dr. Julien Doyon. We are grateful to the patients and control subjects who participated in the present study. Also, we would like to address special thanks to Joanne Roy for her help in various aspects of this research. Thanks are also addressed to Rhonda Amsel for her statistical advice, and to all the members of the Groupe de recherche en réadaptation physique, IRDPQ, site François-Charon, Québec City (Québec), Canada, for their support.

### Abstract

The aim of this study was to examine the role of the striatum and the cerebellum in adapting to a change in context using a visuomotor skill learning paradigm. The performance of patients in the early (Stage 1) or advanced stages (Stages 2-3) of Parkinson's disease (PD), and of a group of patients with damage to the cerebellum (CE) was compared, respectively, to that of a group of aged (ANC) and young (YNC) matched normal control subjects on an adapted version of the Mirror-Tracing Test. In this task, subjects were required to trace a series of complex figures in two conditions: 1) a Practiced condition, in which the figures were composed of the juxtaposition of three simple designs that were individually practiced before testing began, and 2) a Mixed condition requiring adaptation to contextual change, in which new complex triads were created by replacing, at random, one of the three simple figures of the triads in the Practiced condition, by a new simple figure that had never been traced individually before. When compared to their respective control groups, no significant difference in performance between the Mixed and Practiced conditions was observed for the CE and PD groups, whereas patients in the PD Stages 2-3 group showed a significant increase in their mean completion time to trace the triads in these conditions. This suggests that a bilateral striatal dysfunction affects the ability to replace a learned motor plan by a new trajectory motion within a practiced sequence of movements. Furthermore, these results support the existence of an additional functional dissociation between the striatum and the cerebellum in acquiring visuomotor skilled behaviors.

## Introduction

A large body of research in both animals and humans has demonstrated that the striatum and the cerebellum play an important role in the ability to acquire motor skilled behaviors through practice (Doyon, Gaudreau, Laforce, Castonguay, Bédard, Bédard & Bouchard, 1997a; Graybiel, 1995; Graybiel & Kimura, 1995; see Bloedel, 1992; Bloedel, Bracha, Shimansky & Milak, 1996; Doyon, 1997; Leiner, Leiner & Dow, 1993; Moscovitch, Vriezen & Goshen-Gottstein, 1993; Thach, 1996; Thach, Goodkin & Keating, 1992; White, 1997, for reviews). In humans, degenerative conditions affecting the striatum such as in Parkinson's (PD) or Huntington's (HD) diseases, or circumscribed damage to the cerebellum are indeed known to produce a learning impairment on a variety of tasks that require eye-hand (or arm) coordination (Bylsma, Brandt & Strauss, 1990; Harrington, York Haaland, Yeo & Marder, 1990; Heindel, Butters & Salmon, 1988; Heindel, Salmon, Shults, Walicke & Butters, 1989; Roy, Saint-Cyr, Taylor & Lang, 1993; Saint-Cyr, Taylor & Lang, 1988; Saint-Cyr, Taylor, Trépanier & Lang, 1992; Sanes, Dimitrov & Hallett, 1990; see Butters, Salmon & Heindel, 1994; Salmon & Butters, 1995, for reviews), or the coarticulation of finger movements into a repeating sequence (Doyon et al., 1997a; Ferraro, Balota & Connor, 1993; Knopman & Nissen, 1991; Pascual-Leone, Grafman, Clark, Stewart, Massaquoi, Lou & Hallett, 1993; Willingham & Koroshetz, 1993). These clinical findings are further supported by an increasing number of studies with healthy control subjects using brain imaging techniques, such as positron emission tomography (PET) or functional magnetic resonance imaging (fMRI), in which increased neuronal activity reflected by hemodynamic changes in both of these structures, have been elicited in different acquisition stages of a visuomotor skill (Doyon, Karni, Song, Adams, Maisog & Ungerleider, 1997b; Doyon, Owen, Petrides, Sziklas & Evans, 1996; Flament, Ellermann, Kim, Ugurbil & Ebner, 1996; Grafton, Mazziotta, Presty, Friston, Frackowiak & Phelps, 1992; Grafton, Woods & Mike, 1994; Jenkins, Brooks, Nixon, Frackowiak & Passingham, 1994; Passingham, Jueptner, Frith, Brooks & Frackowiak, 1995; Rao, Harrington, Haaland, Bobholz, Binder, Hammeke, Frost, Myklebust, Jacobson, Bandettini & Hyde, 1995; Rauch, Savage, Brown, Curran, Alpert, Kendrick, Fischman & Kosslyn,

1995; Rauch, Whalen, Savage, Curran, Kendrick, Brown, Bush, Breiter & Rosen, 1997; Van Mier, Tempel, Perlmutter, Raichle & Petersen, submitted; see Doyon, 1997; Thach, 1996, for a review).

Although the striatum and the cerebellum are now known to be involved in the incremental acquisition of motor and visuomotor skills, there is increasing evidence from both imaging (Grafton et al., 1994), and lesion studies in humans (Laforce & Doyon, in preparation; Pascual-Leone et al., 1993), which suggest that these structures might contribute differently to this type of learning. For example, using the rotor pursuit task with PET in normal control subjects, Grafton and his colleagues (1994) have demonstrated that the cerebellum is mostly active during the acquisition of this visuomotor skill, whereas the putamen is mainly activated when subjects have achieved asymptotic performance of the skill. Other evidence supporting this notion comes from a recent study by Pascual-Leone et al. (1993), who have compared the performance of patients with PD or with damage to the cerebellum on a serial reaction time task (SRT), and demonstrated that the former had difficulty to translate procedural knowledge into declarative knowledge, while the latter group showed a deficit in both explicit and implicit aspects of sequence learning. These authors have proposed that the normal influence of the basal ganglia on the prefrontal cortex may be required for timely access of information to and from the working memory buffer, while the cerebellum may index and order events in the time domain, and therefore be essential for cognitive functions involving sequences. Finally, in our laboratory, we have recently reported the first double dissociation in functions between the striatum and the cerebellum in visuomotor skill learning by comparing the performance of groups of patients in early (Stage 1) or advanced stages (Stages 2-3) of PD, and of a group of patients with a cerebellar lesion (CE), to that of a group of aged (ANC) and young (YNC) matched normal controls, respectively, using a random version of the Serial Reaction Time task (SRT) as well as an adapted version of the Mirror-Tracing Test (Laforce & Doyon, in preparation). In the former task, subjects were asked to press the button located to the right of the stimulus that was illuminated whereas in the latter, they were required to trace a series of complex figures which consisted of the juxtaposition of three simple figures that they had either

practiced prior to testing (Practiced condition), or had never traced individually before (Unpracticed condition). The results revealed no significant difference between the CE and the YNC groups on the random version of the SRT task, whereas both PD groups were impaired on this task when compared to their ANC group. By contrast, only patients in the CE group failed to show a facilitation effect when tracing the figures in the practiced vs unpracticed conditions. These findings suggest that the striatum plays a critical role in perceptivomotor learning mechanisms based on stimulus-response (S-R) types of associations, whereas the cerebellum is preferentially involved in the ability to integrate separate learned movements into a fluid sequence.

This study reports yet another functional dissociation between the striatum and the cerebellum by examining the effects of contextual change. Adaptation to contextual change has been investigated in several different ways (e.g., Georgiou, Bradshaw, Iansek, Phillips, Mattingley & Bradshaw, 1994; Kimura, Kato & Shimazaki, 1990). For example, it can refer to a signal perceived in striatal neurons in relation to a change in the learning environment (i.e., visual, auditory, state of the organism, location of targets of action, etc.) (Kimura et al., 1990), or to any change in performance caused by the manipulation of contextual visual cues available to PD patients when performing a task (Georgiou et al., 1994). However, in accordance with the notion that the striatum, but not the cerebellum, is preferentially involved in the ability to adapt to a change in context (Graybiel & Kimura, 1995; Wise & Houk, 1994; see Schultz, Apicella, Romo & Scarnati, 1995, for a review), this experiment is based on the model proposed by Marsden and Obeso (1994), who have suggested that novel and external events can capture the attention of striatal regions to signify the need to change the course of movements.

The role of the striatum in adapting to contextual change has been corroborated by a number of neurophysiological investigations which have demonstrated that medium spiny output neurons in the anterior striatum (rostral putamen and caudate) show robust activity in relation to environmental cues (Caan, Perrett & Rolls, 1984; Kimura, 1992; Kimura et al., 1990; Nambu, Yoshida & Jinnai, 1988, 1990; Rolls, Thorpe & Maddison, 1983). This is also consistent with physiological data from Graybiel and Kimura (1995) who suggested that the basal ganglia may be in a privileged position to modify ongoing

motor and non-motor programs depending on particular internal and external conditions. This is further supported by the results of Schultz et al. (1995) who proposed that, in most cases, the activity of striatal neurons can not merely be explained by the physical characteristics of the stimuli presented or the movements performed, but that it rather depends on particular behavioral situations, conditions, or kinds of trials in a given task as well, hence showing some relationship to the context in which the particular events occurred. Finally, the notion that the striatum plays an important role in adapting to contextual change comes from clinical investigations in which it was shown that PD or HD patients have difficulty performing movements in the absence of external visual (contextual) cues (Bradshaw, Phillips, Dennis, Mattingley, Andrewes, Chiu, Pierson & Bradshaw, 1992; Georgiou et al., 1994; Jones, Phillips, Bradshaw, Iansek & Bradshaw, 1992).

The goal of the present study was thus to investigate, in humans, the role of the striatum in adapting to contextual change using a visuomotor skill learning paradigm. Furthermore, by comparing the performance of patients with a striatal dysfunction to those with damage to the cerebellum, this study also attempted to further investigate the possible functional dissociation that exists between these two structures. To this end, the performance of the same groups of PD and CE patients that participated in Laforce and Doyon's (in preparation) study was compared to that of their respective groups of aged (ANC) and young (YNC) matched normal controls on a recent adaptation of the Mirror-Tracing Test. In the latter task, subjects were required to trace a series of complex figures in two conditions: 1) a Practiced condition, in which the figures were composed of the juxtaposition of three simple designs that were individually practiced before testing began, and 2) a Mixed condition requiring adaptation to contextual change, in which new complex triads were created by replacing, at random, one of the three simple figures of the triads in the Practiced condition, by a new simple figure that had never been traced individually before. In accordance with the models suggesting that the striatum recognizes and registers behaviorally significant context in order to adapt the stream of subsequent movements (Graybiel & Kimura, 1995; Marsden & Obeso, 1994; Wise & Houk, 1994; see Schultz et al., 1995, for a review), it was expected that, compared to the

ANC group, only patients in the PD groups would show a deficit in tracing the figures in the Mixed compared to the Practiced conditions, whereas the performance of patients in the CE group would not differ significantly from that of the YNC group. Based on the results of our previous laboratory studies (Doyon et al., 1997a; Doyon, Laforce, Bouchard, Gaudreau, Roy, Poirier, Bédard, Bédard & Bouchard, in press; Doyon et al., 1996), and because the extent and severity of the cognitive impairments associated with PD have been found to be dependent upon the stage of the disease measured using Hoehn and Yahr's scale (1967) (Harrington et al., 1990; Mortimer, Pirozzolo, Hansch & Webster, 1982; Owen, Beksinska, James, Leigh, Summers & Marsden, 1993; Owen & Robbins, 1993; Taylor, Saint-Cyr, Lang & Kenny, 1986), it was also hypothesized that this impairment should be more evident in patients with a bilateral striatal dysfunction (i.e., patients in Stages 2-3 of PD according to the Hoehn & Yahr scale, 1967).

### **Method**

#### **Subjects**

The same five groups of subjects who participated in Laforce & Doyon's (in preparation) study were tested in this experiment. The patients were recruited via the Department of Neurological Sciences and Neuroradiology at the Hôpital de l'Enfant-Jésus, Québec City (Québec), Canada, whereas the aged and young normal control subjects were either acquaintances of the experimenters or volunteers from the community. None of the control subjects had a positive history of a psychiatric or neurological disorder. All of the subjects gave informed written consent for their participation in the study, which was approved by the Review Ethics Board of the Hôpital de l'Enfant-Jésus.

#### **Parkinson's Disease Groups (PD)**

Two groups of patients with a diagnosis of idiopathic Parkinson's disease were included in this study. The first group was composed of 15 patients (5 female, 10 male)

in Stage 1 of the disease as assessed by an experienced neurologist (Dr. P.J. Bédard, Hôpital de l'Enfant-Jésus), using the Hoehn and Yahr's scale (1967). On average, these patients were 58.7 (SD: 9.5) years old, and had 12.8 (SD: 4.5) years of education (see Table 1). The second PD group consisted of 15 patients (7 female, 8 male) in Stages 2-3 of the disease, and who were, on average, 59.3 (SD: 6.3) years old, and had 13.5 (SD: 4.2) years of education. All of these patients were taking optimal levels of levodopa medication at the time of testing. Patients with drug-induced parkinsonism, multiple system atrophy, cerebro-vascular disease, epilepsy, history of alcoholism, head injury or tumor, cerebellar disturbances, or disproportionate oculomotor and autonomic dysfunction were excluded from this study.

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Insert Table 1 about here

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### Cerebellar Group (CE)

A heterogeneous group of 15 patients (mean age [years]: 40.7, SD: 11.8; mean level of education [years]: 11.9, SD: 3.0) with a radiologically-documented lesion to the cerebellum was also tested (see Table 1). Twelve of them had pure cerebellar atrophy (PCA), while the other three had lesions extending into the brainstem or spinal cord. All of these patients showed signs of either dysarthria, ataxia, and/or dysmetria, although the severity of these cerebellar symptoms differed from one patient to the other.

### Normal Control Groups

Two separate groups of normal controls were selected to match the clinical groups with respect to mean age, mean level of education, and sex distribution (see Table 1). They were composed of a group of 15 ANC subjects and a group of 15 YNC subjects that were tested as controls for the PD and CE groups, respectively.

### Basic Neuropsychological Assessment

A short battery of neuropsychological tests was administered to the patients in the three clinical groups in order to eliminate those showing signs of dementia and/or depression. This assessment consisted of the Mini-Mental State Examination (Folstein, 1983) and of the "Vocabulary", "Digit Span", "Picture Arrangement", and "Block Design" subtests of the WAIS-R (Wechsler, 1987), as well as of a French version of the Beck Depression Inventory-Revised (BDI; Bourque & Beaudette, 1982). A home-made General Health Status scale, in which patients had to provide their own subjective estimation of their motor condition (1- Worse than usual, 2- Same as usual, and 3- Better than usual) before testing began, was also completed. This measure allowed to determine that the general physical state of the patients at the beginning of testing did not differ from their overall general health status. Furthermore, there was no clinical evidence of motor deterioration during testing sessions. It should be noted that PD patients in Stage 1 of the disease showed, on average, a score of 11.5 (SD: 9.1) on the BDI, which reflects signs of a mild level of depression. However, these patients were not excluded because 1) Taylor et al. (1986) have demonstrated that such mild depressive states do not interfere significantly with the patients' performance on cognitive tasks, and consistent with this notion, 2) the results of the present neuropsychological assessment revealed that these patients did not suffer an overall deterioration in their level of cognitive functioning. Finally, except for the three clinical groups who showed an impairment on the Purdue Pegboard task, hence reflecting a deficit in fine motor coordination, the results of these patients on the remaining tests of the basic neuropsychological evaluation did not show any particular cognitive dysfunction (see Table 2).

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Insert Table 2 about here

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### Material and Procedure

#### Mirror-Tracing Task: Contextual Adaptation

The capacity to adapt to contextual change was measured with a new visuomotor skill learning paradigm that was developed in our laboratory, based on the original Mirror-Tracing Test. The material and procedure have been described in detail elsewhere (Laforce & Doyon, *in preparation*). In brief, this task required that the subjects learned to trace figures of different shapes while viewing their hand and the figures through the reflection of a mirror (see Figure 1).

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Insert Figure 1 about here

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The present experiment constitutes an extension of the original study by Laforce and Doyon (*in preparation*), and was conducted 15 minutes after the subjects had completed Phase IV of the previous study, in which they were asked to complete three blocks of 12 triads, each block including 6 triads in the Practiced condition (i.e., triads composed of simple figures that were practiced earlier), and 6 triads in the Unpracticed condition (i.e., triads formed by the juxtaposition of simple figures that were never traced individually before). It should be noted that, at this point, subjects had also completed the first three phases in Laforce and Doyon's (*in preparation*) study, in which they were first familiarized with the tracing of simple figures and complex triads (Phases I and II), and were asked to complete 10 blocks of trials, each comprising of the same 18 new simple figures (Learning phase: Phase III).

In the present study, subjects were asked to trace a block of six triads in which, unbeknown to them, one of the three simple figures of each triad in the Practiced condition of Laforce and Doyon's (*in preparation*) study, was changed for another simple figure. Therefore, each triad in this condition, now called Mixed condition, was composed of the juxtaposition of two simple figures that subjects had previously practiced individually (see Phase III of Laforce & Doyon, *in preparation*), and one simple figure

they had never traced before (see Figure 2). The position in which one of the simple figure of the triad was replaced was determined at random. Finally, the subjects' performance on the Mixed triads was compared to that of the triads in the Practiced condition that were traced in the last block of trials in Phase IV of testing in Laforce and Doyon's (in preparation) study. The decision to select the last block of trials was motivated by the fact that results of Laforce and Doyon showed a significant improvement in the completion time required to trace the triads in the Practiced condition from Block 1 to Block 3,  $F(2,1068) = 28.55$ ,  $p < 0.0001$ , and that subjects showed the greatest improvement in Block 3 of testing. Finally, two dependent measures were recorded: 1) the mean completion time (CT) in seconds (i.e., the amount of time required to complete each figure from the beginning to the finishing line), and 2) the mean number of errors (i.e. the number of times a subject crossed the borders of a figure).

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Insert Figure 2 about here

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It is important to note that the level of difficulty of the different sets of triads that were compared in this experiment was controlled based on the results of a pilot study. Although the level of difficulty of the triads in the Practiced and Unpracticed conditions used in Laforce and Doyon (in preparation) had proven to be equivalent in their physical characteristics (accuracy and time required to complete the figures), a new pilot study was conducted to ensure the triads used in the Mixed condition were equivalent to the types of triads used in the Practiced condition. The results of a one-way analysis of variance conducted on the performance of a small group of 5 normal control subjects (mean age [years]: 26.7, SD: 10.3; mean level of education [years]: 14.9, SD: 11.1) revealed no significant difference between these types of complex figures with regards to total length, CT and mean number of errors. On average, the triads in the Practiced condition had a total length of 33.9 cm (SD: 1.6) compared to 32.9 cm (SD: 3.6) for the triads in the Mixed condition. Furthermore, the triads in the Practiced condition took a mean average of 18.2 sec. (SD: 11.1) to trace, whereas the triads in the Mixed condition were completed

in 18.8 sec. (SD: 15.9). Finally, there was no significant difference in the mean number of errors committed when tracing both types of triads (Practiced: 3.00, SD: 5.13, and Mixed: 1.27, SD: 1.46).

## Results

Patients in both PD groups and the CE group were well matched to their respective control groups as separate one-way analyses of variance (ANOVA's) did not reveal any significant difference between them with respect to either age or level of education. There was also no significant difference in the sex distribution of the subjects as measured with a  $\chi^2$ .

In order to assess the ability of these groups to adapt to contextual change, statistical analyses were conducted separately for the mean CT and mean number of errors, by comparing the performance of the clinical groups to that of their respective control groups on the last block of six trials in the Practiced condition of Phase IV in Laforce and Doyon (in preparation), with the block of six trials executed in the Mixed condition of the present experiment.

### Mirror-Tracing Task: Contextual Adaptation

#### Accuracy

A two-way repeated measures analysis of variance (ANOVA) with Group and Condition as between- and within-subjects factors respectively, was performed to compare the number of errors that the two groups of PD patients and the group of ANC subjects made on the two different types of triads (Practiced and Mixed). The results revealed a main effect of Group,  $F(2,42) = 3.36$ ,  $p < 0.05$ , as patients in the PD Stages 2-3 group produced significantly more errors (1.49, SD: 2.13) than the two other groups (ANC: .74, SD: 1.08; PD Stage 1: .52, SD: .87). There was no main effect of Condition, and the

Group x Condition interaction was not significant either, thereby suggesting that the three groups showed the same level of precision in tracing both types of triads.

The results of the analyses comparing the CE and the YNC groups yielded no main effect of Group, although patients in the CE group produced more errors (1.8, SD: 2.38) than the YNC group (.78, SD: 1.11). There was no effect of Condition, and again, the Group x Condition interaction was not significant, suggesting that the two groups did not differ in the number of errors made while tracing the triads in both Mixed and Practiced conditions.

### Completion Time

Figure 3 shows the mean CT in seconds of the two PD groups and their matched controls in tracing the triads in the Practiced and Mixed conditions. The results of the two-way repeated measures ANOVA revealed a main effect of Group,  $F(2,42) = 5.06$ ,  $p < 0.05$ , ANC subjects being significantly faster (6.84, SD: 2.56) than the two PD groups (PD Stage 1: 10.30, SD: 4.69; PD Stages 2-3: 10.6, SD: 6.39). There was no main effect of Condition, and the Group x Condition interaction was not significant, hence suggesting that, as a whole, the three groups did not differ in their ability to trace complex figures in both the Mixed and Practiced conditions.

Because *a priori*, it was hypothesized that PD patients with a bilateral striatal dysfunction would be more affected by this change in context than the two other groups, further contrast analyses were conducted comparing the performance of the PD Stages 2-3 group with that of the ANC group, as well as the PD Stage 1 with the ANC group. As expected, this yielded a significant interaction for the PD Stages 2-3 and ANC comparison only,  $F(1,28) = 4.37$ ,  $p < 0.05$ , hence suggesting a difference in the mean CT of both types of triads between these two groups. Together, this suggests that only patients with a bilateral striatal dysfunction of the striatum were affected by a change in the motor program required to perform the task.

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Insert Figure 3 about here

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Because differences observed in the PD Stages 2-3 group could also be due to the fact that 1) Mixed triads introduced new simple figures that had never been traced before, and 2) the position of such new figures within the triad was randomly determined, we compared the performance of the ANC group on the last block of triads in the Unpracticed condition (i.e., where triads were formed by the juxtaposition of simple figures that had never been traced individually before, see Laforce and Doyon [in preparation]), with that of their triads in the Mixed condition. Results of this analysis revealed a significant difference between these two types of triads,  $F(1,28) = 6.42$ ,  $p < 0.005$ , as the ones in the Mixed condition took significantly less time to complete (6.78, SD: 2.68) than the triads in the Unpracticed condition (9.20, SD: 5.91). These results examined in aged normal controls suggest that, despite the fact that Mixed triads incorporated a new simple figure, and that in such a type of triad, the order of presentation of the simple figures was changed, these were still traced faster than the triads comprising the juxtaposition of new simple figures used in the Unpracticed triads. Consequently, these findings observed in control subjects suggest that the increase in the CT shown by the patients in the PD Stages 2-3 group in the Mixed condition, when compared with triads in the Practiced condition, could not only result from these two alternative hypotheses.

The mean completion time required to trace the last block of triads in the Practiced condition during Phase IV in Laforce and Doyon's (in preparation) study, and those for the block of triads in the Mixed condition for the CE and YNC groups, are presented in Figure 4. Again, a two-way repeated measures ANOVA demonstrated a main effect of Group,  $F(1,28) = 17.30$ ,  $p < 0.0001$ , as the YNC subjects were considerably faster (5.85, SD: 1.95) than the CE group (13.0, SD: 7.83) in tracing the triads. However, the main effect of Condition and the Group x Condition interaction were not significant, hence suggesting that, contrary to the profile observed in PD patients in Stages 2-3, patients with cerebellar damage can adapt their movements to fit a contextual change.

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Insert Figure 4 about here

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**Correlation Analysis.** To determine whether the deficit observed in the PD Stages 2-3 group could be attributed to a cognitive dysfunction, a mood disturbance, or the severity of motor symptoms, a correlation analysis was carried out between the subjects' performance on the triads in the Mixed condition and the dependent measures gathered during the basic neuropsychological evaluation. The latter included scores of the Mini-Mental State Examination, the General Health Status scale, the Beck Depression Inventory, the Purdue Pegboard and the results on the WAIS-R subtests used in this experiment. The results of this analysis revealed no significant correlation, suggesting that the deficit observed in PD patients in Stages 2-3 could not be attributed to those cognitive or psychological variables.

### Discussion

The aim of this study was to examine the distinct contribution of the striatum and the cerebellum to the learning of visuomotor skills and, more specifically, to test one of the current models (i.e., Marsden & Obeso, 1994) which suggests that the striatum would be involved in the ability to adapt to a change in context (Graybiel & Kimura, 1995; Wise & Houk, 1994; see Schultz et al., 1995, for a review). Although based on a limited number of trials, the results revealed that young and aged normal control subjects, patients with a cerebellar degeneration, and PD patients in Stage 1 of the disease, did not show a significant difference in their time to complete the triads that were practiced on several occasions (Laforce & Doyon, in preparation), and the triads that were slightly changed by replacing one of the simple figures (Mixed condition). By contrast, PD patients with a bilateral striatal dysfunction showed a significant deterioration in performance when asked to trace the figures in the Mixed condition. Further analyses also showed that this deficit could not only result from the fact that the simple figure that was replaced was

never practiced before since ANC subjects demonstrated adequate adaptation (i.e., generalization) when tracing the triads in the Mixed condition, and that their mean CT was significantly faster when compared to Unpracticed triads. Finally, the correlation analyses demonstrated that the impairment observed on this task could not be attributed to a general decline in cognitive functioning, mood disturbances, or a motor limitation *per se*. Taken together, these results suggest that a bilateral lesion to the striatum impairs the capacity to generalize a learned ability to a change in the movement or motor program required by the task.

The impairment in contextual adaptation observed in patients with a bilateral striatal dysfunction is consistent with other neurophysiological (Caan et al., 1984; Kimura, 1992; Kimura et al., 1990; Nambu et al., 1988, 1990; Rolls et al., 1983; see Schultz et al., 1995, for a review), and clinical (Bradshaw et al., 1992; Georgiou et al., 1994; Jones et al., 1992) studies supporting the preferential role of the striatum in contextual adaptation. These results are also in accordance with previous behavioral findings which have shown that the extent and severity of the deficits associated with PD, either in the visuomotor skill learning domain (Doyon et al., 1997a, in press, 1996), or in the study of cognitive abilities at large (Harrington et al., 1990; Mortimer et al., 1982; Owen et al., 1993; Owen & Robbins, 1993; Taylor et al., 1986) have been found to be dependent upon the stage of the disease as measured with the Hoehn and Yahr's scale (1967). Finally, the data are consistent with both theoretical models (Burton, 1990; Houk & Wise, 1995; Graybiel & Kimura, 1995; Jueptner, Frith, Brooks, Frackowiak & Passingham, 1997; Marsden & Obeso, 1994; Wise & Houk, 1994) and behavioral evidence (Grafton et al., 1994; Knowlton, Mangels & Squire, 1996; Laforce & Doyon, in preparation; Pascual-Leone et al., 1993), that have demonstrated a dissociation in the mechanisms underlying the contribution of the striatum and the cerebellum in motor learning.

Contrary to the results reported in a study by Laforce and Doyon (in preparation), where it was demonstrated that only patients in the CE group showed a deficit in the ability to integrate separate learned movements into a fluid sequence using a very similar task, the data gathered in the present study show that these patients are not impaired when required to adapt to a change in context. Consequently, even though they did not show

a facilitation effect when tracing the triads that were composed of the juxtaposition of simple previously learned movements, the results of the present investigation demonstrate that they are able to adapt to a change in context without significantly increasing their overall performance in tracing figures, when compared with triads composed of learned simple movements only (i.e., Practiced condition). Taken together, these results can be interpreted as yet revealing another simple functional dissociation within the functions of the cerebellum.

In conclusion, the present findings suggest that, contrary to the cerebellum, the striatum plays a critical role in the adaptation to a change in context. Although very little behavioral evidence on the distinct contribution of the striatum and the cerebellum have been gathered to date in humans (Grafton et al., 1994; Laforce & Doyon, *in preparation*; Pascual-Leone et al., 1993), the results presented in this study are consistent with available theoretical models suggesting that the striatum recognizes and registers behaviorally significant context in order to adapt the stream of subsequent movements (Graybiel & Kimura, 1995; Marsden & Obeso, 1994; Wise & Houk, 1994; see Schultz et al., 1995, for a review). Furthermore, this is in accordance with Marsden and Obeso (1994) who proposed that the striatum can adapt to a change in context by modifying the motor pallido-nigral output so as to interrupt the stream of motor actions and allow new and appropriate motions. Considering the evidence gathered on the role of these structures in visuomotor skill learning, it is believed that further studies aiming at identifying the particular implication of both circuits will be needed to better understand the cerebral networks that support the elaboration and the execution of a learned visuomotor skill.

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Table 1. Subjects' Characteristics.

Variable/Group:	PD: Stage 1* (n=15)	PD: Stages 2-3* (n=15)	ANC (n=15)	Cerebellar (n=15)	YNC (n=15)
Age (years): Mean (SD)	58.7 (9.5)	59.3 (6.3)	53.0 (9.6)	40.7 (11.8)	42.5 (9.4)
Education (years): Mean (SD)	12.8 (4.5)	13.5 (4.2)	13.4 (4.0)	11.9 (3.00)	14.1 (3.3)
Sex (Female/Male)	5/10	7/8	9/6	8/7	5/10
Diagnostic	Akineto-rigid: 2 Tremor: 2 Mixed: 11	Akineto-rigid: 8 Tremor: 1 Mixed: 6	VCA: 4 OPCA: 1 CA: 8 SP: 2		
Duration of the disease	0-5 years: 11 6-10 years: 4 11-30 years: 0	0-5 years: 3 6-10 years: 6 11-30 years: 6	0-5 years: 4 6-10 years: 5 11-30 years: 6		
Lateralization	Left: 7 Right: 8 Bilateral: 0	Left: 0 Right: 0 Bilateral: 15	Left: 7 Right: 2 Bilateral: 6		
Medication	L-Dopa: 15  Anticholinergics Artane: 2 Parsitan: 0	L-Dopa: 15  Anticholinergics Artane: 4 Parsitan: 1			

\* Hoehn & Yahr's Scale (1967).

Legend: VCA: Vascular cerebral accident; OPCA: Olivo-ponto-cerebellar atrophy; CA: Cerebellar atrophy; SP: Spinocerebellar atrophy.

Table 2. Results of the Basic Neuropsychological Assessment for the Clinical Groups.

Test/Group	PD: Stage 1 (n=15) Mean (SD)	PD: Stages 2-3 (n=15) Mean (SD)	Cerebellar (n=15) Mean (SD)	Normative Data
Mini-Mental State Examination	28.90 (1.0)	28.30 (1.4)	27.30 (1.8)	Cutoff: < 27 <sup>1</sup>
General Health Status	2.13 (.35)	2.13 (.35)	2.20 (.56)	Cutoff: < 2
Beck Depression Inventory	11.50 (9.1)*	9.27 (5.1)	7.47 (5.9)	Cutoff: > 9
Purdue Pegboard (Both Hands)	9.13 (1.9)*	8.33 (1.5)*	7.13 (2.8)*	13.1 (1.3) <sup>2</sup>
WAIS-R: Mean Scaled Scores (SD)				
Digit Span	10.50 (3.0)	9.33 (2.7)	8.13 (2.1)	10 (3) <sup>3</sup>
Vocabulary	10.90 (2.8)	11.40 (1.8)	9.40 (1.9)	10 (3) <sup>3</sup>
Picture Arrangement	9.40 (3.3)	9.93 (3.0)	7.73 (2.7)	10 (3) <sup>3</sup>
Block Design	11.50 (3.3)	12.00 (3.9)	9.73 (3.0)	10 (3) <sup>3</sup>

\* Differs significantly from normative data.

Reference: <sup>1</sup> Folstein, 1983; <sup>2</sup> Spreen & Strauss, 1991; <sup>3</sup> Wechsler, 1987.

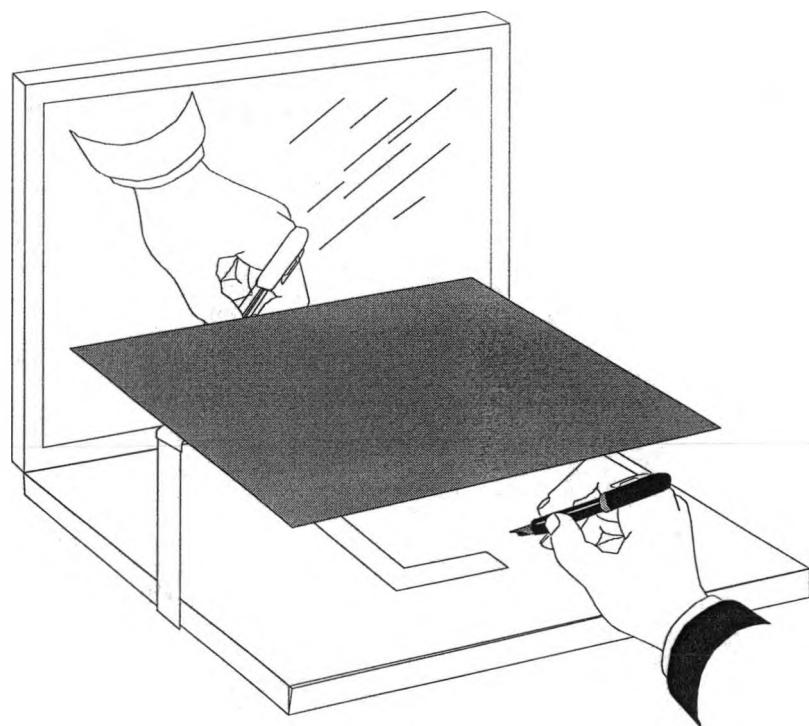
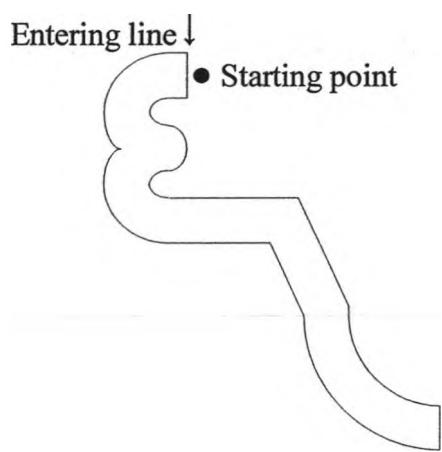
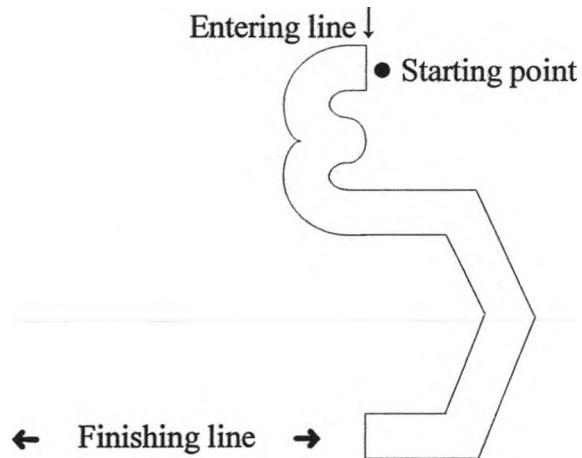
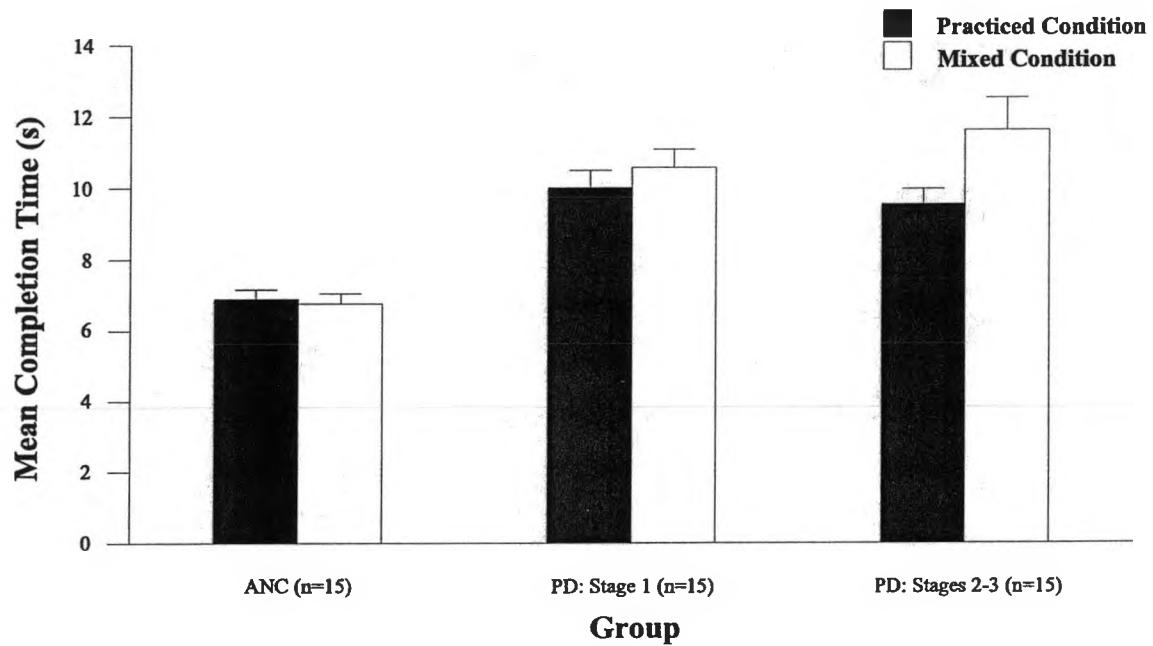


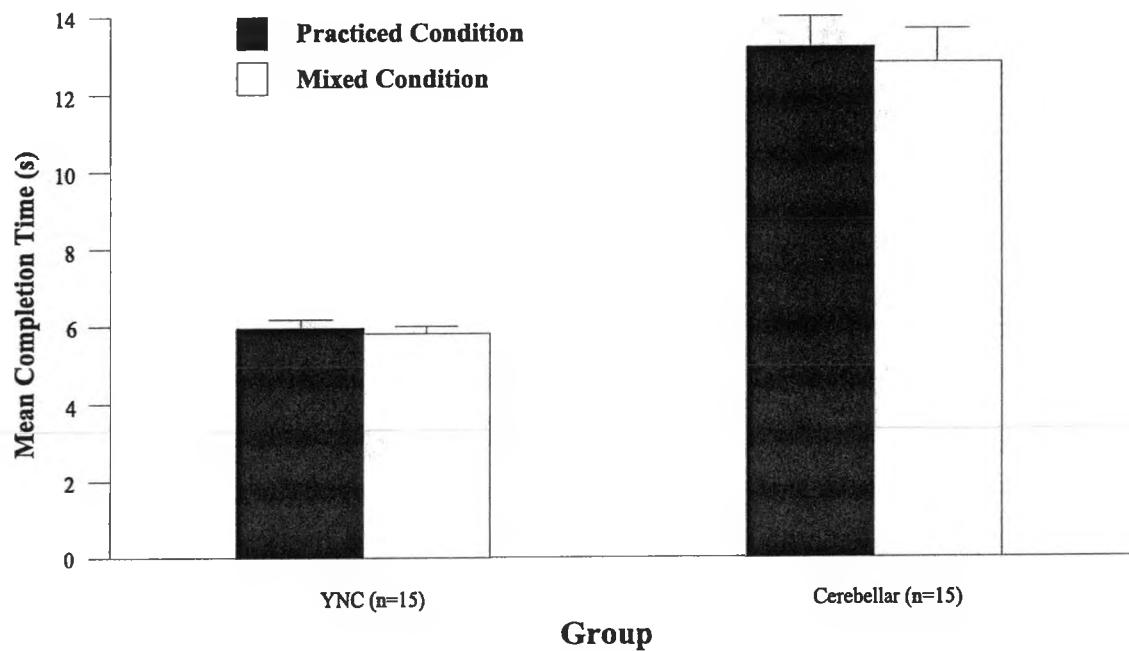
Figure 1. Diagram illustrating the mirror-tracing apparatus.

**A. Practiced Triad****B. Mixed Triad**

**Figure 2.** Examples of the a) practiced, and b) mixed triads used in the new adapted version of the Mirror-Tracing Test. In this task, subjects were asked to trace the complex figures through the reflection of a mirror as quickly as possible, while avoiding to touch the contours. Triads in the Practiced condition were composed of the consecutive juxtaposition of three simple figures learned individually before, whereas triads in the Mixed condition were generated by randomly replacing one of the three simple figures of the triads in the Practiced condition, by a new figure that had never been traced before.



**Figure 3.** Mirror-Tracing Task: Contextual Adaptation. Mean completion times for both groups of Parkinson's disease (PD) patients and the group of aged normal control subjects (ANC) to trace the triads in both Practiced and Mixed conditions.



**Figure 4.** Mirror-Tracing Task: Contextual Adaptation. Mean completion times for the cerebellar patients and the young normal control subjects (YNC) to trace the triads in both Practiced and Mixed conditions.

CHAPITRE VI

DISCUSSION GÉNÉRALE

Dans ce chapitre, les résultats de trois expériences réalisées afin de mieux connaître la contribution du striatum et du cervelet dans l'apprentissage d'habiletés visuomotrices sont d'abord résumés. Par la suite, une intégration générale de l'apport théorique de ces travaux est proposée. Enfin, basées sur les données recueillies dans cette thèse ainsi que sur l'ensemble de la littérature actuelle, des propositions de recherches futures sont présentées.

### Retour sur les résultats des trois études de la thèse

La première étude visait à vérifier si le déficit observé par Doyon et al. (1997a) dans les phases plus avancées de l'apprentissage d'une séquence visuelle répétée chez des patients porteurs d'une dysfonction striatale bilatérale était due à une difficulté au niveau du processus d'automatisation de l'apprentissage. Cette étude a été réalisée à l'aide de la technique de double-tâche. Tel que prévu, les résultats ont montré que seuls les patients en Stades 2-3 de la MP affichent une difficulté à compléter les matrices de Brooks (1967) de façon concomitante avec une séquence visuelle répétée. Ces données suggèrent que les patients porteurs d'une dysfonction bilatérale du striatum ne disposaient pas des mêmes ressources cognitives pour effectuer les deux tâches en même temps, et ce, même après plusieurs présentations de la tâche primaire (i.e., séquence visuelle répétée). En effet, il est important de souligner que ce trouble a été observé chez les mêmes patients qui ont montré un déficit lors des dernières phases d'acquisition de la tâche de séquence visuelle répétée dans l'étude de Doyon et al. (1997a). Dans l'ensemble, ces résultats sont donc en accord avec l'hypothèse selon laquelle le déficit, rapporté par ces derniers auteurs, s'explique par un problème au niveau de l'automatisation de la séquence. De plus, ils suggèrent que le striatum joue un rôle important dans ce type de processus.

L'objectif de la seconde recherche était d'approfondir la contribution distincte du striatum et du cervelet dans l'apprentissage d'habiletés visuomotrices. Basée sur les modèles actuels des mécanismes d'apprentissage propres au striatum (Graybiel, 1995; Graybiel & Kimura; 1995; Knowlton et al., 1996; Marsden, 1987; Marsden & Obeso,

1994; McDonald & White, 1993; Saint-Cyr & Taylor, 1992; Singh et al., 1993; voir White, 1997, pour une recension des écrits), au cervelet (Bloedel, 1992; Gilbert & Thach, 1977; Ito, 1993; Marr, 1969; Thach et al., 1992; Thompson, 1992; voir Thach, 1996, pour une recension des écrits) ainsi qu'à ceux qui ont tenté d'intégrer la contribution de ces deux structures (Burton, 1990; Houk & Wise, 1995; Jueptner et al., 1997; Pascual-Leone et al., 1993; Wise & Houk, 1994), cette recherche visait à explorer la participation possiblement distincte de chacune de ces structures dans l'acquisition d'habiletés à l'aide de deux tâches d'apprentissage visuomoteur. Une version aléatoire de la tâche d'acquisition d'une séquence visuelle répétée, puis une nouvelle version de l'épreuve de tracé-miroir ont été utilisées. Les résultats ont montré que, contrairement aux patients du groupe CE, les deux groupes de patients ayant la MP (Stade 1 et Stades 2-3) affichaient un déficit d'apprentissage à la version aléatoire de la tâche d'apprentissage visuomoteur. À l'inverse, seuls les patients du groupe CE n'ont pas montré d'effet de facilitation lors de la réalisation des figures dans la condition Pratiquée (i.e., figures formées par la juxtaposition de trois figures simples préalablement apprises) vs Non pratiquée (i.e., dessins développés à partir de la juxtaposition de trois figures simples qui n'avaient jamais été tracées auparavant) de la tâche de tracé-miroir. Les résultats obtenus constituent une première dans le domaine et suggèrent une double dissociation fonctionnelle entre le rôle de ces deux structures dans l'acquisition d'habiletés visuomotrices. Ensemble, ces données indiquent que le striatum et le cervelet participent de façon distincte à l'apprentissage d'habiletés. Alors que le striatum semble davantage gérer un apprentissage associatif (S-R) de type perceptivomoteur, le cervelet serait particulièrement nécessaire à la mise en séquence de mouvements appris.

La troisième étude tentait également d'explorer la contribution spécifique du striatum et du cervelet dans le développement des habiletés automatiques en utilisant, cette fois, un modèle récent qui propose que le striatum serait préférentiellement impliqué dans l'adaptation à un changement contextuel (Graybiel & Kimura, 1995; Marsden & Obeso, 1994; Wise & Houk, 1994; voir Schultz et al., 1995a, pour une recension des écrits). Tout comme dans l'expérience précédente, cette recherche a été effectuée à l'aide d'une version adaptée de la tâche de tracé-miroir. Dans cette épreuve, la performance des

mêmes sujets que ceux ayant participé à la deuxième étude a été comparée sous deux conditions soit le traçage de figures complexes formées par la juxtaposition de trois figures simples préalablement apprises (condition Pratiquée), soit celles développées en remplaçant aléatoirement une des trois figures simples préalablement apprises par une nouvelle figure simple (condition Mixte). De façon générale, les résultats n'ont révélé aucune différence significative entre la performance des patients des groupes CE et MP en Stade 1, et leurs groupes de sujets témoins respectifs, et ce, lors des conditions Pratiquée et Mixte. À l'inverse, les patients parkinsoniens de Stades 2-3 ont affiché une augmentation significative dans la réalisation des figures dans la condition Mixte comparée à celle dans la condition Pratiquée. En accord avec les modèles théoriques actuels, ces résultats suggèrent que le striatum joue un rôle important dans l'adaptation à un changement contextuel.

#### Contribution originale de ces travaux

D'une perspective générale, les résultats des études réalisées dans cette thèse apportent deux contributions majeures au domaine de l'apprentissage d'habiletés implicites. Premièrement, à l'intérieur d'un processus qui comprend vraisemblablement plusieurs phases (voir Anderson, 1990; Karni, 1996; Karni et al., in press), les données permettent de préciser que le striatum participe à l'automatisation des apprentissages lors de la phase lente d'acquisition des habiletés. Ces travaux sont en accord avec les études d'enregistrement cellulaire (Brotchie et al., 1991a, 1991b; Graybiel & Kimura, 1995; voir Schultz et al., 1995a, pour une recension des écrits) qui appuient l'existence de cellules du striatum affichant une activité intense lors des phases plus avancées de l'apprentissage moteur. Ils corroborent également plusieurs études d'imagerie cérébrale à l'aide de la TEP ou encore de l'IRMf dans lesquelles on note un changement dans le flux sanguin cérébral avec l'apprentissage d'une séquence répétée de mouvements (Doyon et al., 1996; Grafton et al., 1994; Seitz et al., 1990; voir Doyon, 1997, pour une recension des écrits). Enfin, de concert avec les études qui montrent que le striatum participe aux premières phases de l'apprentissage (Ferraro et al., 1993; Saint-Cyr et al., 1988), ces résultats

suggèrent donc que cette structure est impliquée dans toutes les phases de l'acquisition d'habiletés. Plus récemment, une étude effectuée dans notre laboratoire à l'aide du même protocole de double-tâche que celui utilisé dans cette thèse a permis de montrer que le cervelet serait également impliqué dans la phase d'automatisation des apprentissages (Doyon et al., sous presse). Ainsi, en accord avec les études cliniques (Doyon et al., 1997a, sous presse; Pascual-Leone et al., 1993) et les études d'imagerie cérébrale qui proposent que le striatum et le cervelet participent à l'apprentissage d'habiletés (Doyon et al., 1996; Grafton et al., 1994; Jenkins et al., 1994; Passingham et al., 1995; Seitz et al., 1990), il semble qu'une des contributions possibles de ces structures puissent se situer au niveau de l'automatisation des habiletés apprises par la pratique.

Deuxièmement, les résultats présentés dans cette thèse vont au-delà des nombreuses contributions récentes dans le domaine de l'apprentissage d'habiletés, en identifiant certains mécanismes qui pourraient être à la base de la contribution distincte du striatum et du cervelet dans l'acquisition d'habiletés visuomotrices. Dans le cas du striatum, par exemple, les résultats de la deuxième étude ont permis de montrer que la capacité d'apprentissage perceptivomoteur basée sur des associations de type S-R représente un des mécanismes de base permettant de distinguer la nature de sa participation à l'acquisition d'habitudes. Ces données sont d'ailleurs corroborées par plusieurs recherches dans le domaine physiologique et comportemental chez l'animal (Aosaki et al., 1994a, 1994b; McDonald & White, 1993; Packard et al., 1989; Packard & White, 1990; voir Graybiel, 1995; Graybiel & Kimura, 1995; Marsden & Obeso, 1994; White, 1989, 1997, pour une recension des écrits) où il a été démontré que le striatum participe à cette forme d'apprentissage associatif. Ils sont également en accord avec les résultats d'une étude d'imagerie dans laquelle les auteurs ont observé des changements dans le flux sanguin au niveau du striatum alors que les sujets effectuaient une version aléatoire de la tâche d'apprentissage d'une séquence visuelle répétée (Singh et al., 1993). De plus, ils corroborent les résultats obtenus récemment par Knowlton et al., (1996) qui suggèrent que le striatum fonctionne selon un mécanisme d'apprentissage d'associations qui sont caractéristiques de l'apprentissage d'habitudes. Plus encore, ces données suggèrent que le mécanisme d'apprentissage S-R ne semble pas affecté au début (phase

rapide) mais bien dans les stades plus avancés (phase lente) de l'apprentissage. En effet, les deux groupes de patients parkinsoniens et les sujets contrôles ont montré une diminution significative de leurs temps de réaction de la Session 1 à la Session 2. Par contre, à l'inverse des sujets contrôles qui n'ont cessé de s'améliorer qu'à la Session 4 d'entraînement, le déficit est apparu dès la deuxième session d'apprentissage dans le cas du groupe de patients MP en Stades 2-3 et, lors de la troisième session dans le cas des patients en Stade 1. Ces données permettent donc de postuler que le mécanisme d'apprentissage S-R est possiblement à la base du déficit au niveau de l'automatisation des apprentissages observés chez les patients qui souffrent d'une dysfonction bilatérale du striatum (Doyon et al., 1997a). Enfin, le profil des déficits rapportés plus haut corrobore également les données suggérant que la progression de la maladie est un facteur important à considérer dans ce genre d'étude (Doyon et al., 1997a; Harrington et al., 1990; Mortimer et al., 1982; Owen et al., 1993; Owen & Robbins, 1993; Taylor et al., 1986).

Toujours en ce qui concerne le striatum, les données recueillies dans la troisième étude identifient un autre mécanisme permettant possiblement de dissocier la nature de sa participation dans le domaine de l'apprentissage moteur. Selon les données de cette dernière, il semble que cette structure diencéphalique soit préférentiellement impliquée lors de l'adaptation d'un programme moteur en fonction d'une nouveauté contextuelle. Ces résultats sont en accord avec les recherches neurophysiologiques et neurochimiques (Caan et al., 1984; Kimura, 1992; Kimura et al., 1990; Nambu et al., 1988, 1990; Rolls et al., 1983; voir Schultz et al., 1995a, pour une recension des écrits) ainsi que les quelques études cliniques (Bradshaw et al., 1992; Georgiou et al., 1994; Jones et al., 1992) qui appuient la participation du striatum dans ce type de fonction.

Quant aux mécanismes privilégiés par le cervelet, les résultats de la deuxième étude ont permis de proposer qu'une des contributions spécifiques de cette structure pourrait se situer dans la capacité à mettre en séquence une série de programmes moteurs préalablement appris. Ce type de déficit est corroboré par des études neurophysiologiques qui suggèrent que le cervelet participe à la mise en séquence fluide et continue d'éléments indépendants (Hikosaka et al., 1995; Ito, 1982, 1993; Thach et al., 1992; voir Bloedel

1992; Thach, 1996, pour une recension des écrits). Ces résultats sont aussi en accord avec ceux des études réalisées chez l'animal qui montrent que le cervelet est impliqué dans la modification «en temps réel» de l'activité du système nerveux central, dans le but d'optimiser la coordination des mouvements (Bloedel 1992; Gilbert & Thach, 1977; voir Bloedel et al., 1996, pour une recension des écrits). Enfin, ces données se voient appuyées par une série d'études cliniques qui montrent qu'une dysfonction cérébelleuse affecte l'exécution de séquences motrices (Inhoff & Bisiacchi, 1990; Inhoff et al., 1989; Inhoff & Rafal, 1990).

En résumé, les résultats de l'Expérience I confirment que le striatum participe à la phase d'automatisation des apprentissages. Les résultats obtenus lors d'une seconde étude démontrent, pour la première fois, une double dissociation fonctionnelle entre le striatum et le cervelet lors de l'apprentissage d'habiletés visuomotrices. D'un côté, le striatum serait impliqué dans l'apprentissage associatif de type perceptivomoteur alors que l'intégrité du cervelet serait particulièrement importante dans les apprentissages nécessitant la mise en séquence de mouvements appris. Bien qu'exploratoires, les résultats de la troisième expérience suggèrent que les patients porteurs d'une dysfonction striatale bilatérale, et non ceux ayant une lésion au cervelet, montrent également une difficulté à s'adapter à un changement contextuel lors de l'exécution d'une nouvelle épreuve d'apprentissage visuomoteur. De façon générale, en plus de démontrer que le striatum est impliqué lors de l'automatisation d'habiletés visuomotrices, les données de cette thèse suggèrent que le rôle du striatum et du cervelet diffère quant aux mécanismes privilégiés lors de l'apprentissage d'habiletés visuomotrices.

### Propositions de recherches futures

L'ensemble des travaux réalisés dans le domaine de l'apprentissage d'habiletés visuomotrices, et plus particulièrement les résultats obtenus dans cette thèse, permettent de proposer quelques avenues de recherches qui pourraient contribuer davantage à l'avancement des connaissances dans ce domaine. Tout d'abord, malgré le fait que plusieurs chercheurs ont démontré que le striatum, le cervelet ou encore les deux à la fois,

participant à l'apprentissage d'habiletés motrices, très peu d'auteurs ont porté une attention particulière aux phases d'apprentissage dans lesquelles ces structures sont actives (Doyon et al., sous presse, 1996; Grafton et al., 1992, 1994; Jenkins et al., 1994; Seitz et al., 1990). En effet, jusqu'à très récemment, les recherches dans ce domaine ont révélé que ces dernières pouvaient être impliquées dans diverses phases de l'apprentissage, sans toutefois s'attarder véritablement à l'évolution des acquis propres à chaque structure selon un continuum bien déterminé dans le temps. À mon avis, une telle démarche s'avérerait pertinente afin de mieux cerner la participation du striatum et du cervelet dans l'apprentissage d'habiletés. De plus, elle pourrait représenter une piste de recherche permettant d'identifier d'autres mécanismes pouvant possiblement rendre compte du fonctionnement de chaque structure dans le cadre de l'acquisition d'une habileté.

Plus près des travaux réalisés dans cette thèse, les données rapportés plus haut dans le cadre de la deuxième étude suggèrent qu'un des mécanismes permettant de dissocier la contribution préférentielle du striatum et du cervelet dans l'apprentissage serait la participation prépondérante du cervelet dans la mise en séquence de mouvements appris. Cette interprétation provient du fait que, contrairement aux groupes de patients ayant la MP, les patients porteurs d'une lésion circonscrite au cervelet ne montrent pas d'effet de facilitation dans le traçage de figures complexes constituées de figures simples préalablement apprises (condition Pratiquée), comparativement à des figures complexes élaborées à partir de figures simples que les sujets n'ont jamais tracées auparavant (condition Non Pratiquée). Concrètement, ce déficit se traduit par une différence dans les moyennes de temps mises pour compléter les deux types de figures, les sujets témoins réussissant à bénéficier de l'apprentissage individuel des figures simples afin d'accélérer le traçage des triades dans la condition Pratiquée, contrairement aux patients porteurs d'une dysfonction cérébelleuse. Basé sur l'interprétation selon laquelle cette augmentation reflète une différence au niveau de la mise en séquence de mouvements appris, il s'avérerait extrêmement intéressant de démontrer que ce déficit est provoqué, non pas par une augmentation du temps de traçage des figures simples, mais bien par une augmentation significative des temps au niveau de l'espace théorique (qui demeurerait à préciser) entre les figures d'une triade, et ce, en comparaison avec les temps observés

chez les sujets du groupe contrôle. De façon à mesurer cette hypothèse, l'auteur propose donc de poursuivre l'étude du phénomène identifié dans la deuxième étude en utilisant, cette fois-ci, une présentation informatisée des stimuli à l'aide d'un écran tactile. En plus de mesurer électroniquement le temps passé sur la cible, celui hors cible, ainsi que le nombre d'erreurs, cette version de la tâche pourrait être programmée de façon à permettre la mesure de l'intervalle théorique situé entre chacune des figures simples constitutants les triades. Selon l'auteur, cette méthode permettrait véritablement de préciser la nature du déficit observé dans l'Expérience II.

D'autre part, bien que la troisième étude ait proposé une façon de mesurer l'adaptation contextuelle, d'autres travaux utilisant une plus grande variété de changements contextuels, de même qu'un plus grand nombre d'essais que ceux réalisés dans la troisième expérience de cette thèse, seront nécessaires afin de mieux cerner la nature spécifique de ce type de mécanisme. Aussi, quoique ces recherches se soient concentrées sur trois aspects particuliers de la contribution spécifique du striatum et du cervelet dans l'apprentissage visuomoteur, d'autres études seront nécessaires afin d'approfondir le fonctionnement de ces mécanismes ainsi que d'élargir ces derniers à d'autres fonctions potentiellement gérées par ces mêmes structures. Enfin, il serait intéressant d'adapter ces protocoles dans le cadre d'études d'imagerie cérébrale à l'aide de la TEP ou encore de l'IRMf, afin d'établir des corrélations entre les mécanismes sollicités lors de diverses tâches et les régions corticales et sous-corticales qui participent à cette forme d'apprentissage.

### Commentaire final

La notion de systèmes multiples de mémoire est maintenant bien connue de la communauté scientifique et bénéficie de plusieurs données provenant de travaux réalisés dans divers domaines spécialisés des neurosciences. Dans cette thèse, l'auteur s'est intéressé à l'un de ces systèmes de mémoire qui fait référence aux comportements que l'on apprend par la pratique ou encore de façon implicite. Jusqu'à présent, les études qui ont porté sur cette forme spécifique d'apprentissage suggèrent tant chez l'animal que chez

l'humain que le striatum, le cervelet ainsi que certaines régions corticales associées contribuent à l'acquisition et à la rétention d'habiletés motrices ou autres. Toutefois, jusqu'à maintenant, peu de chercheurs ont tenté d'identifier les mécanismes pouvant être à la base de la participation du striatum et du cervelet dans cette forme de mémoire. Par exemple, les recherches rapportées dans ce manuscrit constituent une première dans le domaine et montrent une double dissociation fonctionnelle entre ces deux structures lors de l'apprentissage d'habiletés visuomotrices. Le fonctionnement normal du striatum serait nécessaire à l'apprentissage associatif de type perceptivomoteur ainsi qu'à l'adaptation à un changement contextuel tandis que l'intégrité du cervelet serait particulièrement importante dans les apprentissages nécessitant la mise en séquence de mouvements appris. Considérant les nombreux modèles physiologiques qui ont été proposés pour expliquer le fonctionnement du striatum et du cervelet, il est à prévoir que d'autres dissociations fonctionnelles entre ces deux structures seront mises à jour dans un avenir rapproché. De plus, en me basant sur les nombreux travaux qui démontrent que le striatum et le cervelet jouent un rôle primordial dans certaines fonctions cognitives, je suis d'avis que les présentes recherches ne sont que le début d'une longue série d'études visant à élargir notre connaissance du rôle de ces deux structures non seulement dans diverses formes d'apprentissage mais également dans le fonctionnement cognitif humain.

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