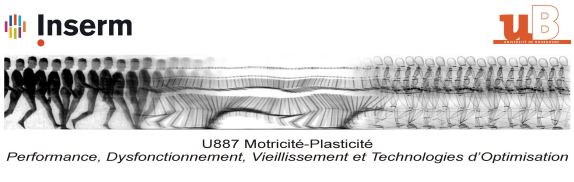
Flexibilité du contrôle moteur dans les mouvements complexes dirigés

Lilian Fautrelle



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Flexibilité du contrôle moteur dans les mouvements complexes dirigés

Présentée par :
Lilian Fautrelle

Sous la direction de :
François Bonnetblanc
&
Frédéric Ricolfi

Devant le jury composé de :

Vercher, Jean Louis, DR, UMR CNRS 6233, Université de la Méditerranée (Rapporteur)
Nougier, Vincent, Professeur, Laboratoire TIMC-IMAG, Université de Grenoble (Rapporteur)
Corneil, Brian, Dr, Gaze Control Lab, University of Western Ontario, Canada (Examinateur)
Assaiante, Christine, DR CNRS UMR 6149, Université de la Méditerranée (Examinateur)
Bonnetblanc, François, MCU, INSERM U887, Université de Bourgogne (Directeur de thèse)
Ricolfi, Frédéric, PUPH, Neuroradiologie, CHU-Dijon (Directeur de thèse)

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Résumé

L'objectif général de cette thèse est d'étudier dans les mouvements complexes, les propriétés psychophysiques de flexibilité d'un programme moteur suite à une perturbation inattendue et certaines de ses bases neurales. Pour ce faire, trois études comportementales et une étude en imagerie par résonance magnétique fonctionnelles ont été menées.

(1)Les principaux résultats de notre première étude démontrent que lors de la réalisation de mouvements complexes, après un déplacement inattendu de la cible visuelle, des corrections motrices peuvent apparaître très rapidement en une centaine de millisecondes dans les muscles de la jambe et du bras. De telles latences pourraient indiquer que les corrections motrices rapides à partir des entrées visuelles pourraient être générées grâce à des boucles corticales de bas niveaux.

(2) Lors d'un déplacement imprévu de la cible visuelle pendant l'exécution d'un mouvement complexe dirigé, les temps de correction sont significativement corrélés entre certaines paires de muscles, indépendamment de leur localisation anatomique ou de leur ordre d'apparition dans la séquence temporelle de recrutement musculaire. Ces résultats suggèrent que le système nerveux central est capable d'utiliser des synergies motrices fonctionnelles et complexes lors de la génération de corrections motrices.

(3) Lorsque la taille de la cible est modifiée de manière imprévisible pendant l'exécution du plan moteur initial, la durée du mouvement augmente, indépendamment de la variabilité de la précision terminale du mouvement de pointage. Ce résultat suggère que les retours sensori-moteurs et une représentation en (quasi) temps réel de la vitesse de l'effecteur sont utilisés pour générer et contrôler le déplacement de la main.

(4) Enfin, lors d'une tâche de rattrapés de balles répétitifs, en manipulant les conditions de prédiction a priori de la masse des balles utilisées, la dernière étude de ce travail expérimental démontre qu'un réseau cérébelleux bilatéral, impliquant les lobules IV, V et VI, est très majoritairement impliqué dans les processus de calcul de l'erreur sensori-motrice.

Dans les boucles corticales classiques impliquées dans la flexibilité motrice, le cervelet est engagé dans la génération de l'erreur sensori-motrice. Néanmoins, il semblerait que d'autres boucles de plus bas niveaux puissent être également employées afin de générer des corrections motrices très rapides. La coordination entre ces différentes boucles reste à être étudiée plus précisément.

Mots clés : flexibilité motrice, erreur sensori-motrice, correction motrice, mouvement complexe dirigé, système nerveux central.

Abstract

The main objective of this thesis is to study the motor flexibility in complex movements when an unexpected event makes the initial motor plan inefficient. In this way, three kinematic and electromyographic studies and a fourth with functional magnetic resonance imaging were realized.

(1)The main result of the first study clearly demonstrate that during complex movements express motor corrections in the upper and lower limbs, with latency responses of less than 100 ms, were revealed by contrasting electromyographic activities in perturbed and unperturbed trials. Such findings could indicate that visual on-going movement corrections may be accomplished via fast loops at the level of the upper and lower limbs and may not require cortical involvement.

(2) When an unexpected target jump occurred, correction times were strongly correlated together for some pairs of muscles independently of their occurrences during the motor sequence and independently of the location of the muscles at the anatomical level. This second study suggests that the CNS re-programs a new motor synergy after the target jumps in order to correct the on going reaching movement.

(3) When the target size is varied during the initial motor plan execution, the movement duration can increase independently of the variability of the final endpoint. These results suggests that when the speed-accuracy trade-off is unexpectedly modified, terminal feedbacks based on intermediate representations of the endpoint velocity are used to monitor and control the hand displacement.

(4) Finally, when catching a falling ball and the possibility of prediction about the ball weight was manipulated, the last study of this thesis showed that both the right and left cerebellum is engaged in processing sensory–motor errors, and more particularly the lobules IV, V and VI.

For classical loops involved in motor flexibility, sensory-motor errors are processed within the cerebellum. However, some shorter sub-cortical loops seem also to be involved for faster motor corrections. The coordination between these different loops needs to be explained more precisely.

Keywords: motor flexibility, sensory motor error, motor correction, goal directed movement, central nervous system.

I. INTRODUCTION

Rattraper un stylo qui roule sur une table avant qu'il ne tombe ou saisir une balle en mouvement sont des gestes quotidiens que nous exécutons sans nous focaliser sur leur contrôle. Cependant, pour accomplir de telles actions, notre cerveau doit résoudre un certain nombre de problèmes liés aux propriétés neurophysiologiques et biomécaniques de notre corps. De plus, un évènement imprévu peut survenir à tout moment et rendre le mouvement initial inapte à assurer la tâche désirée. Par exemple, la balle que nous souhaitons rattraper heurte un obstacle et change inopinément de trajectoire bien que le mouvement pour la saisir soit déjà initié. Avec le temps nécessaire, il est bien évident que nous pourrons ajuster notre mouvement et rattraper la balle.

Le système sensori-moteur humain est capable de s'adapter continuellement aux changements de l'environnement dans lequel il évolue. Pour cela, le cerveau utilise un signal d'erreur. Ce signal est obtenu par le Système Nerveux Central (SNC) en comparant les prédictions sensori-motrices qu'il a émises lors de la génération de la commande motrice (copie d'efference) avec les conséquences sensori-motrices réelles de l'action produite.

Classiquement, pour réaliser une action, le SNC génère une commande motrice à partir de ses intentions et des informations dont il dispose a priori sur les conditions initiales du système et de son environnement. Lors de l'envoi de cette commande motrice aux effecteurs (c'est-à-dire les muscles), une copie interne de celle-ci contenant les prédictions des conséquences sensorielles du mouvement programmé est également établie (cf. Figure 1, flèches bleues). Cette prévision des conséquences sensorielles du mouvement à venir peut alors être comparée aux retours sensoriels réels de l'action réalisée (cf. Figure 1, flèche verte). La différence entre les prévisions (prédictions sensori-motrices) et les retours sensoriels (afférences sensori-motrices) est appelée l'erreur sensori-motrice. Cette erreur offre deux aptitudes majeures au

cerveau dans le contrôle moteur : elle va permettre d'une part de générer des **corrections motrices** du mouvement en ligne lorsqu'un élément perturbateur imprévu intervient pendant l'action et rend le plan moteur initial inadéquat. D'autre part elle va permettre au SNC de réajuster la commande motrice à venir sur la base des erreurs de la commande motrice précédente. Ce processus est appelé **l'adaptation motrice**.

Parce qu'ils interviennent tous les deux sur des échelles de temps très courtes (quelques centaines de millisecondes à quelques secondes), nous regrouperons dans ce manuscrit sous le terme de **flexibilité motrice** les deux grands phénomènes permettant de moduler un comportement moteur en réponse à une perturbation inattendue: les corrections et l'adaptation motrices.

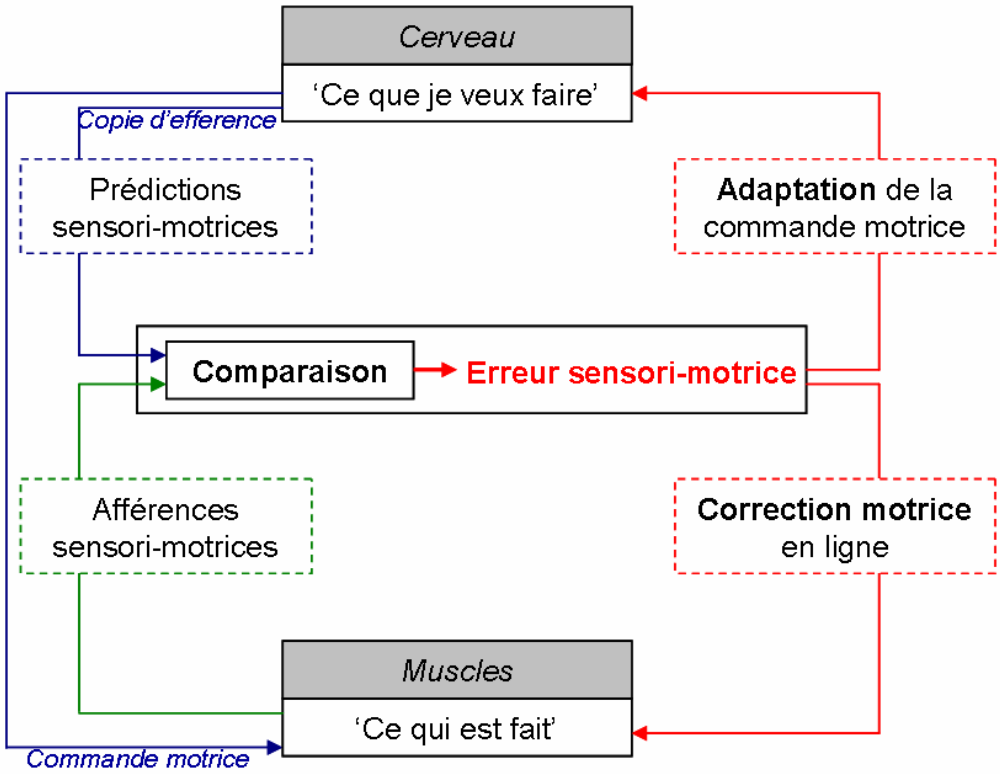

Figure 1 *Schématisation des processus de la flexibilité motrice (Johansson 1998, Desmurget et Grafton 2000, Bastian 2008). Le contrôle moteur nécessite des régulations permanentes face aux modifications de l'environnement. Pour cela, le cerveau génère un signal d'erreur en comparant les sorties prédites d'un certain comportement ('Ce que je veux faire') avec la sortie réelle ('Ce qui est fait'). Ce signal d'erreur va permettre au SNC de générer des corrections motrices en ligne et des adaptations hors ligne essai par essai.*

Ce premier schéma illustre de manière simple les capacités de flexibilité du système moteur humain (cf. Figure 1, flèches rouges) lors de la production de mouvements volontaires. Les processus nécessaires à cette flexibilité motrice nécessitent l'implication de certaines structures cérébrales comme le cervelet qui est impliqué dans le calcul de l'erreur sensori-motrice, ou le cortex pariétal qui est impliqué quant à lui dans l'intégration sensorielle. Néanmoins, ce modèle classique peut voir son fonctionnement questionné quant à la durée de mise en œuvre et aux latences de corrections. En effet, réaliser un mouvement en réponse à un stimulus visuel implique de nombreux processus biophysiques couteux en temps. De ce fait, la durée cumulée de plusieurs périodes de latences (délais de transduction, de conduction, de traitement…) apparaît comme une limite à la capacité de production de corrections motrices en ligne lors de la réalisation de mouvements rapides. Les valeurs de ces périodes de latences sont grandement débattues dans la littérature. De nombreuses études neurophysiologiques et comportementales sur les délais visuo-moteurs et les corrections motrices en ligne exposent des délais contradictoires (Bullier 2001, Maunsell et Gibson 1992, Archambault 2009, Corneil et al. 2004, Gomi 2008). De plus, de nombreuses approches différentes ont permis d'établir plusieurs modèles et plusieurs hypothèses sur les capacités du SNC à adapter le contrôle moteur face à l'apparition d'une perturbation.

L'objectif général de cette thèse est de contribuer à l'étude des capacités de flexibilité du contrôle moteur lors de la production de mouvements complexes dirigés. Dans un premier temps, nous établirons une revue synthétique des connaissances actuelles. Cette première partie relate les principales théories et études neurophysiologiques ou comportementales qui établissent des relations entre une perturbation environnementale et la modification d'un comportement moteur lors de la réalisation de mouvements

dirigés. Dans un second temps, nous présenterons notre travail expérimental qui comporte quatre études différentes. Les trois premières études utilisent des paradigmes de pointages complexes avec sauts de cible et des mesures comportementales comme l'enregistrement de la cinématique du mouvement, des forces de réaction au sol, et des activités électromyographiques de surface. C'est en mesurant et en analysant les latences sur ces différents signaux que nous tenterons d'inférer le type de boucle nerveuse qui intervient dans ces corrections motrices. L'étude des comportements périphériques est un moyen d'étudier les processus nerveux centraux impliqués dans le contrôle du mouvement humain.

La première étude s'attache à déterminer les latences minimales de déclenchement de corrections motrices chez l'homme lors d'une tâche de pointage visuo-manuel complexe. En associant ces délais de corrections avec les délais de conduction des afférences et des efferences ainsi que des traitements neuronaux reportés dans la littérature scientifique, il devient alors possible d'investiguer les circuits neuronaux potentiels impliqués dans les mécanismes de génération des corrections motrices en ligne. Dans la seconde étude, nous nous intéresserons à l'organisation des séquences musculaires impliquées dans la correction en ligne d'un mouvement complexe dirigé impliquant tous les membres et perturbé par un saut de cible. En effet, lors d'études de mouvements de pointage ou de saisie réalisées en position assise, de nombreux auteurs ont rapportés une séquence de recrutement musculaire séquencée de manière proximo-distal (Jeannerod 1986, Ma et Feldman 1995). De tels résultats nous conduiraient à émettre l'hypothèse que les corrections motrice les plus précoces apparaitraient pour les muscles les plus proximaux. Cependant, afin de réduire la complexité du contrôle moteur, il est maintenant bien établi que le SNC développe une organisation synergique des activations musculaires (Bernstein 1967). Pour cela, le SNC est capable de combiner et de

moduler un petit nombre de patrons d'activations musculaires afin de produire une multitude de mouvement (D'Avella et al. 2003, 2005, 2006 ; Musssa-Ivaldi et Bizzi 2000, Torres-Oviedo et al 2006). En conséquence, la seconde étude aura pour but de répondre à la question suivante : suite à une perturbation inattendue survenant au cours d'un mouvement complexe dirigé, le SNC établit-il des corrections rapides sur un mode de recrutement musculaire simple de type proximo-distal ou, au contraire, est-il capable d'établir des liens complexes entre les différentes activations musculaires engagées dans la correction motrice ?

Dans la troisième étude, notre objectif principal est de confronté la flexibilité motrice à un changement de taille de cible pendant la réalisation du mouvement. Il est acquis que lors d'un mouvement de pointage, une relation lie la précision terminale et la vitesse d'exécution du mouvement de pointage (Woodworth 1899). Plus la précision terminale requise lors du mouvement est grande, et plus le mouvement sera lent. Dans la même veine, plus la vitesse du mouvement est grande, et plus la précision terminale est variable (Schmidt et al. 1978, 1979; Harris et Wolpert 1998). Ce principe moteur est appelé le « conflit vitesse-précision » et la relation mathématique liant l'un à l'autre fut explicitement présenté par Fitts (1954). Là encore, en raison de l'importance des délais des informations afférentes et efférentes, certains auteurs défendent l'idée que ce conflit « vitesse-précision » est directement pris en compte par le cerveau dès l'élaboration de la commande motrice (Schmidt et al. 1978, 1979; Meyer et al. 1982, 1988, 1990; Harris et Wolpert 1998). D'autres approches nuancent quant à elles cette idée et émettent l'hypothèse que la position de la main et de la cible peuvent être comparées pendant la réalisation du mouvement (Hoff et Arbib 1993 ; Desmurget et Grafton 2000, Elliott et al. 2001; Bonnetblanc 2008). Dans ce cas, la position terminale de la main découlerait de processus nécessitant l'implication de retours sensoriels. Modifier la taille de la cible pendant le mouvement est un moyen d'étudier

l'impact du « conflit vitesse-précision » sur les corrections motrices en ligne. Nous émettons ici l'hypothèse qu'une prise en compte précoce du conflit vitesse-précision par le SNC dans la commande de correction motrice induira une variabilité de la position finale de la main proportionnelle à la taille de la cible. Au contraire, si des processus nécessitant des retours sensoriels sont impliqués dans la correction en ligne, la variabilité de la position terminale de la main pourrait être indépendante de la taille de la cible. Dans ce cas, la durée du mouvement de pointage après l'apparition de la perturbation pourrait être rallongée.

Dans ces trois premières études, une perturbation visuelle est artificiellement produite de manière imprévisible pendant l'exécution du mouvement engendrant chez les sujets un signal d'erreur sensori-moteur puis le déclenchement de corrections sensori-motrices.

La quatrième étude est conduite quant à elle au moyen d'un protocole expérimental mené en imagerie par résonnance magnétique fonctionnelle (IRMf). D'un point de vue méthodologique, l'IRMf est une technique d'imagerie par résonnance magnétique particulière qui permet d'enregistrer l'activité cérébrale et d'analyser le fonctionnement du cerveau. Cependant, bien que cette technique soit en plein essor dans le domaine des neurosciences, nous souhaitons souligner ici que l'activité cérébrale est enregistrée de manière indirecte. Le signal recueilli avec cet instrument de mesure est la variation des propriétés des flux sanguins cérébraux (appelée variation hémodynamique). Plus particulièrement, tout comme un muscle, les neurones activés par une tâche vont augmenter leur consommation en oxygène. De ce fait, le flux sanguin (perfusion sanguine) augmente. De cette augmentation découle une diminution de la concentration en désoxyhémoglobine. Ce type d'hémoglobine possède des propriétés magnétiques qui permettent à l'appareil IRM de détecter et de mesurer la quantité de cette molécule par unité de volume à l'intérieur du cerveau de

manière non invasive. Une diminution de la concentration en désoxyhémoglobine engendre une augmentation d'un paramètre IRM appelé T2*. En résumé, cet effet enregistré par l'antenne IRM est appelé l'effet BOLD (Blood Oxygen Level Dependant) et représente de manière indirecte l'activité cérébrale du cerveau puisque dans une région cérébrale donnée, le signal mesuré augmente quand l'activité neuronale augmente.

Nous avons vu précédemment que le signal d'erreur sensori-moteur est primordial pour assurer deux fonctions essentielles dans la flexibilité du contrôle moteur : premièrement, il permet le contrôle en ligne et le déclenchement de corrections motrices. Deuxièmement, ce signal d'erreur semble être nécessaire aux processus d'adaptation de la commande motrice sur une base d'essai par essai lors de la production répétée d'une action de même intention. Dans ce dernier cas de figure, les études physiopathologiques ont permis de démontrer une implication fondamentale du cervelet dans les processus d'adaptation (Babin-Ratté et al. 1999, Lang et Bastian 1999, 2001, Nowak et al. 2002, 2007). C'est pourquoi, dans cette quatrième et dernière étude, nous nous intéresserons aux corrélats neuro-anatomiques des aires corticales impliquées dans les processus de calculs de l'erreur sensori-motrice au moyen d'un protocole conduit en imagerie par résonnance magnétique fonctionnelle en nous focalisant plus particulièrement sur le cervelet.

Dans une dernière partie, nous discuterons l'ensemble de ces travaux expérimentaux tout en exposant leurs limites. Pour conclure, nous exposerons les perspectives de ces travaux en confrontant leurs résultats aux modèles et hypothèses présentées dans la partie théorique.

II. CADRE THEORIQUE

1. PRODUIRE UN MOUVEMENT DIRIGE : UNE TACHE COMPLEXE POUR LE CERVEAU

Dans ce premier paragraphe, l'objectif est de rappeler la succession des processus nécessaires pour établir une commande motrice qui engendrera de manière adéquate la réalisation d'un mouvement en direction d'une cible.

Avant toute chose, le cerveau doit localiser spatialement la cible à atteindre. Pour réaliser le lien entre la position de la cible visée et la commande motrice adéquate à envoyer, le SNC doit procéder à des transformations sensori-motrices. Une première solution envisageable pour le SNC est de coder l'emplacement de la cible dans un référentiel spatial indépendant de la position du corps qu'il dirige. Il s'agit dans ce cas d'un référentiel dit allo- ou exocentrique. Une seconde solution consiste à référencer spatialement la position de la cible à atteindre en fonction d'une partie du corps. Il s'agit dans ce deuxième cas d'une représentation dite égocentrée. Au sein de cette représentation peut être soulevé encore un nouveau problème : Sur quelle entité du corps le SNC va-t-il se baser pour déterminer la position à atteindre ? Des entités plutôt fixes durant le mouvement comme la tête ou les yeux, ou l'effecteur principal c'est-à-dire la main dans notre cas ? Quoiqu'il en soit, toutes ces solutions sont potentiellement utilisables par le cerveau afin de réaliser le mouvement. Un premier niveau de complexité dans ce type de mouvements réside donc dans le fait que le SNC doive procéder à plusieurs changements de cadre de référence (Paillard 1971). Pour réaliser des mouvements dirigés avec succès, le cerveau doit transformer des coordonnées d'un objet extérieur au corps en coordonnées intrinsèques (Desmurget et al. 1998).

A ce stade, le SNC doit alors élaborer une trajectoire de la main parmi une infinité de solutions possibles. En effet, il existe de très nombreuses

trajectoires potentielles qui permettent à la fois d'être réalisées par le système biomécanique du corps et d'atteindre la cible avec succès. Si la trajectoire rectiligne, c'est-à-dire la plus courte distance reliant la position initiale de la main à l'objet cible, peut paraître a priori la plus évidente, toutes les trajectoires reliant le point de départ au point d'arrivée permettent d'accomplir la tâche.

Lorsqu'une trajectoire de la main est sélectionnée par le cerveau, celui-ci va devoir gérer un nouveau problème : quelle configuration articulaire choisir afin de réaliser cette trajectoire. Une fois encore, du fait d'un excès de degré de liberté dans le système anatomique humain (Bernstein 1967), les solutions potentielles sont multiples. Par exemple, le membre supérieur de l'homme offre une potentialité cinématique de 7 degrés de liberté tandis que la position de la main n'est repérée dans l'espace que par 3 dimensions. Ce nombre de degré de liberté est décuplé lorsque nous considérons un mouvement du corps entier. Ce problème est également nommé le problème de cinématique inverse. Nous noterons ici que la posture initiale debout présentera une complexité a priori supérieure à un même mouvement réalisé en position assise de part l'ajout de degrés de liberté supplémentaires. Dans ce cas, le SNC doit gérer le maintien de son équilibre de manière plus complexe.

Cet excès de degrés de liberté illustré au niveau articulaire se retrouve au niveau musculaire. Une fois le problème de cinématique inverse résolu par le SNC, celui-ci doit déterminer parmi une infinité de possibilités les activations et les couples musculaires permettant d'obtenir avec succès la configuration articulaire choisie. Il s'agit ici du problème de dynamique inverse. Cette étape est également complexe car le cerveau devra prendre en compte et anticiper de nombreux paramètres dynamiques mis en jeu lors du mouvement comme les couples gravitaires, inertielles, d'interactions inter-segmentaires, auxquels s'ajoutent les forces centrifuge, centripète, et de Coriolis.

En résumé, pour réaliser un mouvement de pointage en direction d'une cible, le cerveau doit dans premier temps passer par de nombreuses transformations sensori-motrices afin de faire correspondre la position spatiale de la cible et la commande motrice à établir. Dans un second temps, le SNC doit résoudre les problèmes de cinématique et de dynamique inverse causés par l'excès de degrés de liberté présent dans le système musculo-squelettique humain. C'est pourquoi, réaliser un mouvement volontaire dirigé est une tâche complexe pour le système nerveux centrale qui doit résoudre une succession de problèmes afin d'élaborer la commande motrice adéquate. Cependant, malgré cette complexité dans l'élaboration d'une commande motrice, nous construisons généralement pour chaque situation une solution privilégiée reproductible d'un essai à un autre. Par quels procédés le SNC résout-il ces problèmes complexes?

Naïvement, nous pourrions émettre l'hypothèse que le cerveau mémorise une commande motrice spécifique pour chacun des mouvements que nous réalisons quotidiennement. Cependant, la variabilité des contextes dans lesquels nous évoluons permet d'affirmer que lors de la production d'un mouvement connu, nous ne produisons pas quelque chose d'absolument nouveau mais nous ne répétons jamais quelque chose d'ancien (Bartlett 1932). Pour rendre plausible cette hypothèse, notre cerveau devrait avoir la capacité de stocker en mémoire une infinité de commandes motrices ce qui, en terme de ressource neuronale n'est pas réalisable (Mussa-Ivaldi et Bizzi 2000, Graziano et al. 2002).

A contrario, de nombreuses études ont montrées que le contrôle des mouvements humain fait appel à des lois invariantes basées sur l'optimisation de certains paramètres (Fitts 1954, Soechting et Lacquaniti 1981, Lacquaniti et al. 1982, Viviani et McCollum 1983, Flash et Hogan 1985, Viviani et Flash 1995). Le cerveau semble donc en mesure d'établir des plans moteur régis

selon ces invariances pour résoudre le problème de complexité de pilotage du corps lors de la production de mouvements dirigés. Une autre solution supplémentaire pour simplifier la complexité du contrôle moteur consiste à créer des liens stables au cours du mouvement entre plusieurs paramètres variables. De cette manière le nombre de degrés de liberté est diminué et le contrôle du mouvement facilité.

2. UNE SIMPLIFICATION DU CONTROLE MOTEUR : LE PRINCIPE DE SYNERGIE

Compte tenu de la complexité de l'élaboration d'une commande motrice causé par la redondance des degrés de liberté du système musculo-squelettique humain, Bernstein (1967) est l'un des premiers auteurs à mettre en avant la capacité du cerveau à regrouper en un seul bloc plusieurs activités musculaires. Cette notion résume le concept de la « synergie ». Flash et Hochner (2005) émettent l'hypothèse que des synergies pourraient se retrouver au niveau cinématique, musculaire, et neuronal.

En étudiant la cinématique du membre inférieur lors de la locomotion chez l'homme et chez le chat, Lacquaniti et al. (1999) démontrent que les trois angles formés par chaque segment de la jambe (pied, tibia, fémur) et la verticale gravitaire co-varient dans un seul et même plan en y décrivant un patron reproductible lors de chaque cycle de marche. Pour ces auteurs, le cerveau semble empêcher ces trois angles de varier indépendamment les uns des autres lors de la réalisation du mouvement. Par cette liaison, le SNC réduit le nombre de degrés de liberté qu'il doit contrôler. Vernazza-Martin et al. (1999) définissent ce phénomène de synergie cinématique comme une relation relativement stable au cours du mouvement entre différents angles segmentaires et reproductible d'un essai à un autre ou d'une tâche à une autre. Si de telles relations synergiques ont été observées pour des tâches cycliques comme la locomotion, des synergies interarticulaires ont également été mises en avant lors de mouvements complexes dirigés. Soechting et Lacquaniti (1981) ou plus récemment Berret et al. (2009) ont en effet clairement démontrés une robustesse des trajectoires tenues dans l'espace des angles inter-segmentaires en dépits de variations significatives de la trajectoire de l'effecteur dans l'espace cartésien. Le cerveau semble donc capable de lier des groupes de variables cinématiques en créant des synergies cinématiques lors de

la planification du mouvement afin de réduire la complexité du contrôle moteur.

La présence établie des synergies cinématiques peut être le reflet d'une organisation synergique au niveau musculaire. Selon Torres-Oviedo et al. (2006) et Mussa-Ivaldi et Bizzi (2000), une synergie musculaire peut se définir comme un ensemble d'activités musculaires basiques pouvant être combinées de manière linéaire et multiple afin de générer un très grand nombre de mouvements différents. De très nombreux travaux sont parvenus à extraire à partir d'un jeu important de données électromyographiques (EMG) une organisation synergique. Pour réduire la complexité du contrôle moteur, une telle organisation semble donc être utilisée par le SNC pour structurer les activations musculaires nécessaires à la réalisation d'une multitude de mouvements qui nécessitent la coordination de nombreux muscles des bras, du tronc et des jambes (Muceli et al. 2010, D'Avella et al. 2005, 2006, Ivanenko et al. 2003, 2004, 2005, 2006, Poppele et Bosco 2003, Mussa-Ivaldi et Bizzi 2000, voir Bizzi et al. 2008 pour une revue).

Enfin, la présence établie des synergies musculaires peut être le reflet d'une organisation synergique au niveau neural. A l'échelle spinale, Mussa-Ivaldi et Bizzi (2000) ont démontré l'existence de mouvements codés sous forme de synergies motrices dans la moelle épinière chez des grenouilles. Ces auteurs parviennent à déclencher chez ces grenouilles préalablement spinalisées un mouvement dirigé de la patte en réponse à un stimulus nociceptif. Dans ces travaux, la précision du mouvement de la patte est maintenue quelque soit la position initiale de celle-ci. Ce résultat souligne l'existence de représentation du corps au niveau spinal. D'après ces auteurs, un réseau neural spinal coderait en général un champ de force convergeant vers un point d'équilibre et la combinaison linéaire des synergies motrices pourrait engendrer un grand nombre de mouvements. Une telle organisation permet au SNC de produire une infinité de mouvements adaptés aux modifications permanentes de

variables comme la localisation de la cible ou la position initiale du corps sans pour autant augmenter la quantité d'informations stockées en mémoire (Mussa-Ivaldi et Bizzi 2000, Bizzi et al. 2008).

Des résultats similaires ont été démontrés par Graziano et al. (2002) au niveau cortical chez le singe. Ces auteurs mettent en avant lors de stimulations invasives du cortex prémoteur et moteur primaire la réalisation de mouvements dirigés vers une même localisation spatiale quelque soit la position initiale du membre effecteur. Cela suggère que le SNC possède la capacité d'atteindre un locus spatial précis quelque soit la trajectoire spatiale et la configuration angulaire du membre effecteur.

L'utilisation de synergies motrices permet donc au SNC d'établir des liens de coordination entre de multiples et différentes entités élémentaires du contrôle moteur (déplacements angulaires, contractions musculaires…). Il en résulte une facilitation du contrôle moteur en réponse au problème posé par la redondance des degrés de liberté.

Cependant, lorsqu'un mouvement en cours d'exécution est rendu inadéquat par une perturbation environnementale, le cerveau est capable lorsqu'il dispose d'assez de temps, de modifier le mouvement afin d'accomplir la tâche avec succès. Ces modifications doivent être rapidement mises en œuvre et le délai de modification du mouvement devient un facteur prépondérant dans la réussite de la tâche. Dans une telle situation, nous pouvons nous interroger sur le mode d'organisation des commandes musculaires ? Est-ce que des lois de types proximo-distal (Jeannerod 1986) ou jambe-tronc-bras (Crenna et Frigo 1991, Stapley et al. 1998, 1999, Bonnetblanc et al. 2004, Bonnetblanc 2008) existent ? Le SNC est il capable d'établir des liens fonctionnels complexes entre les activations musculaires lors de la génération de corrections motrices rapides ?

3. DIFFERENTES APPROCHES POUR DIFFERENTES ESTIMATIONS DES LATENCES NERVEUSES

3.1 LES LATENCES DES CIRCUITS NEURONAUX TRADITIONNELS IMPLIQUES DANS LES TACHES VISUOMOTRICES ISSUES DE LA LITTERATURE NEUROPHYSIOLOGIQUE

Les processus de traitement des informations visuelles par le SNC impliquent différentes aires cérébrales et loci anatomiques. Une fois les informations détectées par la rétine, celles-ci vont devoir circuler et être traitées dans plusieurs endroits du cerveau avant de pouvoir être intégrées à une éventuelle commande motrice. Le parcours de cette circuiterie neuronale par le signal visuel va donc demander un certain temps. La voie neuronale de la perception visuelle consciente aboutie à la projection des informations rétiniennes dans le cortex occipitale, plus particulièrement dans le cortex visuel primaire, via la voie rétino-géniculo-corticale. Chez le singe, suite à un flash lumineux, la première aire corticale sollicitée sera le cortex visuel primaire V1. En effet, 80% des réponses neuronales apparaissent dans cette aire corticale 25 à 65 ms après le stimulus lumineux (Bullier 2001). Pour une tâche expérimentale similaire, Maunsell et Gibson (1992) reportent des délais de 30 à 100 ms entre les stimuli visuels et les activations des neurones du cortex visuel strié. Dans cette simple tâche de perception de stimuli visuels, ces latences pourraient s'expliquer par la relative lenteur du processus de conversion de la lumière en signal électrique (environ 25 ms), appelé délais de transduction (Lennie 1981, Schnapf et al. 1987).

Classiquement, il est considéré que la seconde aire corticale impliquée dans cette boucle du traitement des informations visuelles dans le but de produire un mouvement de la main est le cortex pariétal. En effet, cette structure joue un rôle clé dans l'intégration sensorielle et les transformations nécessaires permettant la mise en relation entre des entrées sensorielles et la commande

motrice adéquate (Duhamel et al. 1997, Andersen et Buneo 2002, Battaglia-Mayer et al. 2003). Dans sa revue, Bullier (2001) reporte un délai de 70 à 180 ms entre un flash lumineux (stimulus) et l'activation des neurones du cortex latéral intrapariétal. Pour nuancer ces latences conséquentes entre un stimulus visuel et les premières réponses neuronales de la boucle corticale classique, nous noterons ici que ces enregistrements ont été effectués sur des singes auxquels ils n'étaient pas demandés de produire un mouvement en réponse aux stimulations. A l'inverse d'une tâche dans laquelle une correction motrice doit rapidement être exécutée sous peine de voir le mouvement ne pas atteindre son but, l'absence de pression temporelle dans cette expérimentation pourrait expliquer la relative lenteur des délais enregistrés.

En associant l'action à la présentation d'un stimulus, une étude neuro-magnétique menée chez l'homme, Senot et al. (2008) mesurent le délai séparant la présentation d'une balle à saisir et le début de la réponse corticale. Les auteurs de cette étude reportent des latences de 40 ms entre le début du stimulus visuel et le début des activations des réseaux neuronaux de la voie visuelle. Dans la même lignée, Archambault et al. (2009) étudient le rôle du cortex pariétal lors du contrôle du mouvement de la main en enregistrant l'activité de neurones de l'aire 5 chez des singes qui réalisent des mouvements de pointages en direction de cibles qui peuvent être déplacées ou non pendant la réalisation de l'action. Leurs résultats reportent que l'activité des neurones enregistrés n'est pas influencée par le signal visuel de la position de la cible lors des 150 ms suivant la présentation du stimulus. Les délais reportés par Senot et al. (2008) et Archambault et al. (2009) à partir de paradigmes expérimentaux qui requièrent une réponse motrice après un stimulus visuel, apparaissent comme un peu plus rapide que ceux reportés par Bullier (2001).

Pour essayer d'apporter une explication potentielle à cette controverse, nous pouvons considérer le contexte dans lequel ces mesures neuronales ont été recueillies. Comme nous l'avons vu, la majorité des données sont enregistrées

sur des singes auxquels aucun mouvement n'est demandé en réponse au stimulus (Maunsell et Gibson 1992, Bullier 2001). Dans l'étude d'Archambault et al. (2009), les singes réalisent des mouvements de pointage du doigt d'une durée comprise entre 500 et 1000 ms. Bien que ces mouvements de pointage soient considérés comme rapides, la pression temporelle appliquée sur les animaux reste faible. Or, Paillard (1996) énonce le fait que la rapidité d'une correction motrice est étroitement liée à la situation d'urgence dans laquelle se trouve le sujet. D'après cet auteur, selon un principe d'urgence, plus le temps disponible pour corriger un mouvement est grand, plus les délais de correction (et donc le temps pris par les processus neuronaux impliqués) seront grands. C'est pourquoi nous pouvons raisonnablement estimer que les latences de la boucle corticale intégrant les informations visuelles dans le cortex strié visuel (V1) et le cortex intrapariétal telles qu'elles sont mesurées et reportées ci dessus peuvent être très vraisemblablement minorées, notamment lors de la réalisation de mouvements de pointage très rapides (< 300 ms). De telles durées de mouvement permettraient en effet d'augmenter significativement la pression temporelle et probablement de diminuer les latences de correction.

3.2 LES LATENCES ISSUES DE LA LITTERATURE COMPORTEMENTALE CHEZ L'HOMME

3.2.a Les paradigmes de sauts de cible non conscients

Afin de mieux comprendre l'implication des processus de contrôle en ligne lors des mouvements complexes dirigés, le paradigme de saut de cible inconscient a été développé dans de nombreuses études au milieu des années 1980s (Pélisson et al. 1986, Goodale et al. 1986, Hoff et Arbib 1993, Prablanc et Martin 1992,). Lorsqu'une cible fixe à atteindre est présentée en périphérie visuelle, le sujet réalise une saccade oculaire. A chaque changement de fixation saccadique, l'image imprimée sur la rétine de l'œil n'est pas traitée consciemment par le cerveau pendant un bref instant. Tout ce passe comme si le signal rétinien n'était pas perçu par le SNC pendant les mouvements saccadiques des yeux. Cette période est appelée la période de suppression saccadique. Dans ce paradigme, le saut de cible est inconscient car il survient pendant cette période de suppression saccadique. De ce fait, la modification de la position spatiale de la cible à atteindre n'est pas perçue consciemment par le sujet qui effectue le mouvement de pointage. Lors de la réalisation d'une saccade oculaire, la position de la cible à atteindre par l'œil est sous-estimée. De ce fait, une seconde saccade dite d'ajustement est réalisée pour fixer l'œil sur la cible. Le principe du saut de cible inconscient consiste à reproduire et à accentuer cette erreur initialement présente dans le système moteur en déplaçant légèrement la cible initiale pendant le pic de vitesse de l'œil (i.e. pendant la période de suppression saccadique) lors de la saccade. Ainsi, le saut de cible intervient pendant la phase initiale d'accélération du membre effecteur. Ce paradigme introduit expérimentalement un biais inconscient dans la planification du mouvement de pointage. En étudiant les réponses comportementales de sujets soumis à ce type de paradigme, les auteurs ont pu développer les connaissances relatives aux mécanismes de rétro-contrôle lors de la production de mouvement dirigé (Pélisson et al. 1986,

Goodale et al. 1986, Hoff et Arbib 1993, Prablanc et Martin 1992, Desmurget et al 1999, Desmurget et Grafton 2000, Desmurget et al. 2001, Sarlegna et al. 2003, 2004, Sarlegna et Blouin 2010).

Bien que les sujets ne parviennent pas à détecter consciemment le déplacement de la localisation spatiale de la cible à atteindre lorsque celui-ci survient aux alentours du pic de vitesse de l'œil lors de la saccade oculaire, ils sont néanmoins capables d'atteindre la cible avec leur main même lorsque le retour visuel du membre effecteur est supprimé (Pélisson et al. 1986). En effet, la trajectoire de la main est redirigée vers la nouvelle position de cible durant la phase initiale d'accélération et ce de manière lisse. Ce qui nous intéressera plus particulièrement dans ces travaux est le délai moyen de 145 ms séparant le saut de cible de la modification cinématique de la trajectoire de la main (Prablanc et Martin 1992). Utilisant le même paradigme, Gaveau et al. (2003) étudient l'effet d'un saut de cible non conscient sur la cinématique de l'œil lui-même. Leurs résultats reportent une modification significative de la vitesse de la saccade oculaire en cours 50 ms après le saut de cible. De tels résultats nous montrent clairement que les informations rétiniennes peuvent être traitées avec des latences plus courtes que celles présentées dans le chapitre précédent.

3.2.b Les paradigmes de sauts de cible conscients

Le paradigme de sauts de cible est également utilisé avec des déplacements de la localisation spatiale de la cible pendant la réalisation du mouvement et donc détectés cette fois ci de manière consciente par les sujets. Dans un tel contexte, le profil de vitesse du membre effecteur incluant la correction motrice n'est plus lisse comme lors des sauts de cibles inconscients, mais présente un double pic de vitesse. Certains auteurs démontrent même que la durée du mouvement perturbée est allongée en moyenne d'une durée égale à celle du temps de réaction initial. Ils suggèrent ainsi la reprogrammation d'un deuxième mouvement retardé (Georgopoulos et al. 1981, Gielen et al. 1984,

Diedrichsen et al. 2005). En ce sens, Flash et Henis (1991) ont développé un modèle démontrant que l'ancien programme moteur n'est pas stoppé et remplacé par le nouveau programme moteur mais que celui-ci est vectoriellement ajouté au premier dans le but d'atteindre la nouvelle localisation de la cible (modèle d'additivité, Flash et Henis 1991).

Concernant les latences séparant l'occurrence du saut de cible et l'apparition de la correction motrice, Paillard (1996) établi entre 150 et 180 ms les délais moyens d'apparition des corrections motrices suivant un saut de cible lorsqu'elles sont détectées sur la cinématique du membre effecteur. Néanmoins d'autres études établissent des délais inférieurs. Pour le même mode de détection de la correction motrice (i.e. calculé sur la cinématique de la main), Day et Lyon reportent des délais de correction motrice situés entre 125 et 160 ms. La cinématique du membre effecteur se situe à l'extrémité de la chaîne de commande. Elle englobe les délais électromécaniques (Schenau et al. 1995) et les délais liés à la complexité inertielle et anatomique des membres. La détection des corrections motrices sur le signal EMG permet d'éliminer ces derniers et de se rapprocher au plus près de la commande motrice et des processus centraux. De ce fait, les délais de correction reportés par la littérature lorsqu'ils sont mesurés sur l'activité EMG apparaissent encore plus en contradiction avec les latences établies par la neurophysiologie. Soechting et Lacquaniti (1983) étudient les modulations des activations des muscles du bras lors de la production de mouvements de pointage perturbé. Leurs résultats reportent une modulation qualitative des patterns EMG 100 ms après le saut de cible. De tels résultats sont en accord avec ceux de Saijo et al. (2005) qui reportent une modification significative de l'activité EMG du fléchisseur de l'épaule et de l'extenseur du coude 102 ms en moyenne après le déplacement de la cible renforçant la contradiction avec les délais présentés par la littérature neurophysiologique.

3.3 QUELLE ORGANISATION NERVEUSE POUR LA FLEXIBILITE MOTRICE ? PLUSIEURS HYPOTHESES

Si les muscles du bras présentent des latences de correction courtes après un saut de cible lors d'une tâche de pointage du doigt, qu'en est-il pour des muscles plus éloignés de la boite crânienne comme les muscles des jambes ? De nombreuses études ont démontré, pour des mouvements perturbés ou non, une séquence de recrutement musculaire simple suivant un ordre proximo-distal pour des pointages du doigt en position assise (Jeannerod1986). Pour des mouvements de pointages non perturbés, dans le cas où les sujets sont en position initiale debout, un autre mode d'organisation partant de l'appui plantaire et allant vers le bras (jambe-tronc-bras) a été démontré (Ma et Feldman 1995, Stapley et al 1998, 1999, Adamovich et al. 2001, Bonnetblanc et al. 2004, Bonnetblanc 2008). Une organisation en séquence proximo-distale suggèrerait donc que les corrections motrices observées dans les muscles du membre supérieur seraient plus rapides que celles qui apparaitraient dans les membres inférieurs ? Au contraire, une séquence d'activation d'ordre jambe-tronc-bras devrait faire apparaître des corrections musculaires précoces dans les muscles des jambes comme le tibialis antérieur par exemple. Est-il possible d'observer des corrections motrices aux latences aussi courtes sur les muscles des membres supérieurs et des membres inférieurs ?

L'apparition de corrections motrices, notamment lors de saut de cible inconscient, démontre clairement la possibilité d'un contrôle moteur continu basé sur un processus de comparaison entre les prédictions sensorielles et les afférences sensorielles réelles. Un tel processus pourrait être utilisé tout au long du mouvement afin d'assurer la flexibilité de contrôle moteur. Néanmoins, ce processus n'apporte pas de solution au problème posé par les délais des afférences sensorielles et de processus nécessaires à leurs intégrations pour l'action. La littérature nous présente deux solutions potentielles et compatibles permettant de répondre à ce problème. Tout

d'abord, Desmurget et Grafton (2000) émettent l'hypothèse de l'utilisation par le cerveau de prédictions des conséquences sensorielles. Selon ces auteurs, de telles prédictions sensorielles permettraient de réduire significativement les délais et permettraient d'expliquer les résultats présentés dans la littérature comportementale.

Ensuite, une deuxième hypothèse suggérée notamment par Gaveau et al. (2003) qui permettrait de résoudre le problème des délais est discutée par Corneil et al. (2004) et Gomi (2008). Il s'agit de l'implication d'une boucle sous corticale de bas niveau peu coûteuse en temps permettant la réalisation de mouvements simples. Plus particulièrement, le colliculus supérieur pourrait solliciter directement une voie sous corticale, la voie tecto-réticulo-spinale pour déclencher très rapidement des corrections motrices à partir d'afférences visuelles.

Dans un premier temps, nous présenterons la notion de modèle interne, l'hypothèse de Desmurget et Grafton ainsi que leur modèle de contrôle. Dans un second temps, nous nous intéresserons à l'implication potentielle d'une boucle de bas niveau capable de générer des corrections motrices rapides pour enfin présenter le modèle de contrôle à niveaux multiples développé par Gomi.

En résumé, le SNC a deux solutions possibles pour palier au problème posé par les délais dans la génération des corrections motrices : Soit (i) le cerveau est capable de prédire les conséquences sensorielles d'un mouvement, soit (ii) le SNC est capable de réduire ces délais eux-mêmes en mobilisant des circuits aux trajets nerveux plus courts et plus rapides impliquant moins de neurones.

4. LE CERVEAU : UN « PREDICTEUR » SENSORI-MOTEUR

4.1 LE CONCEPT DU MODELE INTERNE

Les modèles internes sont des structures ou des processus neuronaux capables de simuler des comportements naturels. Le SNC peut développer des modèles internes de certains phénomènes du monde extérieur, de la dynamique du système biomécanique qu'il commande, ou de transformations mentales (Jordan 1996). De manière complémentaire, Wolpert et Ghahramani (2000) définissent un modèle interne comme un ensemble de connaissances implicites des caractéristiques physiques du corps (cinématiques, musculaires), du monde extérieur, et de leurs interactions. Le terme « modèle » signifie donc que le cerveau modélise l'interaction des systèmes sensoriels, moteurs et environnementaux. Le terme « interne » quant à lui reporte le fait que ces processus sont pleinement intégrés dans le SNC. Physiologiquement, les modèles internes sont des réseaux neuronaux plastiques qui s'actualisent par des phases d'apprentissage. Ces mécanismes neuronaux vont être capables de simuler des propriétés d'entrées et de sorties du système sensori-moteur, dans deux sens différents (Kawato 1999). Il existe deux types de modèles internes aux rôles différents: le modèle interne inverse et le modèle interne prédictif.

Soit le modèle interne reçoit en entrée l'intention de l'action, les conditions initiales du système et de l'environnement, et établi en sortie une commande motrice adéquate. Le modèle interne est alors nommé modèle interne inverse.

Soit le modèle interne est capable de prédire en sortie les conséquences sensori-motrices à partir de la copie de commande en entrée. Le modèle interne sera alors qualifié de prédictif.

4.1.a Le modèle interne inverse

Dans la chaîne des processus permettant l'élaboration d'une commande motrice, le modèle inverse intervient avant le modèle prédictif. Son rôle est de fournir la commande motrice adaptée en connaissant l'état présent du

système, de l'environnement, et l'action désirée. Usuellement, dans le contrôle moteur, le cerveau programme une commande musculaire pour atteindre un objectif. Ce modèle interne a le rôle inverse car il doit, à partir de la connaissance de l'objectif à atteindre et des conditions initiales (cibles, posture …), déterminer la bonne commande musculaire. En effet le modèle inverse doit déterminer les causes (la commande nerveuse) à partir des conséquences souhaitées (intention de l'action). Pour cela, ce modèle intègre en entrée l'ensemble des propriétés du système musculo-squelettique et environnementales et émet en sortie une estimation de la commande motrice en accord avec l'intention de l'action. Il modélise la relation entre les conséquences attendues et les actions à réaliser pour cela (cf. Figure 2, panneau A).

Concrètement, pour réaliser un mouvement du bras en direction d'une cible, le modèle inverse peut utiliser en entrée la trajectoire de la main attendue afin de produire les commandes musculaires appropriées permettant la réalisation de cette trajectoire souhaitée. Pour cela, il va devoir résoudre tous les problèmes de transformations inverses exposés dans le premier paragraphe de ce cadre théorique. Un exemple de données expérimentales qui illustre l'existence des modèles internes inverses est reporté par Shadmehr et Mussa-Ivaldi (1994) qui étudient les mouvements du bras de sujets soumis à un champ de force nouveau et inhabituel. Dans un premier temps, les trajectoires de la main des sujets sont perturbées par la contrainte environnementale, puis elles redeviennent progressivement normales avec la répétition des essais. Dès lors, si le champ de force est stoppé (les conditions environnementales redeviennent conventionnelles), les mouvements du bras se retrouvent de nouveau perturbés mais dans des directions opposées aux forces exercées précédemment (perturbations post-effet). Ces perturbations post effets traduisent bien la présence d'un modèle interne inverse appliqué ici à la

dynamique de l'environnement et de ses interactions avec le bras qui s'est adapté au champ de force artificiel.

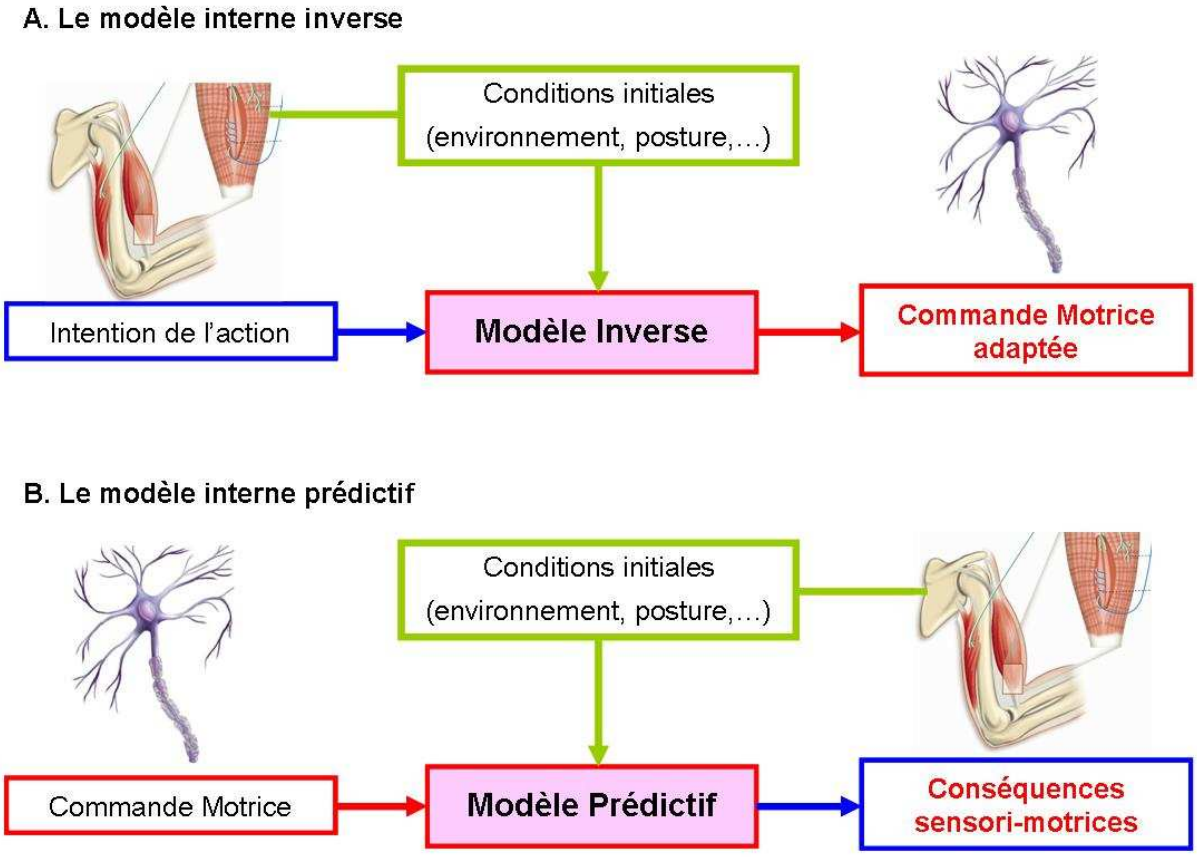

Figure 2 *Illustrations des entrées et sorties des deux différents modèles internes. Le panneau du haut illustre le modèle interne inverse (A) et le panneau du bas illustre le modèle interne prédictif (B).*

4.1.b Le modèle interne prédictif

Le modèle interne prédictif est également présent dans la littérature sous le nom de modèle interne direct. Son rôle est de simuler de manière anticipée les conséquences sensori-motrices (sortie du modèle interne) à partir d'une commande motrice connue (entrée du modèle interne), toujours en prenant en compte l'état présent du système et de l'environnement. Il établit de manière anticipée la relation causale entre les actions motrices et leurs conséquences sensorielles (cf. Figure 2, panneau B). Cette capacité d'anticipation de l'état sensori-moteur futur du système est particulièrement

intéressante dans la mesure où ces prédictions permettraient de compenser les délais présents dans les processus de mesures, de conductions et d'intégrations des conséquences sensorielles lorsqu'elles sont détectées par les capteurs périphériques. Concrètement, lors de la réalisation d'un mouvement du bras, le modèle interne prédictif intègre en entrée l'état présent du système (position, vitesse, inertie…) et la copie de commande du SNC afin d'estimer dans un futur proche l'état de l'effecteur.

Pour conclure, le SNC peut utiliser un modèle prédictif en substitution des afférences sensori-motrices réelles pour déterminer les conséquences d'une commande motrice sur le corps. Le cerveau à donc la possibilité de calculer presqu'en temps réel l'erreur associée à la commande prévue diminuant significativement ainsi les délais de traitements.

4.2 UN MODELE HYBRIDE DE CONTROLE CONTINU

La relative lenteur des boucles de retours sensoriels a souvent conduit les auteurs à émettre l'hypothèse qu'un mouvement complexe comme un mouvement de pointage dirigé est contrôlé de manière totalement programmée et que les boucles rétro actives jouent un rôle uniquement en toute fin de mouvement (Keele 1981, Arbib 1981, Meyer et al. 1988, Milner 1992, Plamondon et Alimi 1997). Néanmoins, d'autres auteurs ont émis l'hypothèse qu'aucun plan moteur n'est a priori construit et que la commande musculaire est actualisée en temps réel grâce à un signal d'erreur qui compare en continue les positions successives de la main et de la cible à atteindre (Hinton 1984). Quoiqu'il en soit, depuis les travaux de Woodworth (1899) sur la précision des mouvements volontaires dirigés, cette controverse entre un contrôle majoritairement programmé et un contrôle sans programmation mais totalement régulé en ligne a été grandement débattue (Paillard 1996 et Desmurget et al. 1998 pour des revues). Dans leur revue, Desmurget et

Grafton (2000) démontrent que ces deux grandes théories lorsqu'elles sont considérées séparément apparaissent comment extrêmement réductionnistes. Hoff et Arbib (1993) développent un modèle de contrôle des mouvements de pointage et de saisie dans lequel le transport de la main est assuré majoritairement par des processus de retours sensoriels au sein desquels des modules de contrôle programmés permettent de palier aux délais (i.e. et donc au retard) des informations sensori-motrices. Leur modèle, qui intègre à la fois un contrôle en ligne et un contrôle programmé, décrit avec succès la cinématique du transport de la main jusqu'à la cible et ce, quelque soit les circonstances ou les perturbations de la localisation de la cible. Dans la même veine, Desmurget et Grafton (2000) développent un 'modèle hybride' du contrôle moteur intégrant à la fois un programme établi et l'utilisation de modèles internes prédictifs permettant l'utilisation des afférences sensorielles dans le but de prédire de l'état 'futur proche' du système. Cet état sensori-moteur 'futur proche' est comparé avec l'intention de l'action et offre au système la capacité de prédiction.

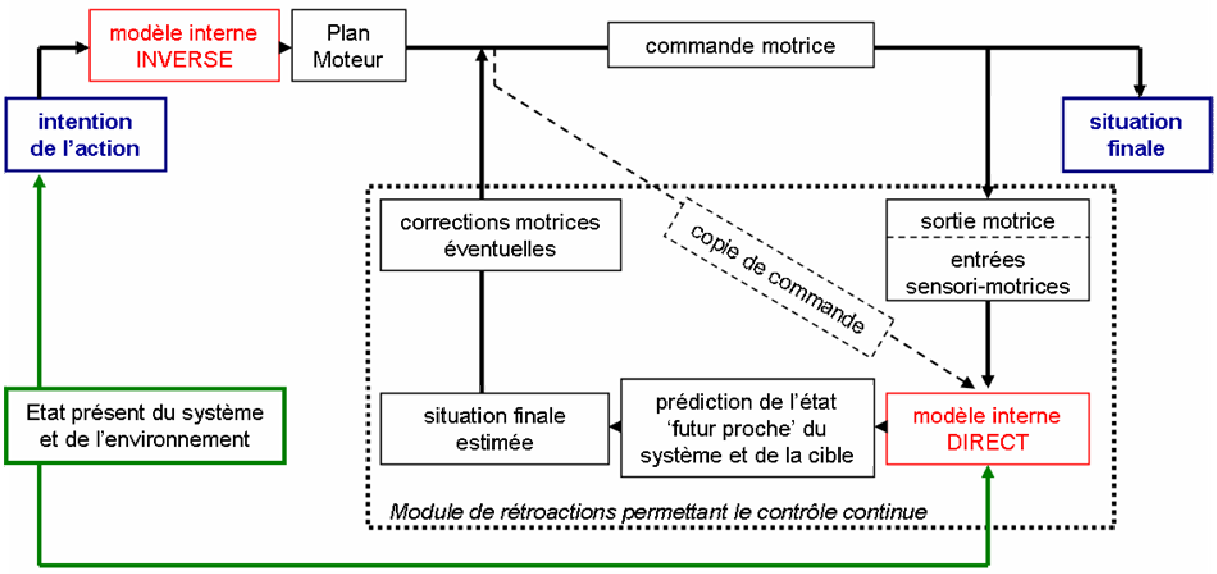

Figure 3 *Modèle hybride de contrôle continue de la main. Ce modèle est une figure originale établie d'après les travaux précédents de Hoff et Arbib (1993), Desmurget et Grafton (2000) et Bastian (2008). Dans le contrôle en ligne du mouvement, ce modèle permet de palier aux retards des informations sensorielles réelles grâce à l'incorporation des modèles internes prédictifs et de leurs capacités de prédictions.*

D'après ce modèle hybride du contrôle continu, lors d'un mouvement du bras dirigé, un plan moteur est initialement programmé grâce à l'intervention d'un modèle interne inverse à partir du but du mouvement (intention de l'action), des conditions initiales de l'environnement et du corps (états présents des systèmes). Lors de l'envoi de la commande motrice, un modèle interne direct va recevoir les informations issues de la copie de commande, des afférences sensori-motrices et de l'état présent de l'environnement pour générer en sortie une prédiction de l'état 'futur proche' du corps. Plus particulièrement, dans notre cas, il s'agira de la position finale estimée de la main. Cette position future estimée est alors comparée à la localisation de la cible. En cas d'erreur, le SNC peut générer des corrections motrices dans un délai court. Le point fort de ce modèle hybride dans le contrôle moteur des mouvements visuo-manuel est de ne pas considérer alternativement et séparément les processus de contrôle programmé et en ligne mais de les intégrer en un seul processus identique et fonctionnel du début à la fin du mouvement (cf. Figure 3). Il permet ainsi de résoudre le problème des délais importants des boucles rétroactives grâce à l'incorporation de modèles internes prédictifs et de leurs capacités de prédictions.

4.3 LES LIMITES EXPERIMENTALES DU MODELE HYBRIDE DE CONTROLE CONTINU

Nous avons précédemment exposé que la flexibilité de contrôle moteur pose au SNC un problème de délais au niveau des afférences sensorielles et de leur intégration. Cependant, le système sensori-moteur humain est capable de se corriger continuellement face aux changements de l'environnement dans lequel il évolue. Le cerveau semble donc capable de palier aux problèmes posés par les délais dans la flexibilité motrice. Nous avons vu dans la section précédente que la capacité de prédiction du cerveau au travers l'existence d'un modèle interne prédictif permet un contrôle du mouvement en partie basé sur un rétro-contrôle. Cependant, cette modalité de fonctionnement semble ne

pas avoir été testée dans des contextes de mouvements très complexes. L'implication simultanée d'un module programmé et d'un module de rétrocontrôle basé sur les prédictions d'un modèle interne direct permet le contrôle flexible des mouvements du bras dirigés. Ce modèle hybride de contrôle continu permet donc dans une certaine mesure de palier à l'importance des délais de traitement des afférences sensorielles. Néanmoins les résultats de cette modélisation sont issus et comparés à des jeux de données comportementales recueillis à partir de mouvements dirigés du bras d'une durée de 300 à 700 ms et réalisés en position assise. Ce contexte de production de mouvements reste relativement simple dans la mesure où (i) l'homme est capable de réaliser des mouvements dirigés beaucoup plus rapides (<300 ms) et (ii) beaucoup plus complexe en terme de degrés de libertés impliqués (par exemple, à partir de la position debout). Nous pouvons alors nous demander si ce modèle de contrôle est généralisable à des mouvements de pointages très rapides réalisés en position debout et perturbés par un déplacement inopiné de la cible pendant la trajectoire de la main ? Nous pouvons également nous interroger sur le fonctionnement d'un tel modèle dans la réalisation de mouvements dirigés perturbés encore plus complexes mettant en œuvre un nombre encore plus grand de degrés de libertés ?

Si la rapidité d'exécution et le nombre de degrés de liberté induisent des régulations au niveau de la commande motrice, modifier la difficulté de la tâche à réaliser influe sur la commande nerveuse. Par exemple, diminuer la taille des cibles à atteindre, c'est-à-dire augmenter la difficulté de la tâche et la précision du mouvement à produire, engendre des modifications de la commande (Woodworth 1899, Fitts 1954). Il semble alors intéressant de vérifier la possible généralisation du modèle hybride de contrôle continue lors de mouvements de pointage en direction de cibles desquelles nous

manipulons la taille pendant la trajectoire de la main. En d'autres termes, ce modèle est-il applicable lors de modifications du conflit vitesse/précision en cours de mouvement ?

Pour résumer, nous pouvons ici soulever la question de savoir si des mouvements de pointage nécessitant des corrections motrices (1) plus rapides, (2) plus complexes en terme de degrés de liberté et de coordinations musculaires impliqués dans le mouvement, ou (3) dans une tâche où le niveau de difficulté est manipulé en cours de mouvement (par exemple : changement du conflit vitesse/précision pendant la réalisation de la tâche), peuvent (i) être contrôlés par le SNC au moyen du modèle 'hybride' de contrôle en ligne et (ii) entrainer des modifications des différents processus impliqués dans ce modèle de contrôle.

5. EXISTENCE DE BOUCLES RAPIDES DANS LE CONTROLE EN LIGNE DES MOUVEMENTS DIRIGES

Après avoir relaté les différentes latences des circuits neuronaux traditionnels impliqués dans les tâches visuomotrices à partir de la littérature neurophysiologique et comportementale, nous avons soulevé le problème que posent ces latences au cerveau dans le contrôle du mouvement en ligne et plus particulièrement dans la génération de corrections motrices. Pour résoudre ce problème, nous avons vu dans la section précédente que le SNC dispose d'une capacité à prédire les conséquences sensori-motrices d'un mouvement pour palier à ce problème des délais. Une seconde solution pour le système nerveux consiste à réduire ces délais eux même en mobilisant des réseaux neuronaux spécifiques aux boucles plus rapides. C'est cette hypothèse que nous explorons dans ce chapitre.

Bien que les réponses motrices à un stimulus visuel soit d'ordinaire lentes, nous avons vu que plusieurs manipulations peuvent considérablement réduire ces temps de réponse. Par exemple, en réponse à un saut de cible inconscient, des corrections motrices rapides sont détectées très précocement sur la cinématique de l'œil (Gaveau et al. 2003) ou de la main (Goodale et al. 1986, Pélisson et al. 1986, Prablanc et Martin 1992, Day et Lyon 2000). D'autres résultats expérimentaux issus d'expérimentations neurophysiologiques invasives chez le primate ont démontrés un recrutement des muscles du cou 50-70 ms après l'apparition de stimuli lumineux (Corneil et al. 2004). Dans la même veine, Schepens et Drew (2003) étudient des mouvements de saisies de la patte chez le chat. Ces auteurs reportent des délais de 130 ms entre la présentation d'une cible à atteindre et l'activation de muscles de la patte. Ces résultats expérimentaux conduisent les auteurs à penser que le mécanisme mis en jeu dans de tels contextes pourrait être radicalement distinct du contrôle

moteur classiquement sollicité lors de la réalisation d'un mouvement de pointage dirigé sans perturbation. Ils émettent alors l'hypothèse de l'existence de boucles sous corticales liant une entrée visuelle à une sortie motrice (Corneil 2004, Saijo et al. 2005, Resvani et Corneil 2008, Gomi 2008, Corneil et al. 2010, Chapman et Corneil 2011).

5.1 MODELE DE CONTROLE A NIVEAUX MULTIPLES

Dans le but de répondre au problème posé par les délais des afférences sensorielles dans le contrôle en ligne d'un mouvement dirigé, une seconde hypothèse est donc émise par de nombreux auteurs (Day et al. 1998, Day et Lyon 2000, Gaveau et al. 2003, Corneil 2004) sur laquelle se greffe un modèle de contrôle développé par Gomi (2008). Il s'agit de l'implication d'une boucle sous corticale de bas niveau peu coûteuse en temps permettant la réalisation de mouvements simples à partir d'afférences sensorielles (notamment visuelles).

Pour corroborer cette hypothèse d'un point de vue neurophysiologique, la littérature présente de nombreuses preuves et discussions sur le rôle du colliculus supérieur dans le contrôle des mouvements des yeux, de la tête et plus récemment, son implication dans le contrôle des mouvements dirigés du bras a été démontrée (Stuphorn et al. 2000). En effet, Dorris et al. (1997) démontre l'implication du colliculus supérieur dans la production de mouvements oculaires très rapides en réponse à une entrée visuelle. De la même manière, le colliculus supérieur permettrait des projections nerveuses directement sur les circuiteries des muscles du bras via la voie poly-synaptiques tecto-reticulo-spinale (Illert et al.1978, Werner 1993, Stuphorn et al. 1999). Cette idée est soutenue par Gomi (2008) qui propose un modèle de contrôle moteur à niveaux multiples.

Dans ce modèle, les signaux d'entrées sont similaires à ceux présent dans le modèle de Desmurget et Grafton (2000), c'est-à-dire l'intention de l'action (le but du mouvement), l'état initiale du système environnemental et du corps. Le

haut niveau de contrôle offre la capacité de produire des plans moteurs très complexes et de s'adapter à de nouveaux problèmes. Il se retrouve en contrepartie très coûteux en temps du fait de la complexité des processus neuronaux mis en jeu. Il ne possède donc pas la capacité d'émettre des corrections motrices rapides en cours de commande. En revanche, le contrôle de bas niveau permettrait à partir des retours sensoriels (et notamment visuels) l'envoi de commandes motrices très rapides au dépend de la flexibilité et de la complexité de la commande musculaire envoyée.

Cependant, Gomi émet l'hypothèse que le manque d'adaptabilité de ces réponses de bas niveau pourrait être compensé par des régulations additionnelles en provenance des centres de haut niveau de contrôle (cf. Figure 4, flèche noire).

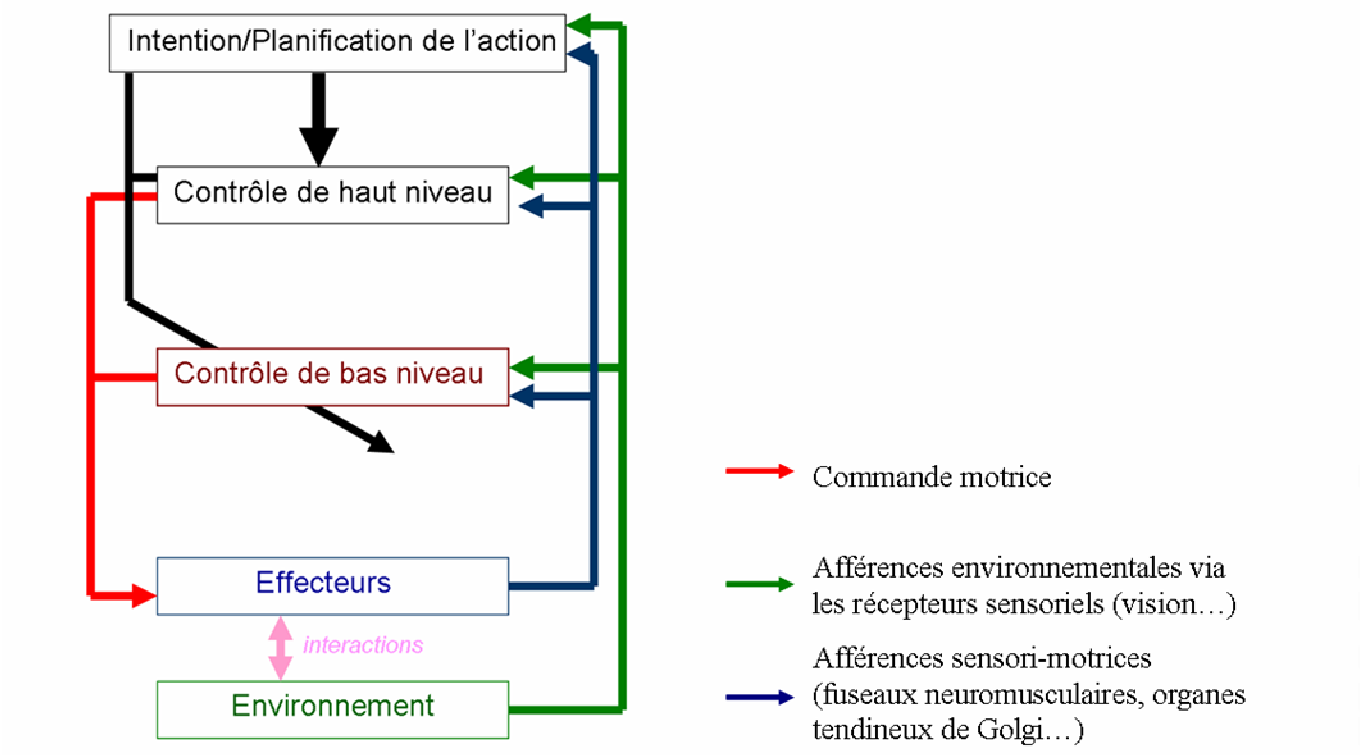

Figure 4 *Modèle de contrôle à niveaux multiples d'après Gomi (2008). Des boucles sous corticales courtes et mettant en jeu un nombre de neurones moins important que dans les boucles de hauts niveaux (flèches rouges) permet des corrections motrices rapides à partir des retours sensoriels et moteurs (flèches bleues et vertes). En contrepartie de cette rapidité, ces boucles ne seraient pas capables de générer des mouvements très complexes. Pour cela, des régulations additionnelles sont possibles par l'intervention de centres supérieurs (flèches noires).*

5.2 LES LIMITES EXPERIMENTALES DU MODELE DE CONTROLE A NIVEAUX MULTIPLES

L'hypothèse d'un contrôle moteur régit par des centres de bas niveaux, strictement distinct du contrôle moteur volontaire traditionnel du mouvement (régit par des centres de plus hauts niveaux) semble donc intéressante. Ce modèle de contrôle à multiples niveaux permettrait donc d'apporter une solution aux problèmes des délais dans le contrôle en ligne des mouvements de pointage dirigés. Il est basé sur de nombreux paradigmes expérimentaux visuomoteurs reportant des latences très courtes entre un stimulus visuel et un mouvement de l'œil, de la tête ou d'un bras. Cependant le fonctionnement de cette boucle sous corticale ainsi que ces propriétés et ces substrats neuronaux soulèvent de nombreuses questions et nécessitent encore de nombreuses études.

Par exemple, la voie tecto-reticulo-spinale qui serait sollicitée par le colliculus supérieur afin de permettre l'envoi d'une commande musculaire précoce après un stimulus visuel dans les muscles oculaires ou les muscles proximaux du bras (les deltoïdes) serait-elle également capable de solliciter des muscles distaux (muscles de la jambe) avec des latences très courtes ? Concrètement, serait-il vraiment possible de mesurer des corrections motrices très rapides (de l'ordre de 100 ms) sur des muscles de la jambe chez l'homme ? Jusqu'à quel degré de complexité du mouvement requis cette boucle sous corticale pourrait-elle être efficiente ? Une augmentation de la coordination des activités musculaires imposée par la tâche devra-t-elle se faire au détriment de la rapidité des corrections motrices ? Ce système de bas niveau serait-il capable de générer des corrections motrices rapides lors d'une tâche de pointage inhabituelle qui contient une modification du rapport vitesse/précision (et donc une modification de la difficulté du pointage) pendant la réalisation de mouvement ?

6. L'ADAPTATION ESSAI PAR ESSAI

Nous venons de voir plusieurs processus impliqués dans la réduction de l'erreur en cours de mouvement. Avec assez de temps, lorsque la réponse motrice dévie fortement de l'intention de l'action, des corrections motrices en lignes sont générées dans le but de diminuer cette erreur. Nous avons également établi que les délais des boucles afférentes représentent un problème majeur dans le contrôle en ligne du mouvement. Néanmoins plusieurs modèles théoriques ont mis en lumière certaines capacités et possibilités du SNC à résoudre ce problème.

Lorsque que le cerveau ne dispose pas d'assez de temps suite à une perturbation, le système nerveux ne parvient pas à corriger en ligne son mouvement et un différentiel sépare l'intention de l'action de l'action réellement produite. Dans le cas où la perturbation perdure, les réponses motrices peuvent être améliorées de manières itératives en répétant plusieurs fois l'action. Ce phénomène d'ajustement progressif de la commande motrice est appelé l'adaptation essai par essai (Bastian 2008). De manière similaire aux processus de correction en ligne, ces adaptations sont basées sur la comparaison hors ligne ('off-line') entre les prévisions sensori-motrices établies par un modèle inverse prédictif et les conséquences sensorielles réelles de l'action produite. Dans le cas d'un essai où cette comparaison aboutit à un différentiel, une erreur sensori-motrice est générée et intégrée aux processus de production de la commande motrice de l'essai suivant. Par conséquent, la capacité de prédiction des conséquences sensori-motrices d'un mouvement, la comparaison de ces prédictions avec les afférences sensori-motrices réelles, et la génération si nécessaire d'une erreur sensori-motrice, sont des processus fondamentaux aussi bien dans le contrôle en ligne d'un mouvement dirigé (Desmurget et Grafton 2000, Magescas et al. 2009) que dans le processus d'adaptation essai par essai (Tseng et al. 2007, Bastian 2008).

6.1 DEFINITION DE L'ADAPTATION ESSAI PAR ESSAI

Le terme « adaptation » est beaucoup utilisé dans la littérature et ne désigne pas toujours rigoureusement les mêmes processus. Dans ce manuscrit, nous choisirons la notion d'adaptation motrice telle qu'elle est définie par Martin et al. (1996) : une adaptation motrice est une modification essai par essai d'un mouvement à partir de retours sensori-moteurs. Cette modification n'altère pas la spécificité de l'action produite mais au contraire modifie au moins un paramètre du mouvement. Une fois une adaptation établie, une désadaptation est nécessaire pour revenir au mouvement initial, toujours sur une base essai par essai. Cette phase de désadaptation permet d'observer des conséquences dites de post-effet (Bastian 2008). Un exemple comportemental classique d'une procédure d'adaptation motrice dans la littérature consiste en une répétition de mouvements de pointage balistiques en direction d'une cible en portant des prismes qui dévient latéralement le champ visuel (Kornheiser 1976, Rossetti et al. 1995, Michel et al. 2008). Lorsque la relation qui lie le cerveau à l'environnement au moyen de la vision est modifiée, le comportement des individus est altéré au niveau moteur, sensoriel et cognitif (Gauthier et al. 2007). Au début du port des lunettes prismatiques, les sujets commettent des erreurs de pointage. Leurs mouvements dévient très significativement dans le sens du biais prismatique. Par conséquent, ces sujets intègrent de nombreux retours sensori-moteurs de l'erreur commise. A partir de ce signal d'erreur, en répétant les mouvements de pointage, les sujets vont améliorer progressivement leur performance en adaptant leur relation entre coordonnée visuelle et production motrice à la situation prismatique inhabituelle. Après un certain temps, les sujets seront capables de produire le mouvement de pointage sans aucune erreur malgré la présence des prismes. A présent, lorsque les prismes sont retirés (i.e. le champ visuel des sujets revient à la normalité), les sujets ne sont pas capables de produire immédiatement un mouvement de pointage sans erreur. En effet, les relations entre coordonnées

visuelles et production motrice s'étant adaptées à la condition prismatique, les sujets vont produire des erreurs de pointages dans la direction opposée à la déviation prismatique utilisée précédemment (voir Gauthier et al. 2007, figure 2). Ce biais opposé à la direction de la déviation est la conséquence post-effet de l'adaptation prismatique essai par essai. Une phase de désadaptation est nécessaire pour produire à nouveau des mouvements de pointages sans erreur en condition normale.

6.2 PROPRIETES DE L'ADAPTATION ESSAI PAR ESSAI

Ce processus d'adaptation, composante de la flexibilité du contrôle moteur, est primordial pour l'homme. Il permet au cerveau d'adapter une action à de nombreux contextes différents sans pour autant apprendre et stocker de nouveaux plans moteurs spécifiques. En effet, ce processus est applicable à de nombreuses tâches motrices élémentaires comme la locomotion (Reisman et al. 2005, Michel et al. 2008), l'équilibration (Horak et Diener 1994), le mouvement des yeux (Wallman et Fuchs 1998) ou les mouvements de saisie dirigés (Shadmehr et Mussa-Ivaldi 1994). L'échelle temporelle de ces processus varie suivant que l'étape soit adaptative ou désadaptative. Elle est de l'ordre d'une dizaine à une centaine de mouvements pour les processus d'adaptation. Davidson et Wolpert (2004) ainsi que Smith et al. (2006) démontrent que les processus de désadaptation sont significativement plus rapides que les processus d'adaptation. Si le nombre de répétition de l'action apparaît comme le critère primordial dans le but d'engendrer une adaptation, le délai temporel séparant chaque réalisation de l'action semble également jouer un rôle. Huang et Shadmehr (2007) montrent qu'un délai court inférieur à 4 secondes entre chaque mouvement permet d'accélérer le processus d'adaptation. Ces auteurs expliquent leur résultat en suggérant que la trace mnésique de l'erreur possède une rémanence de quelques secondes après la fin du mouvement. Ainsi le SNC y a toujours accès lors de l'élaboration de la

commande suivante dans le cas ou les mouvements sont enchainés rapidement.

6.3 LE CERVELET, UNE BASE NEUROPHYSIOLOGIQUE POUR LE CALCUL DE L'ERREUR SENSORI-MOTRICE

A la vue de l'importance du rôle de l'erreur sensori-motrice dans la flexibilité du mouvement volontaire chez l'homme, il semble nécessaire d'essayer de déterminer les centres cérébraux les plus impliqués dans cette tâche.

Dans un premier temps, des études cellulaires sur le fonctionnement spécifique du cervelet ont révélées que cette structure sous-corticale pourrait jouer un grand rôle dans la production d'un signal d'erreur sensori-moteur (Gilbert et Thach 1977, Oscarsson et Sjolund 1977a, b, c, Buisseret-Delmas 1980, Kitazawa et al. 1998, Ramnani 2006 pour revue).

Dans un second temps, cette hypothèse est confirmée et renforcée part les nombreuses études portant sur des populations de patients atteints de lésion du cervelet. Les résultats de ces études confirment le rôle fondamental de cette structure dans le calcul de l'erreur sensori-motrice et l'actualisation des modèles internes où des plan moteurs (Marr 1969, Blomfield and Marr 1970, Kawato et al. 1987, Johansson and Cole 1992, Wolpert and Miall 1996, Kawato and Wolpert 1998, Wolpert and Kawato 1998, Wolpert et al. 1998, Johansson 1998, Morasso et al. 1999, Ito 2000, Blakemore et al. 2001).

6.3.a Etudes cellulaires

Des études anatomo-fonctionnelles ont suggéré que les structures cérébelleuses nommées olives inférieures pourraient jouer un rôle clé dans le calcul de l'erreur sensori-motrice. En effet, d'un point de vue anatomique, ces cellules reçoivent directement en entrée les afférences sensori-motrices via des connexions avec la moelle épinière (Oscarsson et Sjolund 1977a, b, c, Buisseret-Delmas 1980). Ces cellules pourraient donc être capables de comparer les informations de la commande motrice descendante émise par le cortex moteur primaire avec les afférences sensorielles et détecter ainsi les disparités entre ces deux signaux d'entrée (Garwicz 2002, Ramnani 2006). Néanmoins, cette hypothèse reste encore débattue. En effet, Horn et al.

(2004) étudient les décharges des olives inférieures chez le chat lors d'un mouvement de saisie de la patte pendant lequel la localisation spatiale de la cible est perturbée. Les résultats de cette étude ne démontrent aucune activité spécifique de ces cellules lors des conditions avec perturbation. Ces auteurs concluent qu'il est peu probable que les décharges des olives internes fournissent des informations sur l'erreur du mouvement.

Un autre type de cellules cérébelleuses sembleraient être impliquées dans l'élaboration de l'erreur sensori-motrice : les cellules de Purkinje. Des études électrophysiologiques ont démontrées qu'au sein du cervelet, les cellules de Purkinje émettent des décharges complexes lorsqu'elles reçoivent en entrée des conséquences sensorielles imprévues (Gilbert et Thach 1977, Kitazawa et al. 1998). Ces décharges spécifiques pourraient donc se trouver à la genèse d'un signal d'erreur sensori-moteur.

En résumé, l'ensemble de ces études au niveau cellulaires tend à prouver que le cervelet, de part certaines propriétés anatomo-fonctionnelles, joue un rôle très important lors de l'élaboration de l'erreur sensori-motrice. Pour confirmer cette hypothèse, de nombreuses études impliquant des populations présentant une lésion du cervelet ont clairement démontré que la capacité de prédiction était sévèrement diminuée chez ces patients (Babin-Ratté et al. 1999, Lang and Bastian 1999, 2001, Nowak et al. 2002, 2007).

6.3.b Etudes des populations cérébelleuses

L'adaptation motrice met donc en jeu des processus complexes impliquant a priori l'élaboration de prédiction sensori-motrice et a posteriori un signal d'erreur sensori-moteur. Celui-ci permettrait l'adaptation essai par essai via une mise à jour des commandes motrices, peut être au moyen de re-calibrations permanentes des modèles internes et des représentations de l'état des systèmes corporels, environnementaux, et de leurs interactions. Cette capacité d'adaptation est significativement altérée chez les patients présentant des lésions cérébelleuses (Lewis et Zee 1993, Horak et Diener 1994, Babin-

Ratté et al. 1999, Lang and Bastian 1999, 2001, Nowak et al. 2002, 2007, Morton et Bastian 2006). Chez ces patients, les capacités d'adaptation essai par essai en réponse à une nouvelle demande sont nettement détériorées et demandent significativement plus de temps que chez des personnes saines. De plus, les études sur ces populations démontrent également une détérioration majeure du post-effet.

Cette détérioration illustre la diminution de l'efficacité de la prise en compte du signal d'erreur par le SNC lors de la génération de la nouvelle commande motrice. L'actualisation itérative des relations entre les entrées sensorielles et la production motrice est défectueuse chez ces patients. Plus précisément, Morton et Bastian (2006) étudient l'adaptation chez des patients cérébelleux lors d'une tâche locomotrice. Leurs résultats démontrent que les lésions du cervelet détériorent les adaptations et plus particulièrement l'intégration des erreurs passées. L'étape problématique pour ces patients semble donc être l'actualisation des modèles internes impliqués dans le mouvement réalisé. En revanche, les auteurs de cette étude reportent que la capacité de ces patients à corriger en ligne leur mouvement est toujours présente malgré une détérioration significative de la vitesse de correction et de la durée du mouvement. L'ensemble de ces résultats tend à prouver que le cervelet joue un rôle primordial dans l'actualisation de la commande motrice en boucle ouverte.

En résumé, lors de la réalisation répétée d'un mouvement, le cervelet, à partir de l'élaboration d'un signal de non-conformité entre les prédictions et la réalité des conséquences sensorielles (i.e. l'erreur sensori-motrice) semble permettre l'actualisation itérative des modèles internes impliqués dans l'action réalisée. Ces processus de mise à jour d'une commande en boucle ouverte à partir du signal d'erreur résultant d'un mouvement précédent permettent l'adaptation motrice. Néanmoins, si l'implication de la structure globale du cervelet est clairement identifiée dans ces processus, les corrélats neuro-

anatomiques précis impliqués dans l'adaptation motrice et plus particulièrement dans le calcul de l'erreur sensori-motrice restent à préciser.

7. SYNTHESE ET PROBLEMATIQUES

La flexibilité motrice, c'est-à-dire la capacité du cerveau à moduler un comportement moteur suite à la survenue d'un élément imprévu est une composante fondamentale de la motricité. D'un point de vue fonctionnel, le SNC établit un signal d'erreur sensori-motrice en comparant ses prédictions avec la réalité. Ce signal d'erreur permet (i) de générer des corrections motrices en ligne pendant la réalisation d'un mouvement et (ii) l'adaptation essai par essai.

Néanmoins, ces processus soulèvent encore de très nombreuses questions. Les propriétés fonctionnelles ainsi que les substrats neurophysiologiques impliqués dans ces processus sont encore débattus et controversés. Cette thèse est une contribution essayant d'apporter quelques réponses en étudiant expérimentalement la flexibilité du système moteur chez le jeune adulte sain.

Les principales questions posées dans ce travail sont les suivantes :

Problématique générale :

Quelles sont les propriétés de flexibilité d'un programme moteur suite à une perturbation inattendue, de l'expression cinématique aux voies neurales ?

Problématiques spécifiques :

L'homme est-il capable de générer des corrections motrices rapides (de l'ordre de 100 ms) sur les membres supérieurs et inférieurs? Ces délais sont-ils en adéquation avec les données neurophysiologiques conventionnelles ? Quelles solutions neuronales peuvent permettre d'expliquer les délais mesurés ?
(étude 1).

Lors d'une correction motrice, les activations musculaires sont-elles régi de manière réactive et anatomique ou existe-t-il un lien de corrélation plus fonctionnelle entre les délais de ces activations musculaires? (étude 2).

Comment se comportent les processus de corrections motrices en ligne lorsqu'ils sont soumis à un changement de difficulté de la tâche en cours de mouvement. Plus concrètement, quelles sont les conséquences d'un changement de taille de cible pendant la réalisation d'un mouvement de pointage ? (étude 3).

Enfin, quels sont les corrélats neuro-anatomiques cérébelleux des processus de calcul de l'erreur sensori-motrice ? (étude 4).

III. CONTRIBUTIONS EXPÉRIMENTALES

1. POINTING TO DOUBLE-STEP VISUAL STIMULI FROM A STANDING POSITION: VERY SHORT LATENCY (EXPRESS) CORRECTIONS ARE OBSERVED IN UPPER AND LOWER LIMBS AND MAY NOT REQUIRE CORTICAL INVOLVEMENT.

Lilian Fautrelle, Claude Prablanc, Bastien Berret, Yves Ballay, François Bonnetblanc

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1.1 INTRODUCTION

How fast can we correct a planned movement if an unexpected target change makes this planning inadequate? Case studies concerning the processing of visual stimuli are somewhat contradictory. Neurophysiological and electrophysiological data in monkeys suggest slower processing than behavioral data. For instance, in the first stage, 80% of neuronal responses occur in the primary visual area (V1) between 25 and 65 ms after the initiation of a visual signal. The second stage occurs in the lateral intraparietal area (LIP) and responses are observed between 70 and 180 ms after an initiation signal (Bullier, 2001). Similarly, Maunsell and Gibson (1992) have recorded neural activity in the striate visual cortex (V1) 30-100 milliseconds after a light flash. Note that in these cases, neural responses were recorded without the need for the animal to program movement or motor correction. More recently, Archambault et al. (2009) examined the activity of cortical area 5 during a pointing task in which the target location changed when the hand was in mid-air. They reported no change in neuronal discharges until 150 ms after the change in target location. These central delays, however, are not representative of the fast motor corrections observed in human behavioural studies where temporal pressure changes can be more easily applied.

Indeed, turning to double-step experiments in humans, Paillard (1996) assessed hand kinematics and established that minimum correction times of around 150-180 ms were required to influence ongoing movement. Other studies have reported shorter latencies of 100-150 ms (Bridgeman et al. 1979; Georgopoulos et al. 1981; Soechting and Lacquaniti 1983; Gielen et al. 1984; Goodale et al. 1986; Pelisson et al. 1986; Paulignan et al. 1990; Prablanc and Martin 1992; Desmurget et al. 1999; Day and Lyon 2000; Prablanc et al. 2003; Diedrichsen et al. 2005;). Is 100 ms the lowest limit for implementing a correction after the occurrence of a target jump? This question remains legitimate, at least in certain instances.

First, in most of the experiments cited, motor corrections were detected via hand kinematics. This is insufficient to circumvent inertial, anatomical, and neuromechanical complexities of the subjects, especially in complex movements. EMG recordings provide more insight into the neural control of multisegmental motion (Corneil et al. 2004). Second, in most of these experiments the target moved to several locations. If the target movement is large, movement durations are approximately lengthened by the duration of a simple reaction time (RT), namely the time required to initiate the movement after the go-signal (Flash and Henis 1991). However, in the framework of the traditional RT model, it is well established that RTs increase as the number of visual targets increase (Woodworth 1938, Hick's law 1952). Consequently, multiple jumps may result in an overestimation of the time it takes to make a correction; thus, in the case of a single target location (in a simple RT paradigm), motor corrections should appear earlier. Third, movements were always performed from a seated position, and mostly involved arm movements in a pointing task. However, in reaching and grasping tasks, a proximal-to-distal sequence of muscle recruitment is generally observed (Jeannerod 1986; Crenna and Frigo 1991; Ma and Feldman 1995; Adamovich et al. 2001; Bonnetblanc et al. 2004; Bonnetblanc 2008), suggesting that motor corrections could be observed earlier in proximal muscles.

Altogether, these general considerations suggest that latencies in motor correction may be overestimated when considering kinematics alone, particularly if a pointing task involves complex motor coordination. Certain motor corrections may precede pure arm movement corrections and may be triggered more rapidly at the proximal muscle or lower limb level. We investigated the three previously mentioned limitations further, including whether certain motor corrections precede pure arm corrections and whether they are triggered more rapidly. Thus, we designed an experiment in which subjects had to point, from an upright standing position, to a target, which

unexpectedly jumps or moves forward to a constant location, such as in a simple RT model. We then measured, for several muscles, the time it took the individual to correct their arm movement after the target moved.

Finally, based on the above-mentioned contradictions between shorter and longer latencies in motor corrections, Paillard (1996) also suggested that, if movement can be corrected with terminal feedback, early motor corrections are not necessarily involved in the whole correction process. To determine whether correction delays depend on task urgency, we also varied the delay between the go-signal and the target jump. If motor corrections are facilitated with the urgency of the task and if the time-delay is shortened, we should then observe earlier motor corrections when the target change occurs later during the movement.

1.2 EXPERIMENTAL PROCEDURES

Seven right-handed adults (all men, age = [20-25]; mean = 23 years, height = [175-183]; mean = 179.7 m) performed pointing movements with their right index finger. From the starting point, the near and the far targets were located respectively 20, 65 and 90 cm in front of the subject in the sagittal plane and 15 cm below the xyphoid process. The near target could be reached with the arm alone, whereas reaching the far target required an additional forward bending trunk movement. Targets were represented by small visual and tactile 10 x 10 mm square switches, which could be lit (red colour, luminance = 1mcd) and which permitted accurate measurement of time to target contact (cf. Figure 5). Subjects were asked to perform pointing movements as quickly and as accurately as possible when a target was lit, in five conditions. In two normal conditions, either the near or the far target was suddenly lit ("go-signal") and remained lit throughout the pointing movement. In three conditions with target jump (3/11 of all trials), the near target was suddenly lit, as in the control trials, but after a variable delay, it was turned off, whereas the far target, the one located beyond reach, was immediately turned on. This forward target jump occurred 120 ms after the first target was lit (i.e. before movement onset: $t<t_0$), after hand movement onset (i.e., when subjects removed their finger from the starting button, t_0), or 50 ms after hand movement onset (t_0+50 ms). Twenty trials were performed for each of the three conditions with target jumps ($t<t_0$, t_0, t_0+50 ms). Eighty unperturbed trials were also performed for near and far target conditions. A total of 220 trials were pseudo-randomised (20 blocks of 11 trials). Each block contained three perturbed trials (at $t<t_0$, t_0, t_0+50 ms), four trials with a stationary near target and four trials with a stationary far target, with trials randomised within a block. All movements were executed in a dimly illuminated room. Each subject performed six trials before data was recorded, and this always

occurred in the following order: 2 trials in the near, 2 trials in the far and 2 trials in the t_0 condition.

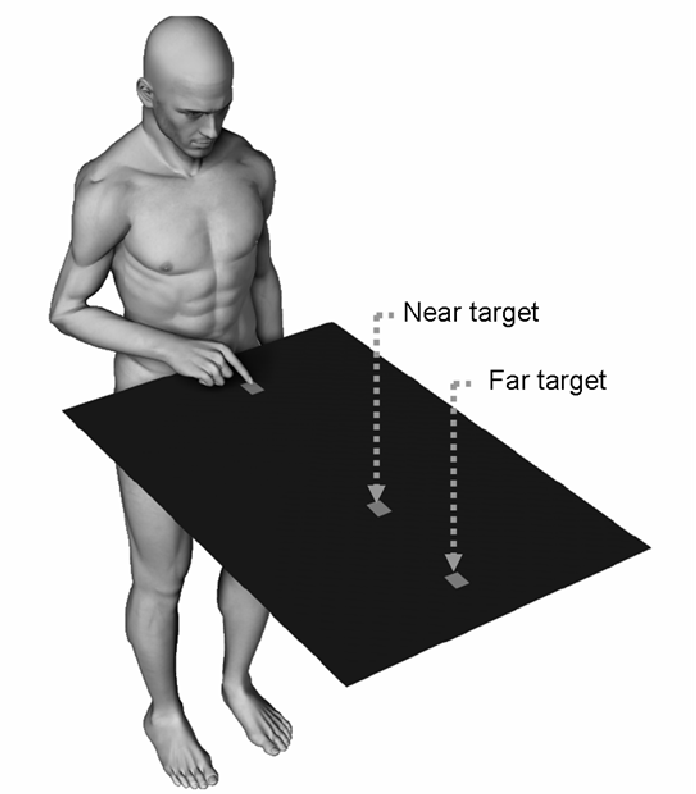

Figure 5 *View from the experimental set-up for the pointing task*

The 3D kinematics of hand movement was recorded with an optoelectronic device (SMART-BTS, Milan, Italy) (120 Hz). The marker was placed on the third phalanx of the right index. All movements were externally triggered. Position signals were filtered (Butterworth 4th order, dual-pass algorithm with a 10 Hz cut-off frequency) before calculating hand kinematics. Velocities and acceleration were computed with a zero phase finite difference algorithm. Statistical analyses were performed using ANOVAs with repeated measures to compare kinematics data from the five experimental conditions (Near, Far, $t<t_0$, t_0, t_0+50 ms). Post-hoc analysis was conducted with the Neuman-Keuls test when necessary.

Surface EMGs were recorded on subjects' right side for the brachio radialis (BRi), biceps brachii (BBi), triceps brachii (TBi), deltoïdus anterior (DAi), deltoïdus posterior (DPi), pectoralis superior (PSi), latissimus dorsi (LDi), erector spinae (ESi) between L3 and L5, rectus abdominis (RAi), biceps femoris (BFi), rectus femoris of the quadriceps (RFi), soleus (SOLi) and tibialis anterior (TAi). All electrodes were placed parallel to the muscle fibres with an interelectrode distance of 2.5 cm. All EMG signals were preamplified at the source before a second stage amplification (SMART-BTS, Milan) and were recorded at a frequency of 960 Hz. Raw EMG signals were first bandpass filtered between 20 and 400 Hz and then full-wave rectified and filtered using an averaging moving-window algorithm (window size: 25 ms) (Bonnetblanc et al. 2004, Bonnetblanc 2008). Trials were averaged for each target location and for stationary or perturbed conditions.

For the $t<t_0$ condition, signals were either synchronised with the "go-signal" (i.e. synchronised with the target jump) or with hand movement onset (in this case, the number of target jumps were averaged). Paired t-tests revealed that both types of synchronisation methods led to similar results for all EMG signals, in terms of detecting correction times ($Ps \geq 0.336$). Consequently, both synchronisation methods were deemed equivalent. For the sake of clarity, results for the $t<t_0$ condition were obtained by synchronising signals with hand movement onset. In the t_0 and t_0+50 ms conditions, signals were synchronised with hand movement onset (i.e. with the target jump). We then performed two types of analysis to assess motor correction times.

The first analysis used integrated EMG data and was performed for each subject individually. For each muscle, EMG signals were integrated per 10 ms intervals (iEMG) from -250 ms before the target jump to 800 ms after. We then compared iEMG values from the three perturbed and near conditions

for each window width; we used t-tests to estimate the time required to correct motor commands sent to a particular muscle after the target jump had occurred (time to EMG modulation within a 10 ms interval). The moment that the P-value was lower than 0.05 for minimum durations of 50 ms, determined the correction time after the target jump, thus avoiding false interference detection (Prablanc et Martin, 1992; Bonnetblanc et al., 2004; Bonnetblanc, 2008). We then computed the correction times for EMG activities and hand accelerations for each perturbed condition and each muscle. Note that repetitive t-tests were not used to answer whether there were differences, but were used to help determine the point at which these differences became significant. There was no summation of the false-positive rate. This difference was subtle, but legitimizing the use of repetitive t-tests in our study. Also, this method has been previously employed in several studies (Prablanc and Martin 1992; Demurget et al. 1999; Bonnetblanc et al 2004; Saijo et al. 2005; Gomi 2008; Gritsenko et al. 2009).

The second method, involving the use of confidence intervals from unperturbed near trials, was also performed on each subject individually. We computed the 95% confidence intervals (±95% CI) across time for all unperturbed near trials. For each perturbed trial, we subsequently measured the time at which values first exceeded this confidence interval for a minimum duration of 50 ms. Ten of 560 trials fell (i.e. 1.7% of all trials) outside of the 95% CI for the near condition; this corresponded to a maximum of 5 out of 80 trials (i.e. 6.3%) for subject D. These outliers were not taken into account when computing the 95% CI for the near condition.

1.3 RESULTS

We examined whether the EMG correlates for motor corrections could be detected less than 100 ms after a target jump in a pointing movement originating from an upright standing position. We also tested how fast they could precede endpoint kinematic arm corrections in some proximal muscles or lower limbs. Therefore, we recorded and analysed both hand kinematics and electromyographic activities of eight muscles located in the legs, trunk and arm.

1.3.a Hand kinematics

We first computed the 95% confidence ellipse area of the finger endpoint (Fep_{area}), to check whether the accuracy of the pointing movement remained the same. There was no significant difference in the five experimental conditions (F (4, 24) = 0.136 P = 0.966). Similarly, the hand RT did not significantly vary among all conditions (F (4, 24) = 0.101 P = 0.991, see Table 1). A Kolmogorov-Smirnov test showed that hand RT did not follow an abnormal distribution for the five experimental conditions for each subject (ds ≤ 0.09, Ps ≥ 0.05). It indicated that subjects did not predict or anticipate the target jumps during the experiment.

One factor, five level (Near, $t<t_0$, t_0, t_0+50 and Far) repeated measures ANOVAs were then undertaken to assess mean movement times, peak velocities, and acceleration durations. Neuman-Keuls post-hoc analysis revealed significant differences in movement times between the near condition and all others, between the far condition and the t_0 and t_0+50 conditions, and between the $t<t_0$ condition and the t_0 and t_0+50 ms conditions (Ps < 0.005). Peak velocities, including time to peak velocities (acceleration durations), were significantly different (see Table 1) between the near and far conditions, the near and $t< t_0$, far and t_0, and far and t_0+50 ms conditions (Ps ≤ 0.001) (Table 1). We assessed the finger trajectories and velocity profiles of

one representative subject under each experimental condition; these profiles were assessed over twenty trials (cf. Figure 6). Second peaks in the velocity profiles indicated later corrections in hand movement, and were markedly visible if target movements occurred at hand movement onset (t_0) or 50 ms later (t_0+50ms). By contrast, these were not visible if the target jumped during hand RTs ($t < t_0$): hand trajectory and velocity profiles exhibited no rebound with this condition.

	Near	$t<t_0$	t0	t_0+50 ms	Far		
Feparea (cm^2)	0.20±0.01	0.19±0.02	0.20±0.01	0.20±0.02	0.20±0.02	$F(4,24)=0.13$	$P=0.97$
Movement time (ms)	285±23	377±51	519±57	574±70	375±31	$F(4,24)=38.28$	$P<0.001$
Hand reaction time (ms)	352±18	351±27	356±23	357±27	352±20	$F(4,24)=0.101$	$P=0.99$
Acceleration duration (ms)	126±31	154±30	127±30	122±30	168±29	$F(4,24)=12.88$	$P<0.001$
Mean velocity (ms^{-1})	1.7±0.2	1.9±0.2	1.4±0.2	1.2±0.2	2.0±0.2	$F(4,24)=16.34$	$P<0.001$
Peak velocity (ms^{-1})	2.9±0.2	3.3±0.3	2.8±0.2	2.7±0.3	3.5±0.2	$F(4,24)=6.86$	$P<0.001$

Table 1 *Hand kinematics variables. The following hand kinematics variables are averaged for the 7 subjects: the 95% confidence ellipse areas of the finger endpoint, the movement times, the reaction times, the acceleration durations, the mean velocities and the peak velocities in the Near, Far, t<t0, t0 and t0+50ms conditions (mean ± standard deviation). For each of these variables, F and P values are also reported.*

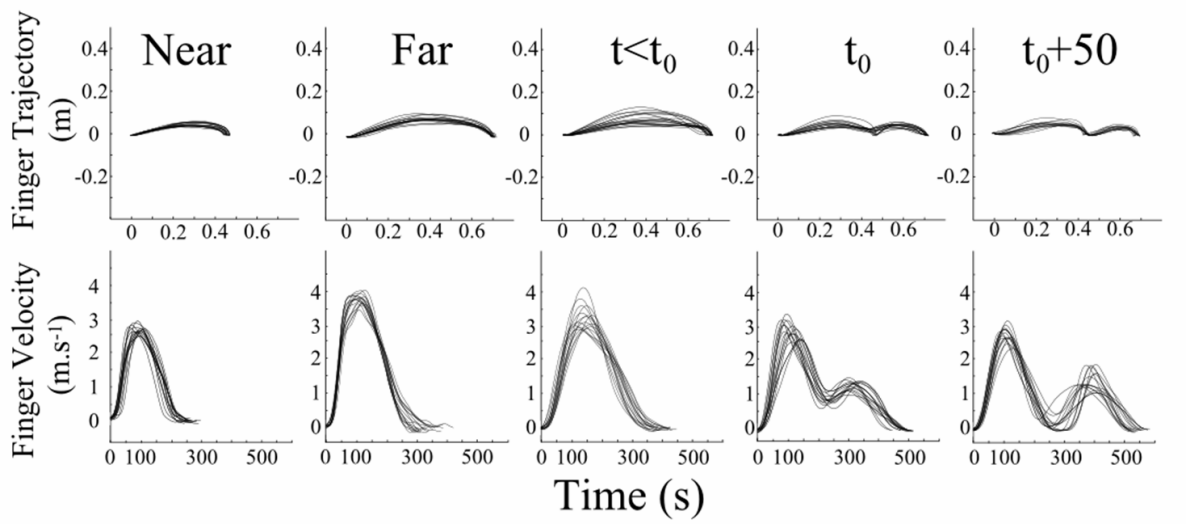

Figure 6 *Hand movement kinematics. Finger trajectories (upper panel) and velocity profiles (lower panel) of a representative subject for the five experimental conditions. For the sake of clarity, two horizontal bars are added to illustrate the ON/OFF pattern of the two targets (black: Near target and grey: Far target). The dimensions are dependent on the occurrence of the two cues.*

1.3.b Correction times detected using hand acceleration

To determine if the target jump induced corrections in the hand acceleration profile during the ongoing movement, we computed the finger acceleration rate and averaged it over a single window frame (120 Hz) for each subject. Each averaged value was subjected to a t-test for independent samples. The target jump induced significant motor correction (cf. Figure 7, A). Data for the near and the three perturbed conditions for one representative subject are presented. The curves were synchronised with hand movement onset. Thus, in the $t<t_0$ condition, the number of target jumps were averaged and listed with their standard deviation. On average for the seven subjects, significant motor corrections of the finger acceleration profile were detected 164 (±10) ms and 168 (±11) ms after the target jump in the t_0 and the t_0+50ms conditions, respectively. Interestingly, these correction times were significantly shorter than the initial RT ($Ps<0.01$) (cf. Figure 7, B). In the $t<t_0$ condition, the time to correction was 345 (±16) ms after the target jump and was associated with a higher finger acceleration peak. In this experimental condition, no significant difference was found between the correction time and the initial RT.

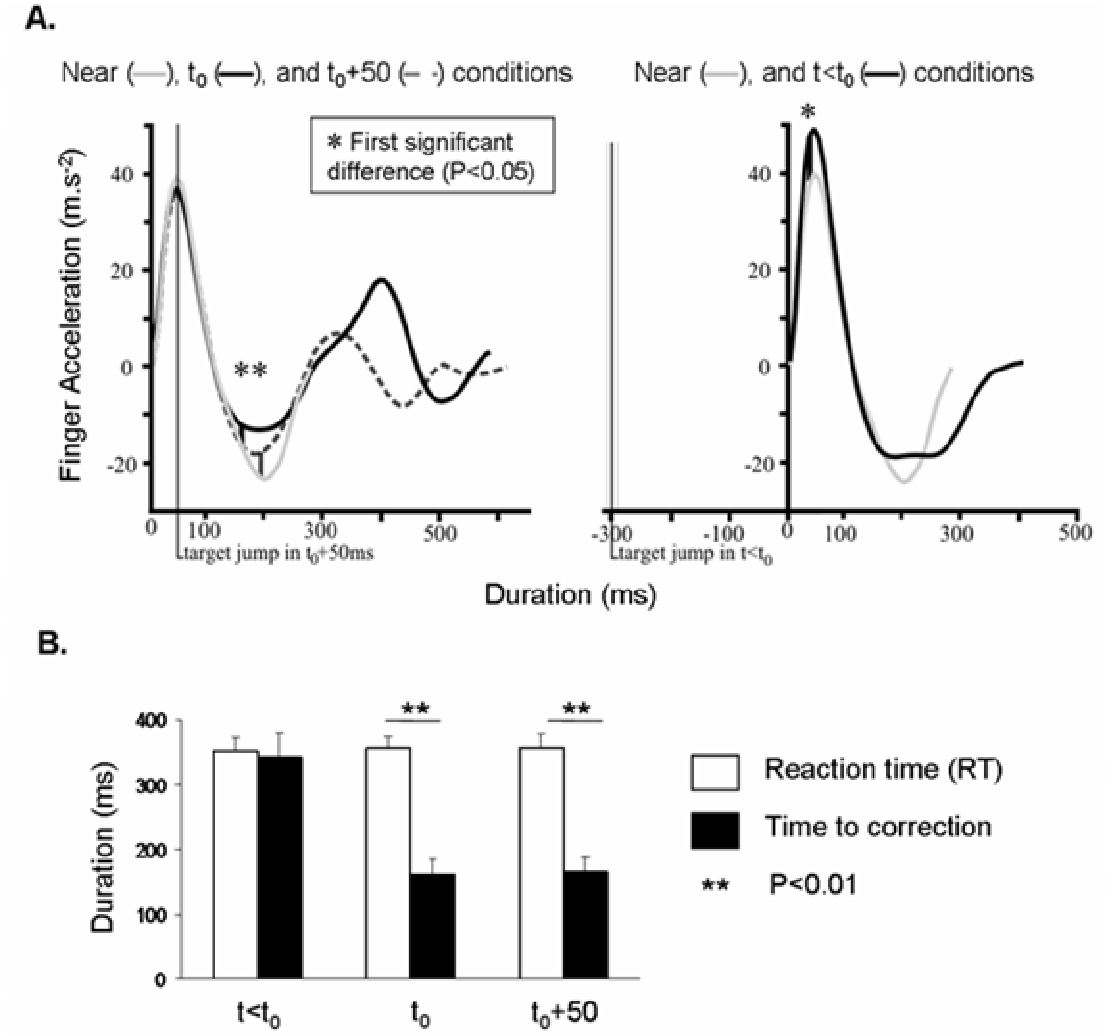

Figure 7 *Acceleration profiles of the hand and reaction times vs. times to motor correction. (A) Acceleration profiles of the hand: Significant modulations measured on the averaged acceleration profiles (using the t-test method) between the near and perturbed conditions for one representative subject, corresponding to motor corrections induced by the target jump. The curves were synchronised with hand movement onset. Thus, in the t<t0 condition, target jump occurrences are averaged and represented with their standard deviation.*
(B) Reaction times vs. Times to motor correction. Comparison between the initial reaction times and correction times for finger acceleration in the three conditions with a target jump.

1.3.c Correction times detected using EMG activities: very rapid corrections were observed for the DAi and TAi muscles.

We performed two methods to determine if the target jump induced corrections in the eight recorded EMG activities during ongoing movement. The first method used a repetitive t-test and the second method used 95% CIs (please refer to the materials and methods section for more detail).

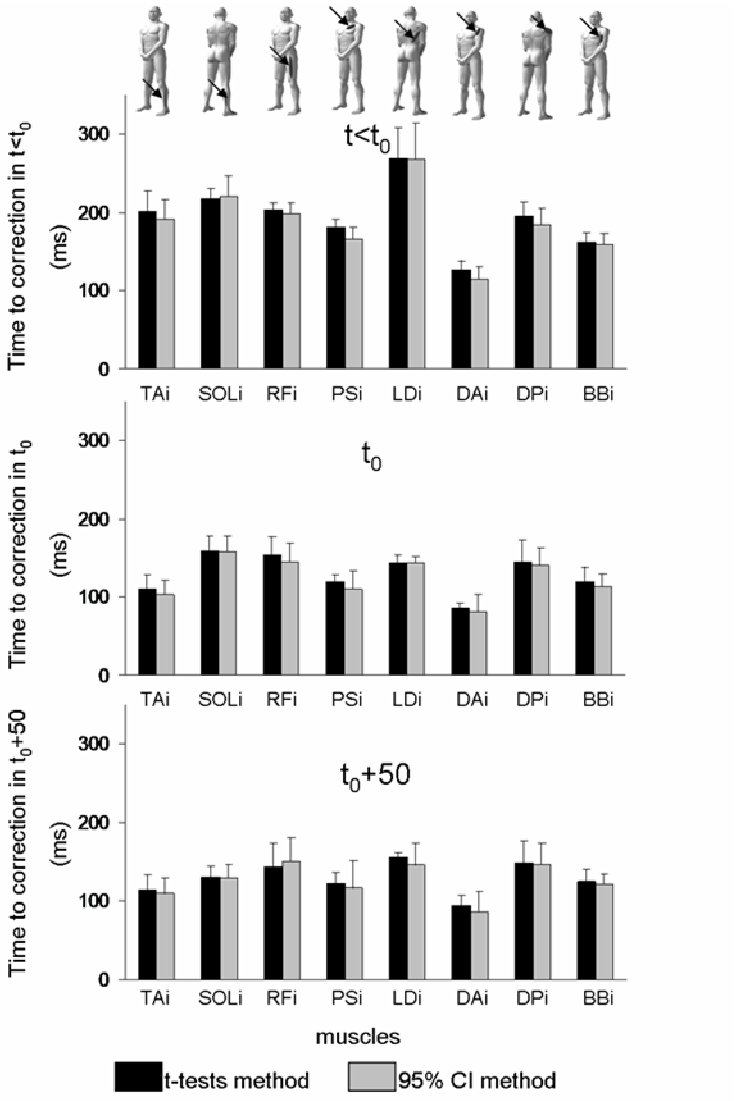

Figure 8 *Mean and standard deviation values for the correction times detected on the EMG activities for all muscles. Histograms of the means and standard deviations of correction times determined using the repetitive t-test method (black bar) and using the 95% CI method (grey bar). Data are presented for all muscles in the three conditions with a target jump. No significant difference was found between both methods.*

Figure 8 presents the means and the standard deviations of the motor correction times determined with the two methods for all muscles under all perturbed conditions. Overall, EMG activities in TAi, SOLi, RFi, PSi, LDi, DAi, DPi, and BBi were all modified after the target jump. No significant differences were found between the results from the two methods, suggesting that the use of a repetitive t-test on integrated EMG signals or the use of 95% CIs were equivalent when determining motor correction times.

More specifically, both methods showed, in four of seven subjects, that DAi and TAi exhibited the most rapid EMG modulations and motor corrections under conditions t_0 and t_0+50 ms; these corrections occurred less than 100 ms after the target jump. We used repetitive t-tests to assess the four subjects with the most rapid responses. Correction times in the TAi were measured at between 85 ms and 95 ms. Three other subjects exhibited significant differences in correction times – between 125 ms and 155 ms – under similar conditions. Seven subjects demonstrated significant correction times in DAi: correctional responses occurred between 75 ms and 105 ms after the target change of location. Figure 9 shows, for a representative subject, the average EMG activity in DAi and TAi muscles under t_0, t_0+50 ms, and near conditions. For illustration purposes only, data are presented from - 100 ms before synchronisation to 250 ms after synchronisation.

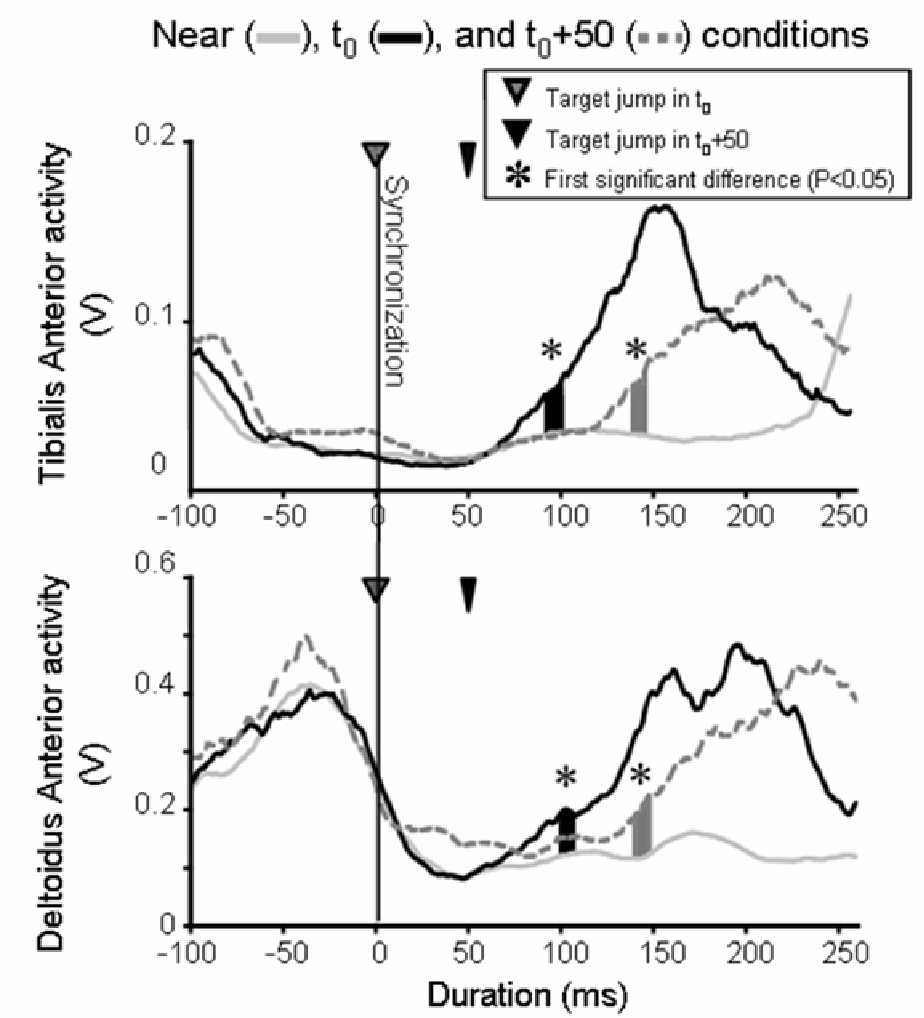

Figure 9 *TAi and DAi EMG activities and the times taken for motor corrections. Significant changes (using t-tests) measured using the magnitude of the EMG activity for the TAi (upper panel) and the DAi (lower panel), for one representative subject. Data are presented for the t0 (black dashed lines) and the t0+50 ms (grey dash-dot lines) conditions. Mean EMG activities in the perturbed conditions are superimposed on those for the near condition (grey dashed lines). For illustration purposes, data are presented from - 100 ms before synchronisation (vertical lines represented hand movement onset) to 250 ms after.*

Results obtained in TAi and DAi muscles with the second method using 95% CI confirmed earlier findings (cf. Figure 10). This figure presents the means and the standard deviations of motor correction times obtained for each subject, to illustrate inter-subject variability. Note that very early "motor corrections", occurring less than 65 ms after the target jump, were only detected in 18 of the 420 perturbed trials (4.5%).

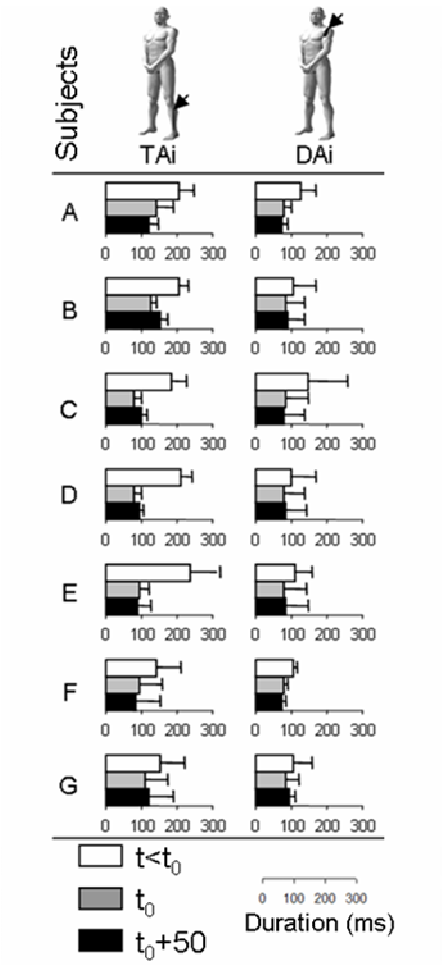

Figure 10 *Time to motor correction for the TAi and DAi muscles in all the subjects. Horizontal histograms with the means and standard deviations for time taken to motor correction for each subject, determined using the 95% CI method. Data are presented for the DAi and TAi muscles, which were the muscles that had the most rapid motor corrections.*

1.4 DISCUSSION

We aimed to determine whether latencies or delays in motor corrections after a target jump are overestimated when kinematics alone are considered, particularly during a complex motor coordination task, such as pointing. Certain motor corrections may precede pure arm movement corrections and may be triggered more rapidly in proximal muscles or lower limbs. During the task, subjects were standing rather than sitting, and the pointing task was made as simple as possible with only two potential targets. Pointing from an upright standing position to a target that suddenly and randomly jumps forward to a constant location triggers certain motor corrections within 100 ms, both at the arm and leg levels. In particular, the DAi muscles in 7/7 subjects and the TAi muscles in 4/7 subjects showed motor corrections less than 100 ms after the target jump occurred.

These results confirm our suggestions that discrepancies in the literature reflect a lack of sensitivity in animal studies and artifactual slowing owing to multiple targets in some human movement studies.

First, our findings clearly contrast those reported in previous electrophysiological and animal studies. This discrepancy is even more surprising if we consider the fact that intra-cortical conduction velocities may often be limited to 1-2 $m.s^{-1}$, thus slowing cortical processing (Bullier et al., 1988). Note that, in animal experiments, methods for imposing temporal pressure are limited.

Second, shorter latencies may be explained by the simpler experimental model used in comparison with other human movement studies. For instance, Day and Lyon (2000) observed longer latencies for motor corrections with hand kinematics (from 190-230 ms). Their study involved pointing at three targets with two possible target jumps. By contrast, Soechting and Lacquaniti (1983) observed shorter latencies with hand kinematics (120-140 ms) for a single random target jump. We used a similar pointing model and report shorter

latencies with EMG activities, suggesting that these signals are useful for accurately detecting motor corrections.

Here, correction times (after the target jump) were shorter than the initial RT (after the go-signal). This effect may be explained by the Hick's law principle (1952). Indeed, if subjects have to initiate their movement, there are at least two possibilities for the location of the target (near or far). However, if the target jumps forward, a single possibility for target location remains (only the far target). There is no spatial uncertainty in this condition. As a consequence, the correction time should be equivalent to a simple RT (Hick 1952, Soechting and Lacquaniti 1983, Flash and Henis 1991). However, these correction times were even shorter than simple RTs measured with hand kinematics for simple finger movements. In the classical studies of Woodworth (1938) and Hick (1952) these simple RTs were equal on average to 185 ms. This contrasts with findings by Soechting and Lacquaniti (1983) who found that the time it takes to correct the trajectory measured with hand kinematics was similar to the RT required to initiate the movement. Altogether, these results strongly suggest that both the simplification of the pointing constraints and the use of the EMG technique may have led to these rapid motor corrections. Moreover, Soechting and Lacquaniti experiment subjects were seated and only had to move their arm to reach the target. By contrast, our study subjects were standing, thus reaching the target with their hand involved complex coordination of the whole body, which was initiated in the TA (Bonnetblanc et al. 2004, Bonnetblanc 2008).

This latter aspect is important, including the fact that motor corrections with approximately the same latency were observed at both arm and leg levels. In this case, TAi activity cannot be a by-product of corrections made by the arm, which are triggered through the reflexive mode. In five of seven subjects, motor corrections in the TAi were observed less than 20 ms after those

observed in the DAi. This is inconsistent with the time lapse required to generate a mechanical change from upper to lower limbs and to trigger a reflexive response. This time lapse is also not sufficiently long enough for the mechanical displacement of the upper limb to occur, as the hand kinematics is not yet modified. It rather suggests that there is no hierarchical processing of upper over lower limb motor corrections and that motor flexibility in rapid movements probably involve a complex coordination of the whole body schema. These results are thus important in the understanding of motor correction organisation in more complex and ecological movements.

Indeed, in case of urgency, one may suggest that it would be easier to send a motor command to the arm to rapidly correct the focal movement, but as the whole body is involved in the pointing task, the TAi must also be recruited to facilitate the displacement of the centre of mass and to initiate the bending forward motion. In our study, DAi and TAi contractions were limited to a few degrees of freedom. The DAi makes the hand move toward the far target with a trajectory in the sagittal plane, whereas the TAi initiates a forward bending motion of the subject with the foot as a fixed support. This may explain why rapid motor corrections within 100 ms were only observed in these two muscles and not in the other ones. Other muscles may be solicited with greater variability, as their involvement is not fixed in space. This may explain inter-subject variability. Indeed, the variability we observed between subjects at the EMG level may also be explained by large differences in movement requiring complex coordination. Coefficients of determination were very low ($R^2<0.44$) between correction times measured using the DAi and TAi EMG activities and those measured using hand acceleration, suggesting that the time to correct the movement at the muscle level was not representative of the time to correct the movement at the kinematics level. In other words, the subjects may use various types of muscular coordination to correct their

movement. This interpretation is reinforced by the fact that inter-subject variability, measured by the coefficient of variation, for RTs was lower than that observed for times required to make a correction (0.07 vs 0.26). However, the observed inter-subject variability at the level of EMG activities may also be explained by several other factors. For instance, differences in attention levels or the ability to alert or react may explain this variability. To investigate whether these were indeed the reasons for these differences, we compared correction times measured using DAi and TAi EMG activities and RTs measured on the same muscles. We found very low coefficients of determination (R^2<0.38). This suggested that the time to initiate the movement was not representative of the time to correct the movement, lending further support to this hypothesis. As a consequence, the motor coordination sequence employed to correct the movement may be an important factor influencing inter-subject variability in our experiment.

Another (unlikely) functional interpretation of these rapid motor corrections is that these fast EMG modulations are non-specific and are similar to an alarm response. In this case, we would probably observe distributed EMG modulations (not on agonistic muscles only) of the same latencies for all target jump conditions. However, motor corrections were delayed if the target jump was triggered during the RT before hand movement onset. This is in accordance with Paillard's hypothesis (1996), which suggests that if movement is corrected with terminal feedback, early motor corrections are not necessarily involved in the whole correction process.

Under such pre-defined conditions in which a single target jump is involved, the cortical processing of the visual signal may be very simple and rapid, with the subjects being able to pre-plan a particular motor correction and perform it at the occurrence of the visual input, despite the fact that they do not know

when the target jump will occur. This may facilitate information processing, especially in the parietal cortex, in which retinal signals are known to be transformed into motor coordinates (Johnson et al. 1996; Duhamel et al. 1997; Burnod et al. 1999; Buneo et al. 2002). Consequently, the cortical loop involved in the motor response could be faster and involve fewer synaptic relays than in conditions with several possible targets for the jumps.

An alternative suggestion, and one we advocate, is that motor corrections following the target jump may also be triggered by lower level loops involving few synaptic relays. In contrast to the slow signal processing within the cortex, some studies have shown quicker adjustment in cat limbs during goal-directed movement, suggesting that subcortical structures are involved in these rapid motor corrections (Alstermark et al. 1987; Petterson et al. 1997; Petterson and Perfiliev 2002). These authors suggest that visual control is exerted via ponto-cerebellar pathways. In a patient with a complete agenesis of the corpus callosum, Day and Brown (2001) observed similar adjustments in latency, irrespective of the target jump direction or the hand used; once again suggesting that visual control was not necessarily cortical.

Gaveau et al. (2003) have more recently reported very fast motor corrections using eye kinematics, occurring only 50 ms after visual double-step stimulation during saccadic eye movements. These authors suggest that the superior colliculus could be involved in these functional corrective loops. Similarly, Corneil et al. (2004) demonstrated that visual target presentation elicits a time-locked, lateralised recruitment of neck muscles at extremely short latencies (55-95 ms) in the orientation response. These authors suggested that the superior colliculus engaged the tectoreticulospinal pathway to move the head independently of gaze shift. Interestingly, neurons of the dorsal Superior Colliculus have been shown to display persistent levels of low-frequency activity in advance of target presentation (Glimcher and Sparks 1992; Basso

and Wurtz 1997; Dorris and Munoz 1998). Moreover, the superior colliculus has also unequivocally been shown to be a key structure in so-called express saccades. Lesions of the superior colliculus abolish express saccades but still admit the monkeys to perform fast regular saccades (Schiller et al. 1987).
Finally, working with reaching movements of the arm, Saijo et al. (2005) have shown that a sudden visual background displacement induces motor corrections at the arm level with 100 ms EMG latencies. These quick responses seem to be functional, as subjects were unable to cancel the initial correction even if instructed to move in an opposite direction. Altogether, these results have recently led Gomi to develop an integrated model of multilevel motor control (Gomi, 2008), in which some implicit low level visuomotor controls exist and interact with higher ones. At such a low level, fast reactions are automatically triggered; this is, however, detrimental to the flexibility and complexity of higher-level motor adjustments. Although we cannot make unequivocal conclusions on the nature of the loops involved in the motor corrections we measured, their short latencies appear to be with this model, at least with respect to the initiation of the motor correction process.

In these types of corrections, parts of the networks identified by PET functional neuroanatomy are known to involve the posterior parietal cortex and the cerebellum (Desmurget et al., 1999; Desmurget et al., 2001). Our findings suggest that there are potential rapid cortical or subcortico-spinal corrective loops that remain to be identified in the rapid motor correction process.

1.5 ACKNOWLEDGEMENTS

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We also sincerely thank Pr Roderick Nicolson for his reading of this study.

2. MUSCULAR SYNERGIES DURING MOTOR CORRECTIONS: INVESTIGATION OF THE LATENCIES OF MUSCLE ACTIVITIES.

Lilian Fautrelle, Yves Ballay, François Bonnetblanc

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2.1 INTRODUCTION

Considering the large number of muscles that can theoretically be involved in a complex movement, Bernstein (1967) suggested that the Central Nervous System (CNS) could simplify the 'problem of redundancy' by grouping the functioning of muscles in more global units. Such a strategy would reduce the number of degrees of freedom that the CNS has to manage. It is now well established that a small number of muscular activations may combine to produce infinity of movements (D'Avella et al. 2003, 2005, 2006). More specifically, Mussa-Ivaldi and Bizzi (2000) and Torres-Oviedo et al. (2006) defined muscular synergies as the set of muscles recruited by a single neural command signal, i.e. a set of basic activations that may generate a large repertory of movements. This concept of muscle synergies has been accepted as a CNS strategy used to perform planned movements such as walking, reaching, grasping, pointing and many other motor tasks (D'Avella et al. 2003, 2005, Poppele and Bosco 2003, Ivanenko et al. 2006, Bizzi et al. 2008, Fautrelle et al. 2010). This hypothesis has received a great deal of experimental as well as theoretical support (Flash and Hochner 2005, Nori and Frezza 2005 for a modeling approach). All of these works have highlighted the use by the CNS of muscular synergies as a strategy to plan complex movements requiring the coordination of many arm, trunk and leg muscles.

Typically, muscular synergies are extracted from the overall EMG activities by using principal component analysis or nonnegative matrix factorisation (PCA Joliffe 1986, NNMF Lee and Seung 1999). PCA or NNMF are standard statistical techniques generally used to extract a low dimensional structure from a high-dimensional dataset, by means of a linear technique. Mathematically, the method involves the eigenvalue decomposition of a dataset covariation matrix in order to find the principal directions in high-dimensional space. In the context of muscle synergies, these methods have

been used as a dimensionality reduction tool applied to the muscle space. Physiologically, the underlying assumption is that two correlated EMG signals could belong to the same synergy and that, in general, a specific EMG signal could originate from a linear combination of different synergies. Therefore, these covariation analyses allow the experimenter (i) to find a simpler organization in EMG activities and (ii) to quantify the whole motor strategy in terms of muscles synergies (principal components). Generally, PCAs or NNMF are performed on smoothed (EMG) waveforms which are obtained by using a low-pass filter with a 5 Hz cut-off frequency. However, in this case, the major temporal representation of the EMG data may be lost, given that the 5Hz low-pass filter is applied to rectified signals which merely represent muscle burst activity that corresponds to the joint angular displacements. As such, PCA or NNMF may not be sensitive enough to detect brief bursts of muscle activity. For example, Grasso et al. (1998) examined EMG activity during forward/reversed gait and showed that the first principal component may account for only 50% of the EMG variance and up to 7 principal components had to be used to explain 95% of the inter-trial EMG variance. In addition, PCAs were performed exclusively to extract synergies from unperturbed movements that were executed in a stable environment at a comfortable (quite slow) speed. In this case, EMG signals are time-normalized during PCA or NNMF. This latter procedure renders precise detection of occurrences of motor corrections impossible. Finally, we cannot be sure that linear co-variations extracted from NNMF and PCA are purely representative of motor synergies. For instance, PCA or NNMF performed on EMG signals recorded on both agonist and antagonist muscles during a stretch reflex would extract two synergies: one for the activation of the agonist and the other for the inhibition of the antagonist. Paradoxically, the stretch reflex and the associated combination of agonist and antagonist EMG signals is the clearest evidence and the simplest example of what a single synergy is. Its circuitry is

well-known and its temporal organization is stable. By contrast, a method based on the precise detection of the temporal organization between both activation and inhibition would detect strong regularities that would allow classifying this motor sequence as a single synergy.

In more natural conditions, planned movements can be altered at any time if the target location is changed during execution. Given enough time, humans are able to produce fast motor corrections when unexpected events occur during the execution of a movement (Georgopoulos et al. 1981, Soechting and Lacquaniti 1983, see Paillard 1996 for a review). Motor corrections are usually investigated in the literature by means of a double step pointing experimental paradigm. This framework has indeed been widely employed to understand the numerous processes of feedback control occurring between the eye and the hand during pointing movements (Pelisson et al. 1986, Hoff and Arbib 1993, Desmurget and Grafton 2000). To perform such online motor corrections, the CNS uses certain sensory feedback information like the retinal error, which can basically be compared to the efference copy (Prablanc and Martin 1992, Blouin et al. 1995, Desmurget et al. 1999, Gaveau et al. 2003). Moreover, such experimental paradigms have also been used to study the temporal delays between the occurrence of a visual perturbation during the initial movement plan and the motor correction. For instance, Paillard (1996) established that minimum delays allowing feedback or feedforward control to influence the ongoing movements are classically centred on 120–150ms when measured on hand kinematics. When measured on EMG signals latencies inferior to 100ms can be observed both in upper and lower limbs (Fautrelle et al 2010). In this study, our aim was to develop a simple method to determine the precise latencies or delays of each muscle activity in response to a random change in the target location. As muscle synergies would be involved in the following motor corrections, there should exist a temporal link between certain muscle activities, and synergies should be characterized by

correlations between the latencies of muscle activities. Consequently, we designed an experiment in which participants were asked to point from an initial sitting position to a target that unexpectedly jumped forward and upward at the same time. The target localization used during the target jump constrained participants to involve their leg, thigh, trunk and arm muscles to perform the task successfully. The investigation of electromyographic activities will thus enable us to determine the temporal aspects of muscular synergies used by the CNS to perform these motor corrections in the whole body.

2.2 EXPERIMENTAL PROCEDURES

2.2.a Subjects

Eight right handed participants [all men, 30.5±3 years old, 70±6 kg, 1.76±0.02m] volunteered for the experiment. None of the participants had a previous history of neuromuscular disease. The entire experiment conformed to the Declaration of Helsinki and informed consent was obtained from all participants according to the guidelines of the University of Burgundy.

2.2.b Experimental setup and pointing conditions

Participants were initially seated on a 0.50mhigh stool and performed pointing movements with their right index. The starting point, the near and the far targets were represented by small, visual and tactile 10mm×10mmsquare switches, which could be lit and allowed an accurate detection of time to contact. The starting point was located to the side of the participant's right knee at a 0.50m distance from the floor, and the near target was located in front of the participant's eyes, in the saggital plane, 0.60m in front of and 0.50m higher than the starting point. The far target was located at a total distance of 1.10m from the starting point, 0.90m in front of and 0.80m higher than the starting point. Consequently, the near target could be reached from a seated position whereas the far target necessitated a sit to stand pointing movement (cf. Figure 11). Participants were asked to perform their movements as quickly and as accurately as possible when a target was lit, in three experimental conditions. In two normal conditions, either the Near or the Far target (9/21 of all trials for both conditions) was suddenly lit ("go-signal") and remained lit throughout the pointing movement. In the perturbed condition ("Target Jump" condition, 3/21 of all trials), the near target was initially lit and upon hand movement onset, was turned off and the far target was immediately turned on. The overall trials (126 trials, 6 blocks of 21 trials) were pseudo randomized. Each block contained nine trials in the Near

condition, nine trials in the Far condition and three trials in the Target Jump condition. Therefore, fewer than 15% of the overall trials were perturbed, a frequency which did not allow participants to anticipate the target jump. Finger kinematics, center of pressure (CoP) displacement, movement onset and offset, and EMG activities for 16 muscles were recorded and analyzed.

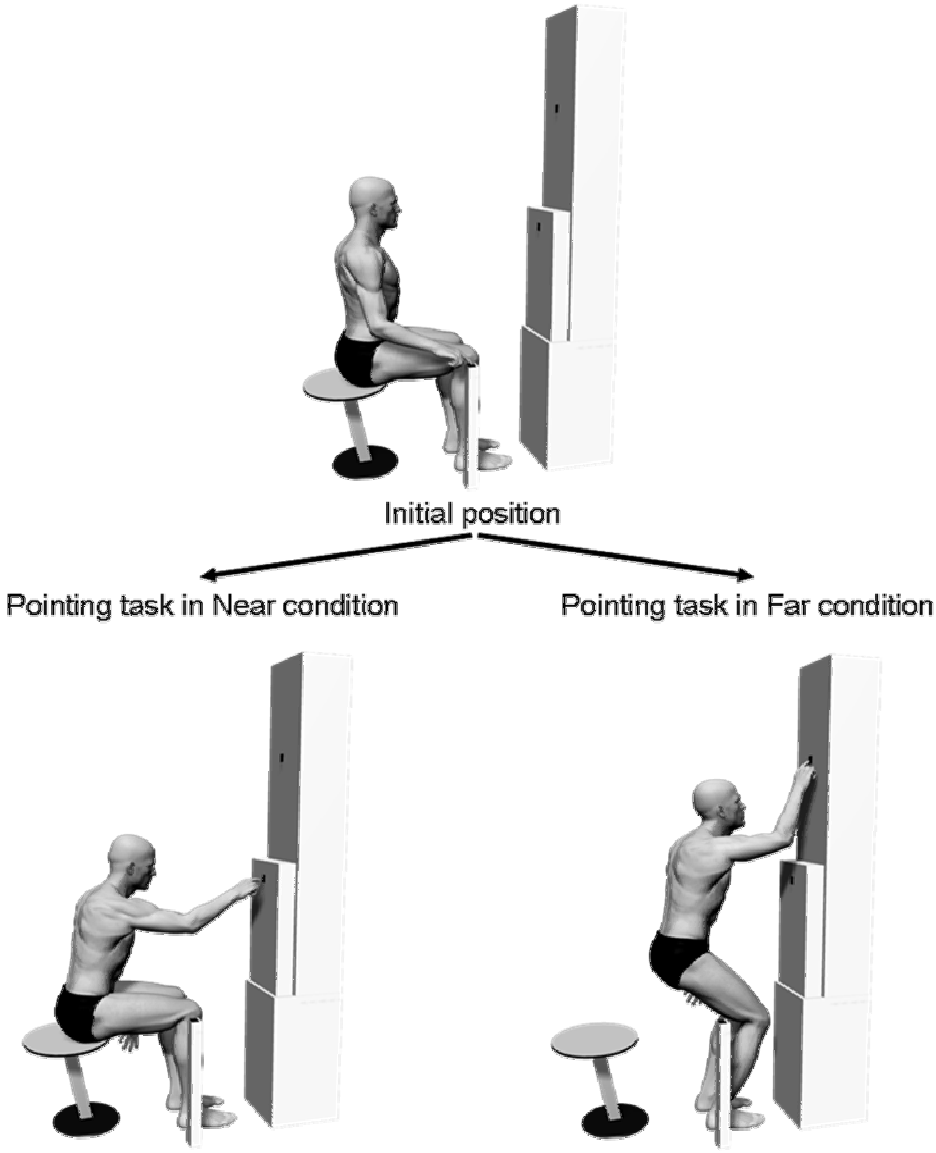

Figure 11 *View from the experimental set-up of the pointing task with the initial position for the three conditions (top) and the final position of the participants when pointing at the near (bottom left) or the far target (bottom right).*

2.2.c Recording and analysis of kinematics

The 3D kinematics of the hand movement was recorded with an optoelectronic device (SMART-BTS, Milan, Italy) (120 Hz). The marker was placed on the third phalanx of the right index. All movements were externally triggered. Position signals were filtered (Butterworth 4th order, dual-pass algorithm with a 10Hz cut-off frequency) before calculating the hand kinematics. Velocities and accelerations were computed with a zero phase finite difference algorithm. Acceleration duration (i.e. the time between hand movement onset and its peak velocity), peak velocity and mean velocity were also computed and averaged for each subject and each condition. Statistical analyses were performed using ANOVAs with repeated measures to compare kinematics data from the three experimental conditions (Near, Far, Target Jump). Post hoc analyses were conducted with the Neuman-Keuls test when necessary. In this paper, we use the term "correction time" to indicate the time lapse between the target jump and the beginning of the motor correction. In order to determine the correction time after the target jump on the hand kinematics, the hand acceleration profile between the Target Jump and the Near conditions were compared at each value using t-tests. Note that repetitive t-tests were not used to establish whether there were differences, but were used to help determine the point at which these differences became significant. There was no summation of the false-positive rate. This difference was subtle, but legitimized the use of repetitive t-tests in our study. In addition, this method has been employed in a number of previous studies (Prablanc and Martin 1992, Desmurget et al. 1999, Bonnetblanc et al. 2004, Saijo et al. 2005, Gomi 2008, Gritsenko et al. 2009, Fautrelle et al. 2010). The moment that the P-value was lower than 0.05 for minimum durations of 50ms determined the correction time after the target jump, thus avoiding false interference detection (Prablanc and Martin 1992, Bonnetblanc et al. 2004, Bonnetblanc 2008, Fautrelle et al. 2010).

2.2.d Hand movement reaction time and movement time

The tactile switches used in our experimental setup sent analogical signals at a sampling frequency of 960 Hz. The reaction time was computed as the duration between the "go-signal" and hand movement onset. The movement time was computed as the time lapse between hand movement onset and offset. In order to check whether learning influenced our results, we performed regression analyses on the hand reaction times and movement times for the 54 trials in both unperturbed conditions and the 18 trials in the perturbed condition in each subject. We then compared the values of the obtained slopes to zero.

2.2.e Center of pressure (CoP) recordings and analyses

CoP positions were recorded using a force platform (Kistler, France) at a sampling frequency of 960 Hz. Recorded position signals were low-pass filtered using a digital fifth-order Butterworth filter at a cut-off frequency of 5Hz (Matlab filtfilt function). The amplitude of the CoP displacements was computed on the antero-posterior (AP) axis for all the trials. As in our analyses of hand reaction time and hand movement time, we performed a regression analysis for the A-P CoP displacement in the three conditions and for each subject and compared the values of the obtained slopes to zero. Similarly, to determine the correction time for the A-P CoP displacement, the acceleration profiles of the CoP in the Near and the Target Jump conditions were compared for each value using t-tests. The first instant at which the P-value was lower than 0.05 for a minimum duration of 50 ms determined the beginning of the motor correction of the A-P CoP displacement.

2.2.f EMG recording and analyses

The participants were instructed to selectively activate each recorded muscle individually to determine the positioning of the surface electrodes (Kendall et al. 1993). In addition, the skin was shaved and cleaned with alcohol to ensure low resistance. The interval between each electrode was two centimeters.

Surface EMG activities (SMART-BTS, Milan, Italy) were recorded (960 Hz frequency) on the subject's right side for the tibialis anterior (TAi), soleus (SOLi), rectus femoris (RFi), vastus lateralis (VLi) and the biceps femoris (BFi) at the leg level, the rectus abdominis (RAi), erector spinae (ESL5i) between L3 and L5, erector spinae (ESL1i) between D11 and L1, pectoralis (PSi), latissimums dorsi (LDi), and the trapezoid (TR) at the trunk level, the deltoïdus anterior (DAi), deltoïdus posterior (DPi), biceps brachii (BBi), triceps brachii (TBi) and the brachio radialis (BRi) at the arm level. Raw EMG signals were first bandpass filtered between 20 and 400 Hz and then full-wave rectified and filtered using an averaging moving-window algorithm (window size: 25 ms). Trials were averaged for each pointing condition and for each subject. In this paper, we use the term "initiation time" to indicate the delay between the illumination of the first target (the "go-signal") and the beginning of significant muscular activity. To determine the initiation time of the sixteen muscles recorded, the EMG values after the illumination of the first target and the EMG baselines were compared for each value using t-tests for each muscle in each condition. The EMG baselines were computed as the mean integrated activity of each muscle from −2s to −1 s before the first target was lit and when the participants maintained the initial position. The first instant at which the P-value was lower than 0.05 for a 50 ms minimum duration determined the beginning of the muscle activation necessary to perform the pointing movements. Similarly, in order to determine the correction time of the sixteen recorded muscles, the EMG values in the Target Jump condition and the Near condition were compared for each value by means of t-tests and applied to each muscle. The first instant at which the P-value was lower than 0.05 for a 50 ms minimum duration determined the beginning of the motor correction in response to the perturbation. This latter analysis was performed to determine the latencies of muscle activities. In order to assess whether latencies of the whole motor sequence used to correct the movement were

similar to those used to initiate the movement, we performed linear correlations between values of correction times and initiation times for each subject. Correlations between values of initiation times obtained for each experimental condition were also performed. The main limitation of our method is that the EMG amplitude or gain of the motor correction is not investigated. Consequently, the main discussion of the obtained results can only concern the temporal aspects of the motor sequence. In order to further investigate the aspects linked to the variation in EMG amplitude induced by the target jump, we computed the integrated EMG values for the first 50 ms after the correction time detected for each muscle in the perturbed condition divided by the integrated EMG values computed for the same temporal interval in the unperturbed condition. This index allows us to estimate the EMG amplitude or gain of the motor corrections. Finally, to determine whether correction times, initiation times and EMG amplitude of motor corrections were organized in a synergetic manner and thus linearly correlated between pairs of muscles, correlation coefficients were computed between values obtained for each subject and each muscle, for the 120 possible combinations (16 muscles×15/2).

2.3. RESULTS

2.3.a Hand kinematics

First, we checked whether learning significantly influenced our results. Regression analyses were performed on hand reaction times, hand movement times and CoP amplitudes. Results revealed that the obtained slopes were not statistically different from zero for any of these parameters, in any experimental condition ($P > 0.85$ for hand reaction time, $P > 0.87$ for hand movement time and $P > 0.45$ for CoP amplitude) demonstrating that learning did not influence our results. Second, we ensured that hand reaction times were not different in the Near and Target Jump conditions, that is to say that the target jump was not anticipated. No significant differences were found between the Near, the Far and the Target Jump conditions ($F(2, 14) = 1.01$, $P = 0.389$). Similarly, the peak velocity of the finger did not vary significantly among the three experimental conditions ($F(2, 14) = 1.005$, $P = 0.390$). In contrast, main effects were found for movement time, the acceleration duration of the finger, and for the CoP A-P amplitude (see Table 1 for the statistical values). Neuman-Keuls post hoc analyses revealed more precisely that movement time was inferior in the Near condition, that the acceleration duration was superior in the Far condition, and that the mean velocity was inferior in the Target Jump condition ($Ps < 0.01$). All these results are summarized in Table 2.

	Near	Far	TJump	*F*-value	*P*-value
Movement Time (ms)	464 ± 89	733 ± 99	874 ± 83	$F(2, 14) = 464.69$	$P < 0.001$
Hand Reaction Time (ms)	340 ± 42	347 ± 67	340 ± 53	$F(2, 14) = 1.0100$	$P = 0.389$
Acceleration Duration (ms)	163 ± 31	211 ± 42	172 ± 41	$F(2, 14) = 26.349$	$P < 0.001$
Mean Velocity ($m\,s^{-1}$)	1.46 ± 32	1.41 ± 0.26	1.22 ± 0.15	$F(2, 14) = 11.916$	$P < 0.001$
Peak Velocity ($m\,s^{-1}$)	2.89 ± 0.5	2.82 ± 0.35	2.91 ± 0.49	$F(2, 14) = 1.0053$	$P = 0.390$
CoP A-P Amplitude (cm)	5.3 ± 1.6	15.0 ± 2.4	18.7 ± 2.1	$F(2, 14) = 68.936$	$P < 0.001$

Table 2 *Hand kinematics and A-P CoP displacements parameters.The following hand kinematics parameters are averaged for the 8 subjects: movement times, reaction times, acceleration durations, peak velocities of the finger and amplitude of the CoP A-P displacement in the Near, Far, and Target Jump conditions (mean±standard deviation). For each of these parameters, F and P values are also reported.*

Figure 12 presents the velocity profile of the hand movement, the A-P displacement of the CoP and the electrical activity of the sixteen recorded muscles for a typical trial. Data recorded in the three experimental conditions were superimposed for each recorded signal, from two hundred ms before hand movement onset to hand movement offset. The following overall analyses and more particularly the detection of the correction time from EMG activities were performed from this kind of data for all subjects in all conditions.

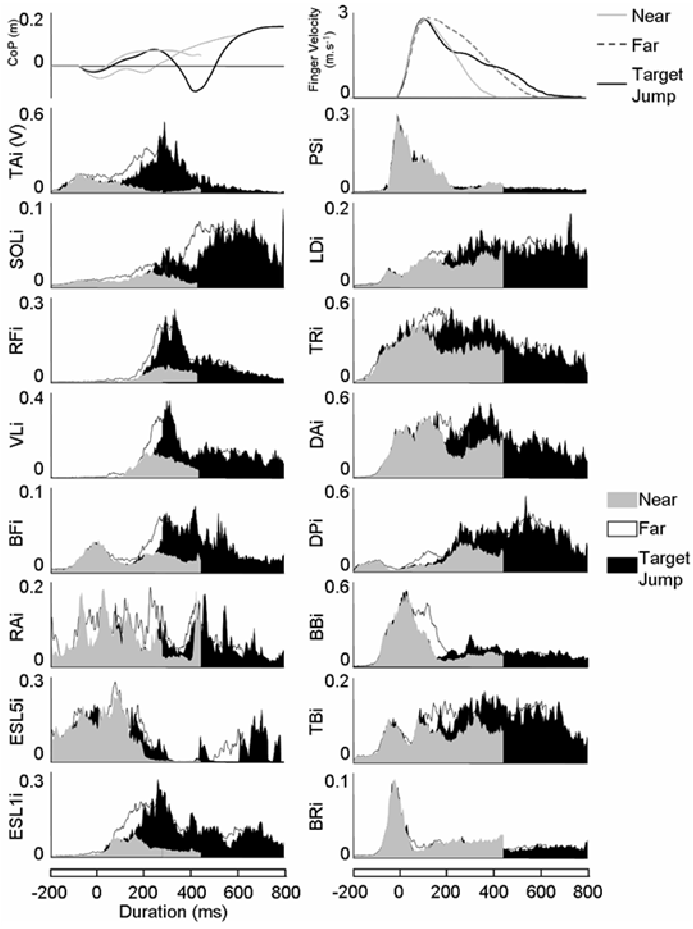

Figure 12 *Raw data of the A-P displacement of the CoP (m), the velocity profile of the hand movement (ms−1), and the EMG activity of the sixteen recorded muscles (V). Kinematics signals are filtered with a dual-pass algorithm with a 10Hz cut-off frequency (Butterworth 4th order), CoP positions are low pass filtered at 5 Hz, and EMG signals are bandpass filtered between 20 and 400 Hz, full-wave rectified and then filtered using an averaging moving-window algorithm (window size: 25 ms). Data are synchronized to the hand movement onset and represented from 200ms before the onset to the offset. The following overall analyses and more particularly the detection of correction time in EMG activities were carried out using this kind of typical data.*

2.3.b Correction times

For all participants, overall recorded parameters were significantly modified after the target jump. On average, correction times increased from 170 (±30) ms for the EMG activity of the TAi to 343 (±38) ms for the hand kinematics. Interestingly, although the order of the muscle recruitment differed more or less widely between participants, the first three significant correction times were always found for the TAi, the TRi, and the DAi in this order for all participants. Means (±SD) of correction times determined for all these parameters are shown in Figure 13.

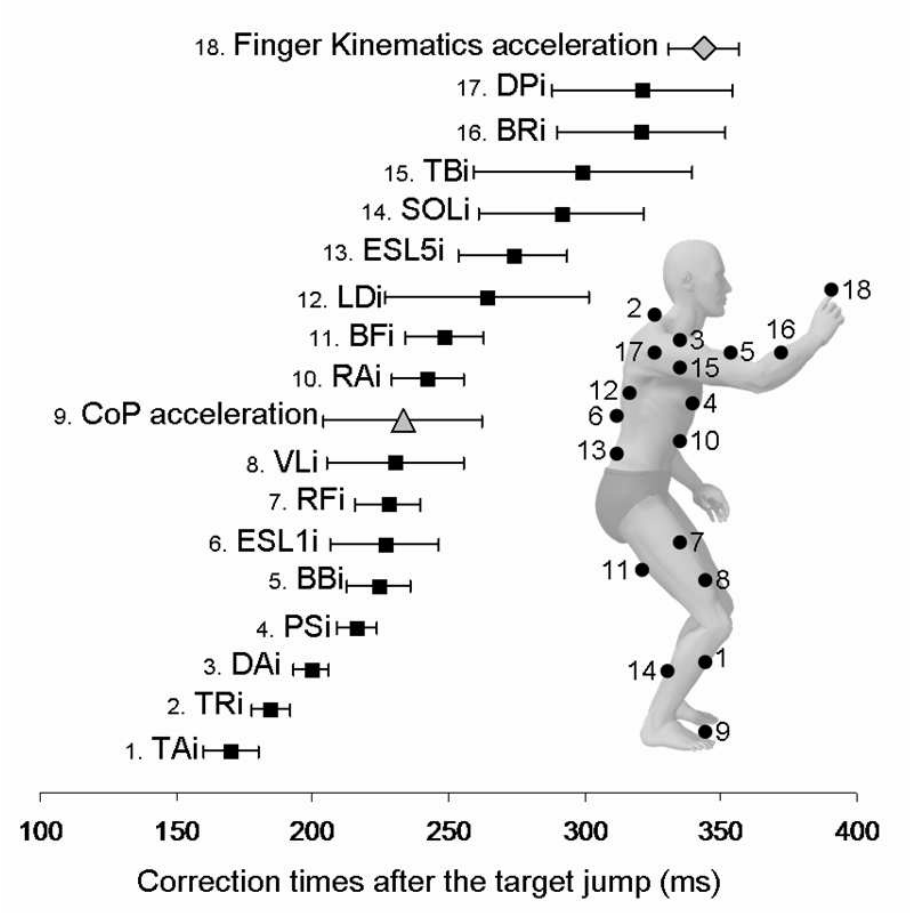

Figure 13 *Correction times computed on finger acceleration, CoP acceleration and EMG activities. Average (±SD) of the correction times reported in ascending order for kinematics, CoP and EMG recordings. Concerning the duration axis, the origin (0) corresponds to the target jump occurrence. For the sake of clarity, the temporal scale begins here at 100ms after the target jump. Each correction time is numbered and reported on the human schemata to facilitate location of the muscles in the human body.*

2.3.c Correction times versus initiation times

We wanted to determine whether correction times and initiation times were differently ordered. Figure 14 shows clear differences between the order of correction times and initiation times for most muscles. Correlation coefficients were very low when regression analyses were carried out on correction time and initiation time. In contrast, correlation coefficients were much higher and significant when initiation times were correlated together for all experimental conditions.

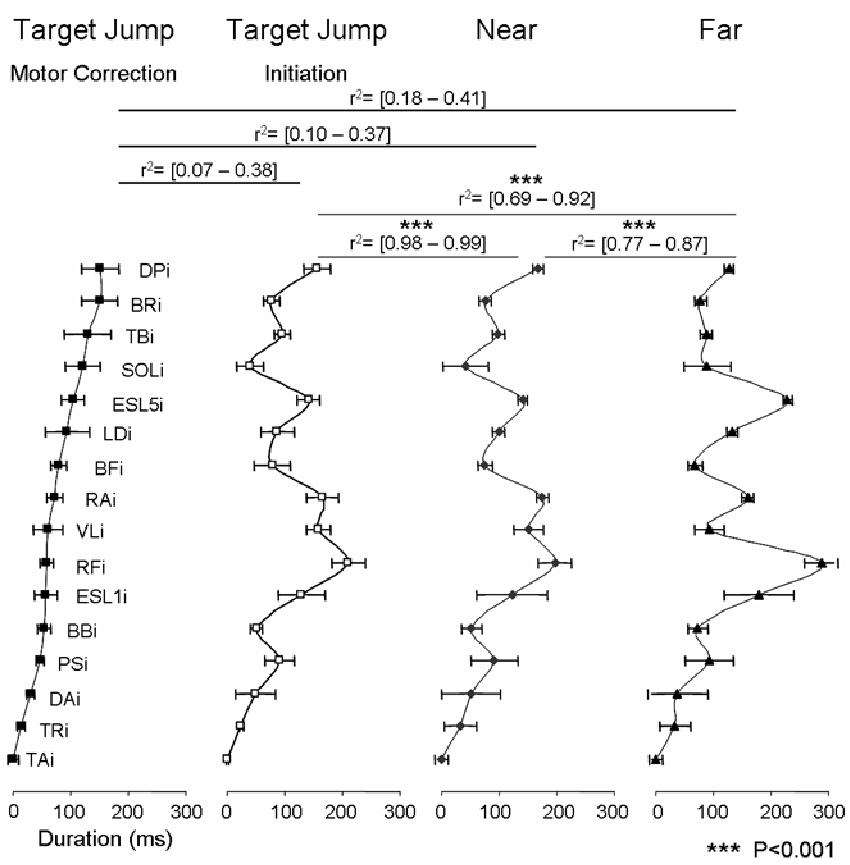

Figure 14 *Muscular synergies used to initiate or correct the pointing movement. The muscular synergy reported in the left-hand column corresponds to the average (±SD) of the correction times after the visual perturbation in the target jump condition. The muscular synergies reported in the second, third and fourth columns correspond to the averages (±SD) of the Target Jump initiation, the time to initiation in the Near and in the Far conditions. These muscular synergies were those used to initiate the pointing movement after the go signal (the lit target) in the three experimental conditions. The origin (0) of the temporal axis is the first muscular activation occurrence, i.e. the TAi activation, for all subjects in all conditions. To compare these four muscular synergies, the correlation coefficient r2 between each pair of synergies was computed for each subject and the range of the obtained results is given on top of the graphs.*

2.3.d Correction times were correlated between pairs of muscles independently of their location or their occurrences

We found fourteen significant correlations in correction times between pairs of muscles ($r > 0.71$; $P < 0.01$) involving ten different muscles located in the arm, the trunk and the leg. Figure 15 shows the ten muscles (namely the TAi, SOLi, RFi, VLi, ESL5i, ESL1i, TRi, DPi, BBi, TBi) whose correction times present at least one significant correlation with those of another muscle. These correlations ($P < 0.01$) are represented between two muscles by a straight line and the r-coefficient is reported along the line. The six muscles which revealed no significant correlation are presented in the box on the right. Importantly, these correlations between correction times for some pairs of muscles were independent of their occurrence and their order. We found, for example, a significant correlation between the TAi (correction time = 170±30 ms) and the ESL5i (correction time = 274±60 ms), and between the BBi (correction time = 224±34 ms) and the DPi (correction time = 321±88 ms). A difference of 100ms was indeed observed between the correction times of the TAi and the ESL5i and between those of the BBi and the DPi. Similarly, these correlations were also independent of the spatial localization of the muscles in the human anatomy. For instance, Figure 15 demonstrates that the correction times measured for the TAi, which is located in the leg, were closely correlated with those of the TRi, located near the neck ($r = 0.97$).

2.3.e Correlations of correction times and initiation times between pairs of muscles

We found eight significant correlations in initiation times ($r > 0.70$; $P < 0.01$) involving ten different muscles located in the arm, the trunk and the leg (namely the TAi, SOLi, RFi, BFi, ESL5i, ESL1i, PSi, DPi, DAi, and the BBi). All correlations are summed up in Figure 16 A and B both for correction times and initiation times and are represented on two separate bodies. Muscles for which at least one significant correlation with another muscle was observed are represented in black and linked by a straight line. These results

demonstrate that initiation times were correlated between fewer pairs of muscles located primarily in the lower body whereas correction times were correlated between more pairs of muscles located either in the lower or the upper body.

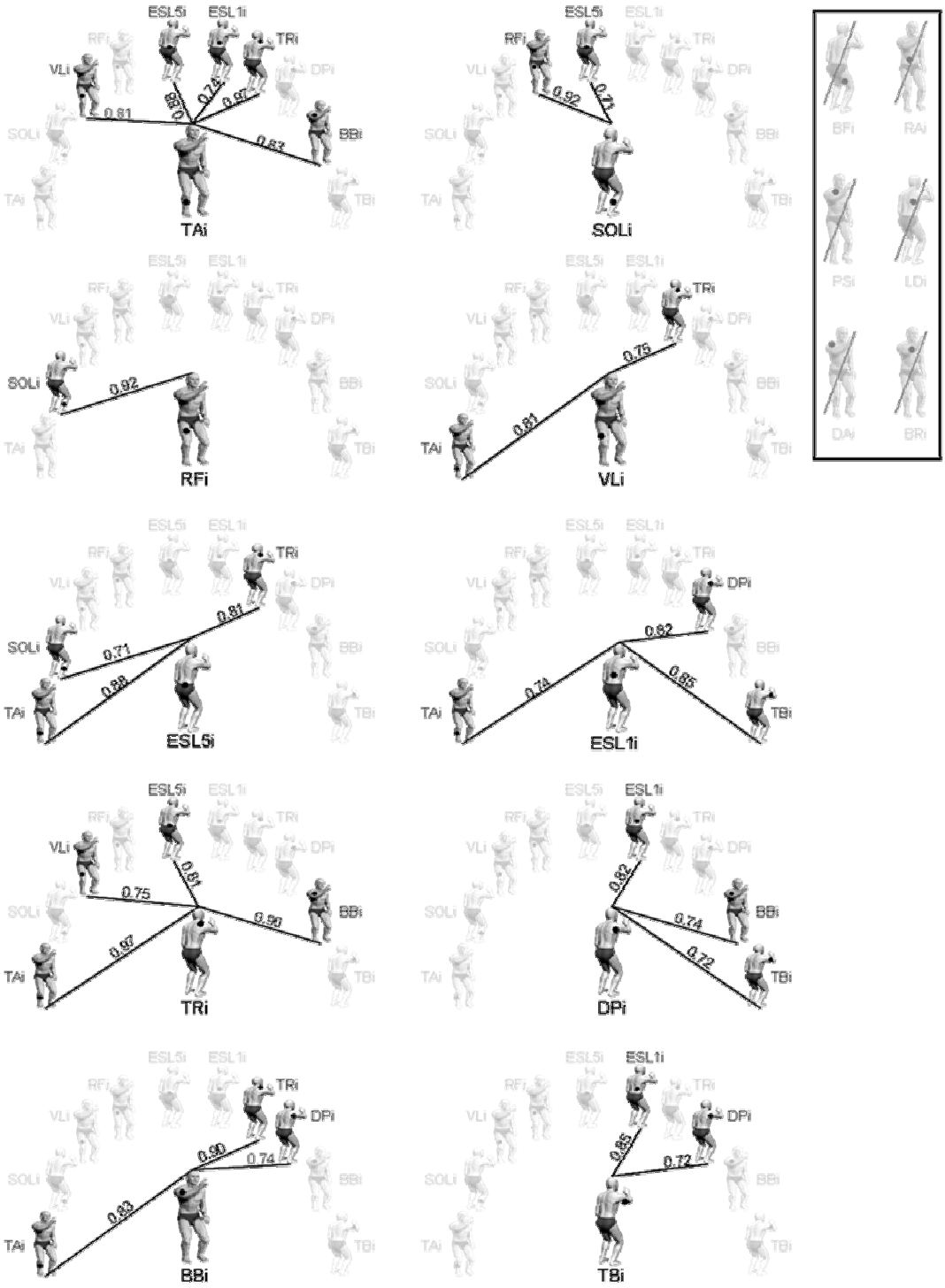

Figure 15 *Correlations in correction times for each muscle. Correction times for each muscle and each subject are taken from the correlation matrix. For each muscle, significant correlations are represented by a link between each pair of correlated muscles. The values of the significant r-coefficients are reported along the link for each correlation. The six muscles showing no significant correlations are reported in the gray box.*

2.3.f Correlation of normalized EMG amplitudes of the motor corrections

We found 10 significant correlations in normalized EMG amplitudes ($r > 0.71$) involving nine different muscles located in the arm, the trunk and the leg (namely, the TAi, VLi, RFi, BFi, RAi, LDi, TRi, DAi and the BBi). All correlations are summed up in Fig. 16C. Muscles for which at least one significant correlation with another muscle was observed are represented in black and linked by a straight line. These results demonstrate that the normalized EMG amplitudes of the motor corrections were correlated mostly between different pairs of muscles. These correlations should be interpreted with caution as the normalization is here limited to allow a comparison of the EMG activity between muscles. They give only a global idea and mainly show that the muscles in which correction or initiation times were correlated are not necessarily those in which normalized EMG amplitudes of the motor corrections are.

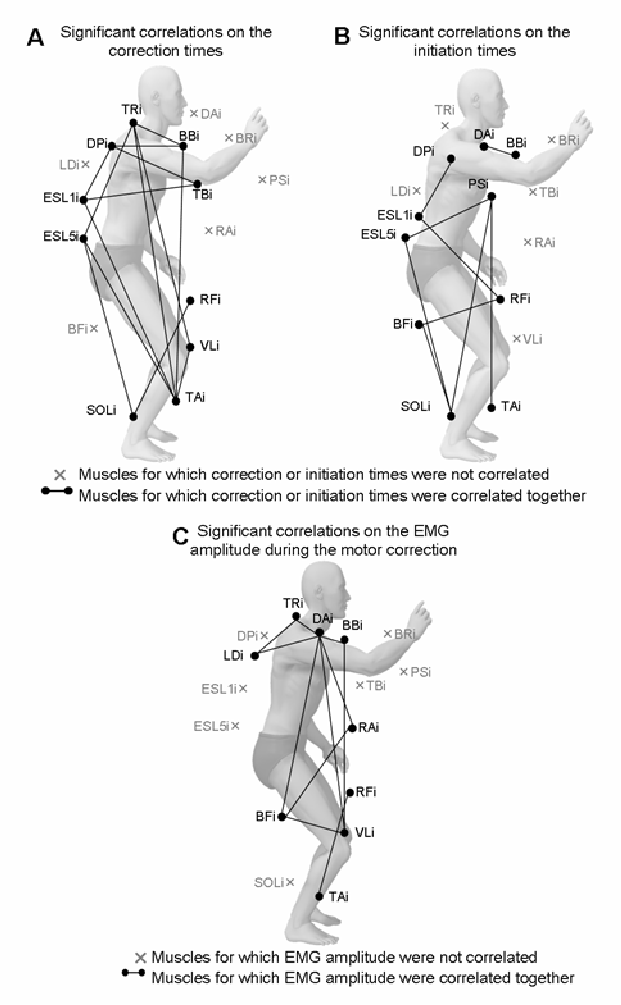

Figure 16 *Significant correlations computed on correction times, initiation times and amplitudes of the motor corrections.*
Significant correlations computed on correction times, initiation times, and amplitudes of the motor corrections. The significant correlations in correction times represented on a single body (A) are compared: (i) to the significant correlations in initiation times (B) and (ii) to the significant correlations in integrated EMG amplitude for the 50ms after the beginning of the motor corrections for each muscle (C). A black link between two muscles represents a significant correlation. The muscles showing no significant correlations are represented by a cross and reported in gray.

2.4. DISCUSSION

Our aim was to characterize muscle synergies during movements involving large motor corrections by precisely determining the latencies of muscle activities. We hypothesized that, due to synergies, we should observe correlations between these latencies. In our task, participants were asked to point from an initial sitting position to a target that unexpectedly jumped forward and upward at the same time. Using a simple statistical method based on repetitive t-tests used to contrast EMG signals in the perturbed and unperturbed conditions, our results demonstrated that: (1) both initiation times together and correction times together were strongly correlated for certain pairs of muscles, independently of their occurrences during the motor sequence and independently of the location of the muscles at the anatomical level, (2) latencies of muscles activities were not similarly organized between the initiation and the correction of the movement despite the fact that this correction was triggered very soon after movement initiation, (3) initiation times were correlated between fewer pairs of muscles primarily located in the lower body whereas correction times were correlated between more pairs of muscles located either in the lower or the upper body.

2.4.a Movement initiation and correction

During unperturbed and rapid pointing movements performed from an upright standing position, it has been observed that the TAi initiated the whole pointing movement before the hand movement onset. In these cases, the integrated EMG activity of this muscle was even shown to be proportional to the target size at least 200 ms before the hand movement onset and independently of the kinetic constraints applied to the trunk movement (Bonnetblanc et al. 2004, Bonnetblanc 2008). In the present study, we also observed that the TAi was the first muscle to be activated during both movement initiation and correction, suggesting that the role of this muscle was critical in facilitating the forward displacement of the CoM in advance of

the hand displacement (Fautrelle et al. 2010). In reaching and grasping tasks, a proximal-to-distal sequence of muscle recruitment is generally observed (Jeannerod 1986). This is clearly not the case during more complex movements. While the TAi initiated the movement or the correction, the order of muscle activities did not follow a bottom-up sequence. We identified no obvious reason to explain this order. Moreover, the trapezoid (TRi) was the second most rapidly involved muscle both during movement initiation and motor corrections, likely suggesting an orienting response, and showing significant activity only 20 ms after that of the TAi. At this point, it is important to note that the corrections observed in one muscle are probably not a by-product of those observed in another muscle, triggered by means of a reflexive mode. These short delays, combined with the major distance between muscles, are strongly inconsistent with this hypothesis. Indeed, many motor corrections were triggered at time intervals of less than 20 ms in very distant muscles and many intervened before the CoP acceleration was modified. In addition, there was no obvious relationship that could be explained by connections at the spinal level (e.g. reciprocal inhibition, etc.). This suggests rather that there is no hierarchical processing of upper over lower limb motor corrections and that motor flexibility in rapid movements probably involve a complex coordination within the body schema. These results are thus important in the understanding of motor correction organization and their implementation within the motor command in complex and ecological movements.

2.4.b Somatotopic organization of synergies in the primary motor cortice and synchronization of correction times and initiation times between muscles

Interestingly, we observed that both initiation times together and correction times together were strongly correlated for some pairs of muscles. Importantly, these correlations were observed for pairs of muscles independently of their occurrences during the motor sequence and

independently of the location of the muscles at the anatomical level. Our method thus proved very simple and very useful in investigating the precise latencies of muscle activities. By definition, these correlations were strongly illustrative of the muscular synergies involved during movement initiation and movement correction. At the level of the Primary Motor Cortice (M1), muscles appear to be controlled as a coupled functional system, rather than individually and separately (Capaday 2004, Graziano and Aflalo 2007). This conclusion is sustained when looking carefully at the pattern of intrinsic connections between motor cortical points. Indeed, the somatotopic organization reveals differentiated as well as undifferentiated motor points, involving in these latter cases several muscles, and suggests a more complex representation for muscles and muscle synergies in the motor cortex than previously thought. Our results are in line with an undifferentiated representation of motor synergies in M1. Indeed, modulations exerted on the descending command at the spinal level would rather desynchronize EMG activity in the muscles. More specifically, it is unrealistic to consider that various differentiated motor cortical points are solicited in the brain at different instants and synchronized at the spinal level. The synchronization we observe in our data instead emerges at the level of M1. According to Capaday "the selection of movement-related muscle synergies was more likely a dynamic process involving the functional linking of a variety of motor cortical points, rather than the selection of fixed patterns embedded in the motor cortical circuitry". The main mechanism invoked in the functional linking of motor cortical points was disinhibition. Thus, synergies could emerge from the recruitment of various motor cortical points by selected excitation as well as by selected release from inhibition (Capaday 2004). In this vein, it would be interesting to investigate whether repetitive transcranial magnetic stimulation applied over M1 at a subthreshold intensity would inhibit the motor points and desynchronize and delay the motor corrections between some muscles

that are usually synchronized together. The principal limitation of our method is that it does not permit precise investigation of the relationship between EMG signals in terms of magnitude. However, this investigation is also limited when using PCA. Indeed, in this case, signals are normalized in amplitude. In addition, while PCA determines the level of similarities that envelops of EMGsignals share between some muscles, this level of similarity is nevertheless strongly dependent on the cut-off frequency of the low-pass filter that is applied. The lower the cut off frequency, the lower the number of principal components that explain the variability of the EMG signals. Our method characterizes the temporal relationships between several EMG activities that are representative of muscle synergies and does so in a manner which is much more direct and precise.

2.4.c Movement correction involves more synergies than movement initiation

Finally, we observed that initiation times were correlated between fewer pairs of muscles located primarily in the lower body, whereas correction times were correlated between more pairs of muscles located either in the lower or the upper body. Based on a qualitative analysis, Soechting and Lacquaniti (1983) observed in a simple arm reaching task with only two degrees of freedom that EMG activities between the BBi and DAi became more closely coupled during the corrective process responsible for altering the trajectory of the movement. Using a quantitative approach, we generalized this result to a much more complex pointing task involving many muscles that were not located close to each other. This suggests that coordination during motor correction was achieved by means of a reduction in the number of degrees of freedom of the movement. This finding may be explained in two ways that cannot be disentangled. First, an increased level of urgency may induce a more linked control of the muscles as a whole during the corrective process. In addition, a decreased level of spatial incertitude may explain this effect. Indeed, discussing the effect of urgency on motor coordination, Paillard

(1996) suggested that unexpected changes of location, once the initial planning process is already started, will result in a quick remodulation of the relative duration of the coordinating program. In other words, change in the kinematics of a complex movement, triggered by visual information about change in target location, might reflect a regulation of the relative timing of the motor schemata involved in the completion of this complex movement. Concerning the effect of the degree of spatial uncertainty in our experiment, if subjects have to initiate their movement, there are at least two possibilities for the location of the target (near or far). However, if the target jumps upward and forward, a single possibility in terms of target location remains (the far target only). There is no spatial uncertainty in this condition. This may explain amore coupled control of the whole pointing movement. In connection with this last point, we would predict a diminution in synergies and correlations between latencies of muscle activities as the number of target jump possibilities increases. In conclusion, it is possible to detect and use latencies of muscle activities to easily characterize muscle synergies. This synchronization between certain muscle activities seems to be a representation of the somatotopic organization of synergies in M1. It seems that movement correction involves a tighter temporal coupling between muscle activities than is the case in movement initiation. This temporal coupling may also increase according to the urgency to complete the task or with a decrease in spatial uncertainty.

2.5 ACKNOWLEDGEMENTS

We sincerely thank the two anonymous reviewers for their very precise and stimulating comments about this study.

3. POINTING TO DOUBLE-STEP VISUAL STIMULI FROM A STANDING POSITION: MOTOR CORRECTIONS WHEN THE SPEED-ACCURACY TRADE-OFF IS UNEXPECTEDLY MODIFIED IN-FLIGHT. A BREAKDOWN OF THE PERCEPTION-ACTION COUPLING.

Lilian Fautrelle, Guillaume Barbieri, Yves Ballay, François Bonnetblanc

3.1 INTRODUCTION

In 1899, Woodworth demonstrated that the terminal variability of a movement was influenced by the speed of execution (Woodworth 1899). These pioneer works have led to the idea that the time required to complete a fast and accurate movement is a function of the amplitude and the target size. For instance, when a subject has to point as fast and as accurately as possible, the speed of execution will be to the detriment of the final precision. Conversely, the more precision required, the more the speed of execution will be compromised. This phenomenon is called the "speed-accuracy trade-off" and Fitts described this relationship by the law: $MT = a + b \cdot Log2(2A/W)$, where A and W are the movement amplitude and target width, respectively and Log2(2A/W) is the index of difficulty (ID) of the pointing task (Fitts 1954; Fitts and Peterson 1964).

In the case of rapid movements, it has been suggested that the relationship linking movement time (MT) to movement amplitude and especially to target size is already present in the movement planning phase (Schmidt et al. 1978; 1979; Meyer et al. 1982; 1988; 1990; Harris and Wolpert 1998). In these models, the terminal variability increases proportionally according to the initial force that is required and its initial duration. More specifically, Harris and Wolpert (1998) suggested that pointing movements are planned to minimize the variance of the final position of the hand. Motor output signals are corrupted by noise and the terminal variance is thus a function of the output signal amplitude. In this vein, Bonnetblanc et al. (2004) demonstrated that, when pointing from an upright standing position, the electromyographic (EMG) activities of lower limb muscles that preceded the hand movement onset by 200 ms were proportional to the target size. As a whole, based on the idea that afferent and efferent delays are too long, these interpretations suggest that the speed-accuracy trade-off is already planned at the initial stages of motor control.

However, goal-directed movements can be altered at any time if, for instance, the target location is changed during execution. Given enough time, humans are able to produce fast motor corrections when unexpected events occur during the execution of a movement (Georgopoulos et al. 1981; Soechting and Lacquaniti 1983; see Paillard 1996 for a review). Thus, one possible limitation of previous interpretations may be that they underestimate feedback processes (Elliott et al. 2001; Bonnetblanc 2008). In particular, to nuance the role of feedforward processes in the speed-accuracy trade-off, Hoff and Arbib (1992 ;1993) have suggested that the hand and target positions could be compared on-line in a predictive mode. Similarly, Desmurget and Grafton (2000) suggested that feedforward models could serve to monitor hand displacement with respect to the target on-line, in order to detect motor errors and trigger motor corrections.

Motor corrections are usually investigated by means of a double step pointing paradigm. This paradigm has been employed to understand the numerous processes of feedback control occurring between the eye and the hand during pointing movements (Pelisson et al. 1986; Hoff and Arbib 1993; Desmurget and Grafton 2000). To perform such online motor corrections, the CNS uses certain sensory feedback information like the retinal error, which can basically be compared to the efference copy (Prablanc and Martin 1992; Blouin et al 1995; Desmurget et al. 1999; Gaveau et al. 2003). Such experimental paradigms have also been used to study the temporal delays between the occurrence of a visual perturbation during the initial movement plan and the motor correction. For instance, Paillard (1996) established that minimum delays allowing feedback or feedforward control to influence the ongoing movements are typically around 120–150ms when measured on hand kinematics. Interestingly, in these experiments, movements were always performed from a seated position, and mostly involved arm movements alone. However, when a more complex coordination is required, one that

necessitates the involvement of lower and upper limbs together to reach the target, motor corrections were measured on EMG signals with latencies inferior to 100 ms both in upper and lower limbs (Fautrelle et al. 2010a). In a similar case, it was also demonstrated that correction times measured on EMG signals were strongly correlated for certain pairs of muscles, independently of their occurrences during the motor sequence and independently of the location of the muscles at the anatomical level. These findings point to the existence of muscular synergies associated with motor corrections (Fautrelle et al. 2010b).

Double-step paradigms often involve changes in target location alone. Few experiments have tested correction processes involving target size changes (e.g. Paulignan et al. 1991; Castiello et al. 1993; 1998). In these latter studies, grasping movements (and not pointing movements) were studied, and targets were also simultaneously displaced as their size was modified. In consequence, the target size was never the sole modification. Nevertheless, this particular condition may be employed to investigate how changes in target size may influence motor corrections during a pointing movement.

More specifically, we hypothesized here that if the speed-accuracy trade-off is specified before triggering a corrective movement that is purely ballistic, we should observe a terminal variability that is proportional to the target size. Alternatively, if feedback corrections are involved, the final variability may be independent of the final target size and the final approach may be lengthened. In addition, in order to better document the motor correction processes that occur when the speed-accuracy trade-off is varied unexpectedly, we also recorded EMG signals for several muscles, and measured the time it took the individual to correct their movement after the perturbation.

3.2 MATERIALS AND METHODS

3.2.a Subjects

Seven right handed participants [all men, 28.5 ± 5 years old, 74 ± 5.5 kg, 1.76 ± 0.03 m] volunteered for the experiment. None of the participants had a previous history of neuromuscular disease. The entire experiment conformed to the Declaration of Helsinki and informed consent was obtained from all participants according to the guidelines of the University of Burgundy.

3.2.b Experimental setup and pointing conditions

Subjects were asked to perform pointing movements with their right index finger at four potential targets. The starting point, the center of the two concentric near targets and the center of the far targets were located respectively 12, 55 and 80 cm in front of the subject in the sagittal plane and 10 cm below the xyphoid process. Targets were represented by a visible, bright red circle 2 cm in diameter for the small targets and 20 cm in diameter for the big targets (cf. Figure 17). Small and big targets were represented by 30 LED and 90 LED respectively (red color, luminance 2 mcd). The entire experiment took place in the dark. The near targets could be pointed at with the arm alone, whereas pointing at the far targets required an additional forward bending movement of the trunk. Subjects were asked to perform pointing movements as quickly and as accurately as possible when a target was lit. Altogether, twelve conditions were tested. In four normal conditions, the Small Near (N), the Big N, the Small Far (F) or the Big F was lit ("go signal") and remained lit throughout the pointing movement. In the four conditions involving target size change only (without distance change), a target was initially lit and at the onset of hand movement, was turned off while the other concentric target was immediately turned on. Four situations were then possible: Big N to Small N, Small N to Big N, Big F to Small F and Small F to

Big F. Finally, target size and/or distance could be used in combination to perturb the pointing movement at hand movement onset. The four final experimental conditions were thus added: Small N to Small F, Small N to Big F, Big N to Small F, and Big N to Big F. The order of the conditions was randomized in each block of twelve trials and ten blocks were performed by each subject (120 trials, 10 blocks of 12 trials per subject). Finger kinematics, movement onset and offset and EMG activity for 16 muscles were recorded and analyzed.

Signals were all synchronized to the hand movement onset (t=0).

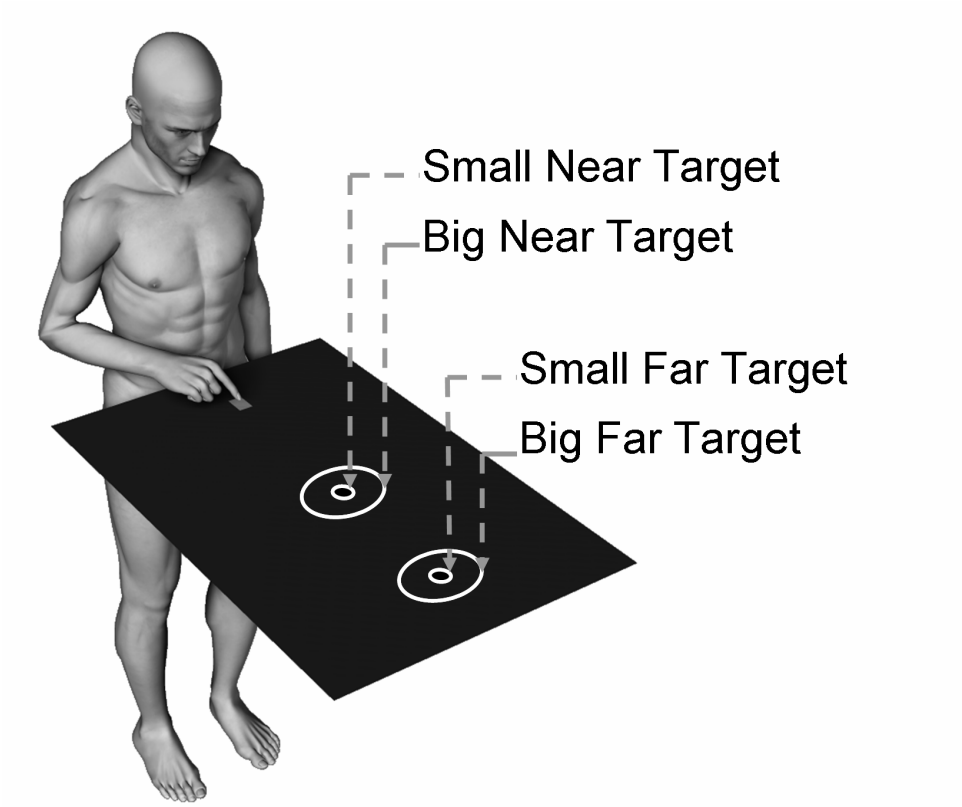

Figure 17 *View of the experimental set-up for the pointing task showing a subject in initial position and the four possible targets.*

3.2.c Kinematic recording and analyses

An optoelectronic device recorded the 3D kinematics of the hand movement (SMART-BTS, Milan, Italy; 120 Hz). The marker was placed on the third phalanx of the right index. All movements were externally triggered. Position signals were filtered (Butterworth 4th order, dual-pass algorithm with a 10 Hz cut-off frequency) before calculating the hand kinematics. Velocities and accelerations were computed with a zero phase finite difference algorithm. Hand movement onset was determined by means of the tactile 10x10 mm square switch used as starting point and allowed an accurate measurement of time to release (sampling frequency of 960 Hz). Hand movement offset (i.e. the end of the pointing movement) was determined from the end of the recording when the linear tangential velocity surpassed 3% of the maximal peak velocity (the maximal velocity). Acceleration duration, (i.e. the duration between the hand movement onset and its peak velocity) and peak velocity were computed and averaged for each subject in each condition. Moreover, reaction time was computed as the duration between the "go-signal" and the hand movement onset. MT was computed as the duration between hand movement onset and offset.

3.2.d Correction time computed on the hand kinematics.

In the following, we use the term "correction time" to indicate the delay between the target jump and the beginning of the motor correction (Fautrelle et al. 2010 a, 2010 b). In order to determine correction time after the target jump on the hand kinematics, the hand velocity profile between the eight perturbed conditions and the four corresponding normal conditions were compared at each value using t-tests. More precisely, the Small N to Big N, Small N to Small F, and Small N to Big F experimental conditions were compared with the Small N condition. The Big N to Small N, Big N to Small F, and Big N to Big F conditions were compared with the Big N condition. Finally, the Small F to Big F condition was compared with the Small F

condition and the Big F to Small F condition was compared with the Big F condition. Note that repetitive t-tests were used, not to determine whether there were differences, but rather to determine the point at which these differences became significant. There was no summation of the false-positive rate. This difference is subtle, but legitimizes the use of repetitive t-tests in our study. This method has been previously employed in several studies (Prablanc and Martin 1992; Desmurget et al. 1999; Bonnetblanc et al 2004; Saijo et al. 2005; Gomi 2008; Gritsenko et al. 2009; Fautrelle et al. 2010a, 2010b).

A P-value lower than 0.05 for minimum durations of 50 ms determined the correction time after the target jump, thus avoiding false interference detection (Prablanc et Martin, 1992; Bonnetblanc et al., 2004; Bonnetblanc, 2008).

3.2.e EMG recording and analyses

Subjects were instructed how to selectively activate each recorded muscle individually to determine the positioning of the surface electrodes (Kendall et al. 1993). In addition, the skin was shaved and cleaned with alcohol to ensure low resistance. The interval between electrodes was two centimeters. Surface EMG activities (SMART-BTS, Milan, Italy) were recorded (960Hz frequency) on the subject's right side for the tibialis anterior (TAi), soleus (SOLi), rectus femoris (RFi), vastus lateralis (VLi) and the biceps femoris (BFi) at the leg level, the rectus abdominis (RAi), erector spinae (ESL5i) between L3 and L5, erector spinae (ESL1i) between D11 and L1, pectoralis (PSi), latissimums dorsi (LDi), and the trapezoid (TR) at the trunk level, the deltoïdus anterior (DAi), deltoïdus posterior (DPi), biceps brachii (BBi), triceps brachii (TBi) and the brachio radialis (BRi) at the arm level. Raw EMG signals were first bandpass filtered at between 20 and 400Hz and then full-wave rectified and filtered using an averaging moving-window algorithm (window size: 25 ms). Trials were averaged for each subject in each experimental condition.

3.2.f Correction time and initiation time computed on the EMG activity.

In the following, we use the term "initiation time" to indicate the delay between the lighting of the first target (the "go-signal") and the beginning of significant muscular activity. To determine the initiation time in terms of the sixteen recorded muscles, the EMG values after the lighting of the first target and the EMG baselines were compared for each value using t-tests for each muscle in the four unperturbed conditions. The EMG baselines were computed as the mean integrated activity of each muscle over 1 second from -2s to -1s before the first target was lit and after participants had adopted the initial position. Similarly to correction time, the first instant at which the P-value was lower than 0.05 for a 50 ms minimum duration determined the beginning of the muscle activation necessary to perform the pointing movements.

To determine the correction time after the target jump for the sixteen recorded muscles, we compared the EMG values of these sixteen muscles for the eight perturbed conditions and the four corresponding normal conditions, using t-tests at each value (please see the section on hand kinematics for more details on the comparative experimental conditions). Once again, the first instant at which the P-value was lower than 0.05 for a 50 ms minimum duration determined the beginning of the motor correction in response to the perturbation. This latter analysis was performed to determine the time-latencies of muscle activities between the perturbation and the muscular corrections. To assess whether latencies of the whole motor sequence used to correct or to initiate the movement were similar or different in each experimental condition, we performed linear correlations between these motor sequences (Fautrelle et al. 2010 b).

Finally, our aim was to further investigate modulations of EMG amplitude induced by unexpected changes in the speed-accuracy trade-off. To do so, we computed the integrated EMG values for the first 50 ms after the initiation time and the correction time for the first muscle activated in the leg (or in the

trunk depending on the experimental condition), and in the arm. Statistical analyses were performed using ANOVAs with repeated measures to compare data from all experimental conditions taken together or separately when necessary. Conditions were clustered to separate conditions without perturbation, conditions with target size perturbations only and conditions with at least distance perturbations.

3.3 RESULTS

We examined the effects of unexpected, in-flight changes in the speed-accuracy trade-off on motor corrections during hand pointing movements performed from an upright standing position. Both hand kinematics and EMG activities were recorded and analyzed to investigate latencies and amplitudes of motor corrections. Figure 18 illustrates typical data for one subject and shows mean velocity profiles and EMG traces ± 95% CI for the DAi and TAi in all conditions.

3.3.a Hand kinematic: potential learning effects

We first checked whether learning could have influenced our results. We performed regression analyses in each experimental condition on hand reaction times, hand MT, and accuracy of the finger endpoints (X and Y coordinates of the finger endpoint). Results revealed that the obtained slopes were not statistically different from zero for any of these parameters, in any of the twelve experimental conditions (N=7; $P > 0.55$ for the hand reaction times, $P > 0.67$ for the hand MT, $P > 0.76$ for the Fep X-coordinate and $P > 0.77$ for the Fep Y-coordinate). All these statistical analyses suggested that learning did not influence our results.

3.3.b Hand kinematic: pointing conditions did not influence reaction time or final precision except when the final target was far and big.

In order to determine whether reaction times or final precision was different between the different conditions, we first performed one ways ANOVAs (with experimental conditions as the sole factor with 12 levels). These one-way ANOVAs were performed on reaction times, 95% confidence ellipse areas of the finger endpoint (Fep CE area) and on the X-Y coordinates of the finger endpoint for each subject in all conditions (cf. Table 3).

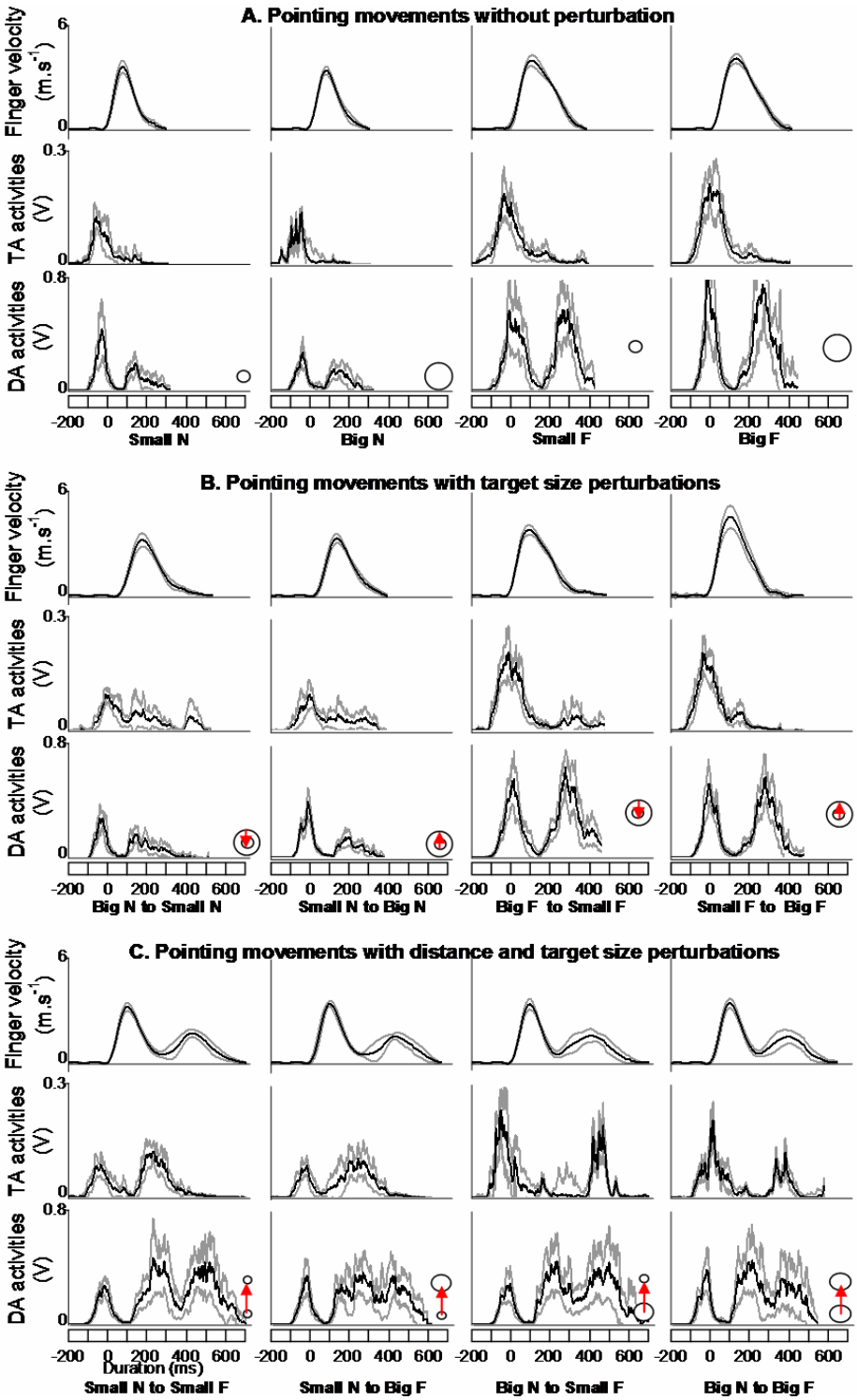

Figure 18 *Raw data from recorded measures. Raw data from the velocity profile of the hand movement (m.s-1), the activity of the TAi and the DAi (V) in the A) pointing movements without perturbation (upper panel), B) pointing movements with target size perturbations (middle panel), and C) pointing movements with target size and distance perturbations (lower panel). Kinematics signals are filtered with a dual-pass algorithm with a 10 HZ cut-off frequency (Butterworth 4th order) and EMG signals are bandpass filtered between 20 and 400 Hz, full-wave rectified and then filtered using an averaging moving window algorithm (window size: 25 ms). Data are synchronized to the hand movement onset and are represented from 200 ms before the onset to the offset.*

A. Pointing movements without perturbation

	Small N	Big N	Small F	Big F	Statistical analyses: *size*	*amplitude*	*size*amplitude*
Movement Time (ms)	255 ± 25	245 ± 16	372 ± 33	317 ± 33	**	**	*ns*
Hand Reaction Time (ms)	335 ± 37	345 ± 37	335 ± 30	332 ± 30	*ns*	*ns*	*ns*
Acc Duration (ms)	127 ± 13	129 ± 9	156 ± 15	157 ± 19	*ns*	**	*ns*
Peak Velocity (ms^{-1})	3.3 ± 0.3	3.4 ± 0.3	3.9 ± 0.3	4.0 ± 0.4	*ns*	***	*ns*
FepCE center X-coor	54 ± 1.0	55 ± 1.0	85 ± 1.3	81 ± 2.6	*ns*	*ns*	***
Fep CE center Y-coor	1.0 ± 0.1	1.0 ± 0.2	1.3 ± 0.1	1.0 ± 0.1	*ns*	*ns*	*ns*
Fep CE area (cm^2)	1.8 ± 0.1	2.1 ± 0.2	2.0 ± 0.1	2.0 ± 0.2	*ns*	*ns*	*ns*

B. Pointing movements with target size perturbations

	Big N to Small N	Small N to Big N	Big F to Small F	Small F to Big F	Statistical analyses: *size*	*distance*	*size*distance*
Movement Time (ms)	381 ± 50	376 ± 61	462 ± 40	380 ± 25	*	*	*
Hand Reaction Time (ms)	346 ± 35	349 ± 30	355 ± 18	359 ± 38	*ns*	*ns*	*ns*
Acc Duration (ms)	127 ± 10	123 ± 6	156 ± 11	150 ± 11	*	*	ns
Peak Velocity (ms^{-1})	3.4 ± 0.3	3.4 ± 0.2	4.2 ± 0.4	4.2 ± 1.1	ns	***	ns
FepCE center X-coor	56 ± 0.2	58 ± 0.3	87 ± 1.6	84 ± 0.1	*ns*	*ns*	***
Fep CE center Y-coor	1.0 ± 0.1	1.2 ± 0.1	1.0 ± 0.1	1.0 ± 0.2	*ns*	*ns*	*ns*
Fep CE area (cm^2)	1.8 ± 0.2	1.8 ± 0.1	1.8 ± 0.1	2.1 ± 0.2	*ns*	*ns*	*ns*

C. Pointing movements with target size and distance perturbations

	Small N to Small F	Small N to Big F	Big N to Small F	Big N to Big F	Statistical analyses: *Initial target size*	*Final target size*	*Initial*final target sizes*
Movement Time (ms)	502 ± 46	505 ± 32	544 ± 27	449 ± 34	*ns*	*	*ns*
Hand Reaction Time (ms)	351 ± 31	338 ± 30	334 ± 38	333 ± 35	*ns*	*ns*	*ns*
Acc Duration (ms)	133 ± 17	141 ± 18	128 ± 21	134 ± 14	*ns*	*ns*	*ns*
Peak Velocity (ms^{-1})	3.4 ± 0.2	3.3 ± 0.2	3.6 ± 0.2	3.2 ± 0.2	*ns*	*ns*	*ns*
FepCE center X-coor	89 ± 1.0	86 ± 2.1	88 ± 1.0	85 ± 1.0	*ns*	*ns*	***
Fep CE center Y-coor	0.9 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	*ns*	*ns*	*ns*
Fep CE area (cm^2)	2.0 ± 0.1	2.0 ± 0.1	1.9 ± 0.1	2.1 ± 0.2	*ns*	*ns*	*ns*

Table 3. *Hand kinematics variables in three different statistical plans. Conditions without perturbation (n=4, upper panel), with target size perturbations only (n=4, middle panel) and with target size and distance perturbations (n=4, lower panel) are analyzed separately The following hand kinematics variables are averaged for the seven subjects: the movement time, the hand reaction time, the acceleration duration, the peak velocity, the X, Y coordinates, and the area of the 95% confidence ellipse of the finger endpoints (mean ± 95% confident interval). For each of these variables, statistical effects are also reported (ns P>0.05, * P<0.05, ** P<0.01, *** P<0.001).*

Results demonstrated no significant effect for reaction times, 95% confidence ellipse areas or Y coordinates of the finger ($F(11, 66)= 0.97$, $P=0.47$, $F (11, 66) = 1.48$, $P=0.16$ and $F (11, 66) = 0.75$, $P = 0.69$ respectively). Concerning the final precision, we analyzed separately conditions in which the final position of the target was near (n=4) with those in which the final position was farther (n=8). Results revealed no significant differences for X coordinates of the finger (i.e. the antero-posterior axis) in the near conditions ($F (3, 18) = 2.42$, $P = 0.1$). However, in the far conditions, the final positions of the finger were nearer to the starting point (3.25 ± 0.5 cm on average) when the final target was bigger in comparison to the four other conditions in which the final target was smaller ($F (7, 42) = 6.8$, $P<0.001$).

3.3.c Hand kinematic: movement time

At this stage it is important to not that we performed three separated statistical plans and analyzed separately conditions without perturbation (n=4), with target size perturbations only (n=4), and with target size and distance perturbations (n=4). These results are summed-up in Table 3 and Figure 19 (upper panel). Please note that these separated analyses were also performed for dependant variables analyzed previously.

3.3.d Hand kinematic, conditions with no perturbation: target distance and target size influence MT.

Results of the ANOVA revealed a main effect of target distance ($F (1, 6) = 35.17$, $P<0.01$), a main effect of target size ($F (1, 6) =28.9$, $P<0.01$) but no target distance × target size interaction ($F (1, 6) =1.09$, $P=0.33$). This suggests that hand MT decrease when the size of the final target increases and when the distance of the final target decreases. Figure 19a sums up this finding (left panel).

3.3.e Hand kinematic: conditions with target size perturbation only: target distance and target size interact.

Results of the ANOVA revealed a main effect of target distance ($F(1, 6) = 10.40$, $P<0.05$), a main effect of final target size ($F(1, 6) = 7.57$, $P<0.05$) and an interaction of a target distance × final target size ($F(1, 6) = 6.03$, $P<0.05$). A decomposition of this interaction showed that MT increased more in the far condition when the target changed in-flight from a big to a small size, in conditions in which only the target size was modified in-flight. Figure 19a sums up this finding (middle panel).

3.3.f Hand kinematic: conditions with target size and distance perturbations: final target size influences MT

For conditions in which the target distance was modified, results of the ANOVA revealed no effect of initial target size ($F(1, 6) = 0.02$, $P=0.9$), a main effect of final target size ($F(1, 6)=7.46$, $P<0.05$), and no significant effect of initial × final target size interaction ($F(1, 6)=1.96$, $P=0.21$). These results showed that MT increased when the size of the final target decreased in-flight in the far condition. Figure 19a sums up this finding (right panel).

3.3.g Hand kinematic: correction times

We performed two separated statistical plans and analyzed separately conditions with target size perturbations only (n=4), and with target size and distance perturbations (n=4). These results are summed-up in Figure 19b (lower panel).

3.3.h Conditions with target size perturbation only: correction times increase when the target size is modified in-flight from small to big.

Results of the ANOVA revealed a main effect of target distance ($F(1, 6) = 11.9$, $P<0.01$), a main effect of final target size ($F(1, 24) =10.6$, $P<0.05$) and no target distance × final target size interaction ($F(1, 6) =1.02$, $P=0.35$). Figure 19b sums up this finding (middle panel). When hand MT and hand correction times were analyzed together, results revealed that when target size

only was modified in-flight, corrections occurred later when the target was modified from a small to a big size. However, these latter corrections induced shorter hand MT.

3.3.i Hand kinematic: conditions with target size and distance perturbations: correction times are shorter when the target distance is modified in-flight toward a bigger final target size.

Results of the ANOVA revealed no main effect of the initial target size ($F(1, 6) = 0.69$, $P = 0.43$), a significant main effect of the final target size ($F(1, 6) = 6.0$, $P < 0.05$) and no initial × final target size interaction ($F(1, 6) = 2.4$, $P = 0.17$). Figure 19b sums up this finding (right panel). When hand MT and hand correction times were analyzed together, results revealed that when the target distance was modified in-flight, corrections occurred roughly simultaneously in the four conditions but that MT was longer when the final target was small.

3.3.j EMG activities: sequences of initiation or correction times

We wanted to determine whether initiation or correction times were differently ordered among the conditions. Figure 20 shows similar orders in initiation times for most muscles in the pointing conditions without perturbation (upper panel) and similar orders in correction times in the pointing conditions with at least a distance perturbation (lower panel). In these two cases, correlation coefficients were high and statistically significant when regression analyses were carried out. Movement initiations or corrections seemed to begin roughly at the level of the lower limbs. Interestingly, however, we observed different sequences in correction times in the pointing conditions with a target size perturbation alone (i.e. without distance changes). Correlation coefficients were very low in this case and movement corrections were initiated rather at the level of the upper limbs.

Movement initiation and correction began in the lower limbs when there was no perturbation or when the target location was changed. By contrast,

movement corrections began instead in the upper limbs when the target size only was modified.

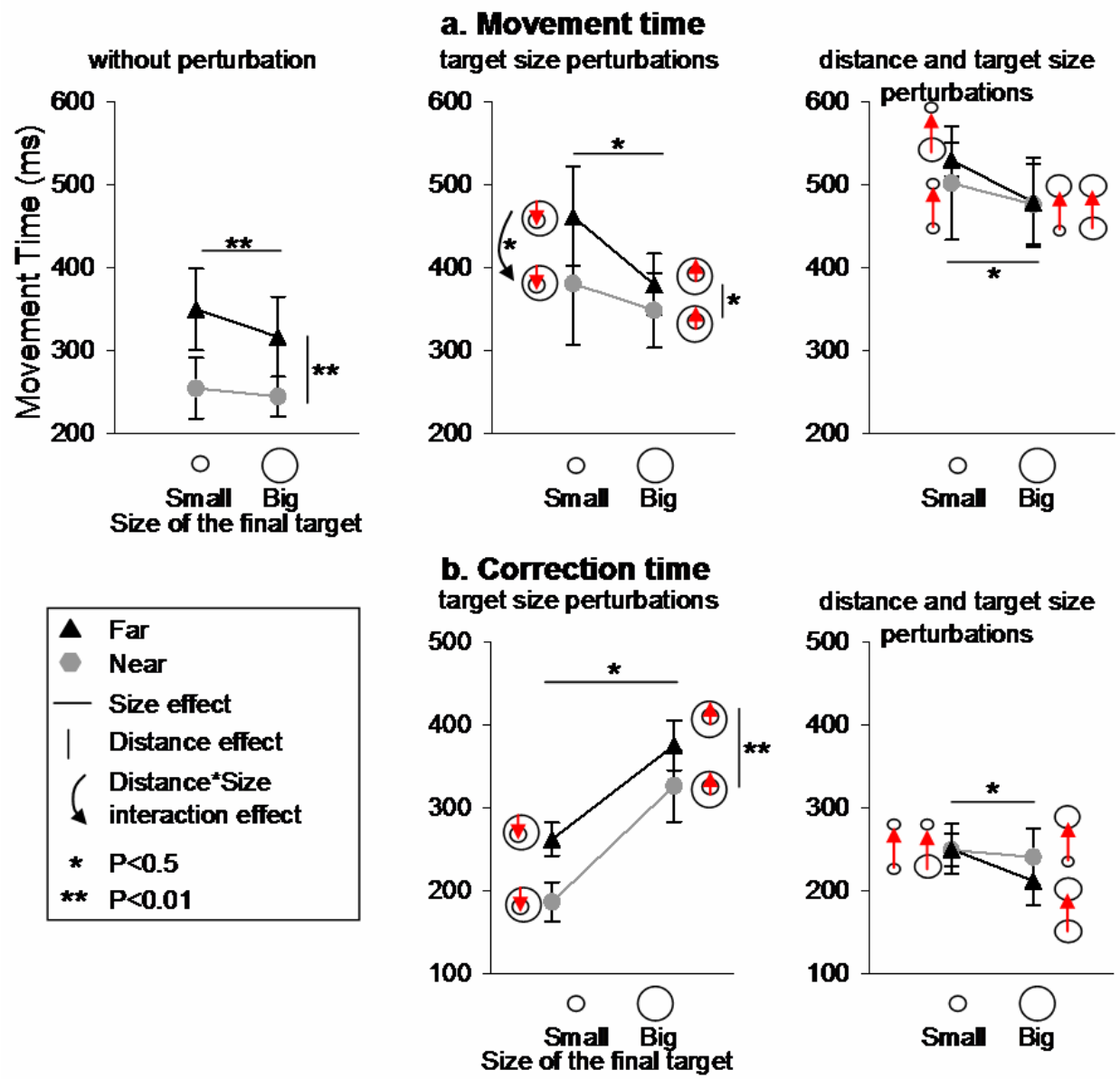

Figure 19 *Movement time and correction time depending on the final target size in all the experimental conditions. Upper panel (3 statistical separated plans): movement times (ms) were reported here according to the size of the final target in the four conditions without perturbation together (left graph), in the four conditions with target size perturbations (middle graph) and in the four conditions with distance and target size perturbations (right graph). Lower panel (2 statistical separated plans): correction times (ms) were reported according to the size of the final target in the four conditions with target size perturbations (left graph) and in the four conditions with distance and target size perturbations (right graph). Here, statistical analyses were conducted for each graph with a 2 (target sizes) x 2 (distances) repeated measures ANOVA. Size, distance and interaction effects are reported.*

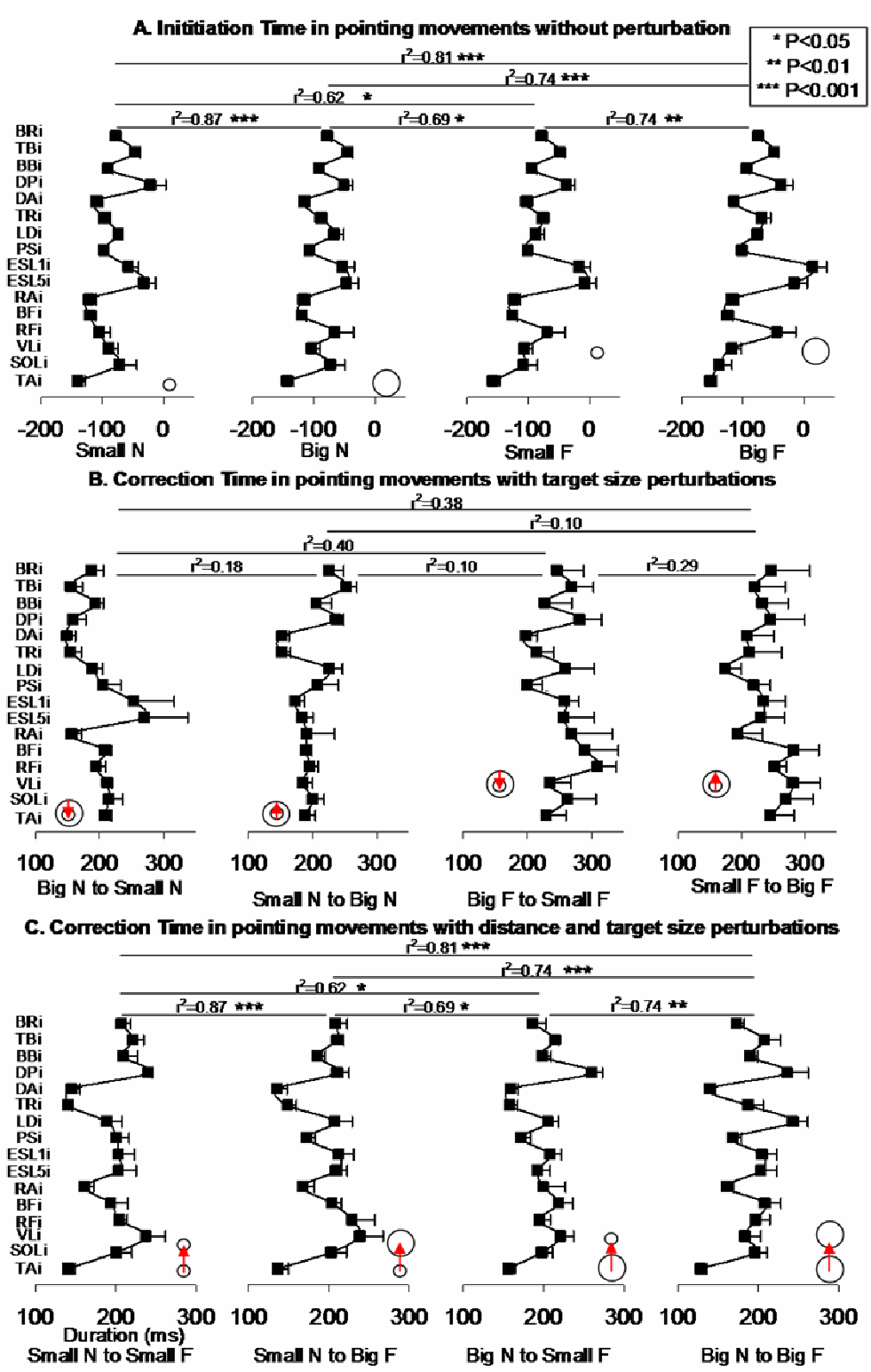

Figure 20 *Muscular Synergies used to initiate or to correct the pointing movement. The four muscular synergies reported in the upper panel correspond to the average (±95%CI) initiation time in the four pointing movements without perturbation. The four muscular synergies reported in the middle panel correspond to the average (±95%CI) of the correction times after the visual perturbation in the four pointing movements with target size perturbations. Similarly, the four muscular synergies reported in the lowerpanel correspond to the average (± 95%CI) of the correction times after the visual perturbation in the four pointing movements with distance and target size perturbations. The order of the muscles on the ordinate axis remained the same across the twelve graphs. The origin (0) of the temporal axis corresponds to the hand movement onset. To compare the muscular synergies in each panel, the correlation coefficient r2 between each pair of synergies was computed and reported.*

3.3.k EMG activities: comparison of correction times measured on EMG traces between the perturbed conditions.

In order to determine for which mode of perturbation motor corrections were observed earlier we compared correction times measured on EMG traces between perturbed conditions with changes in target size and perturbed conditions with both changes in target size and location. We performed t-tests between values obtained for the fastest motor corrections (any muscles) observed in these two sets of conditions (cf. Figure 20). Results revealed that for any muscles, the first motor corrections to be observed were of similar latencies between all conditions ($ts<=1.7$, $p>=0.13$) except for the Big F to Small F and Small F to Big F ($t>=2.44$, $p<=0.05$) for which the first motor corrections were significantly delayed in comparison to the other conditions. In other words, for the conditions in which the target size only was modified, motor corrections were observed later when the target was located in the far workspace.

3.3.l EMG activities: integrated EMG activity of the TAi and DAi, 50 ms after movement initiation and correction

Obviously, EMG modulations in these two muscles are observed when the target distance is modified. In consequence, we focused here only on the effects of the target size with respect to EMG activity. Results are summed up in Figure 21. This figure shows that in the conditions without perturbation, the integrated EMG activity of the TAi increased with the target size within -158 to -140 ms before the hand movement onset ($T=2.63$, $P<0.05$ and $T=2.52$, $P<0.05$ for the N and F distances respectively). That of the DAi also increased within -117 and -104 ms before the hand movement onset, but only for the N distance ($T=3.35$, $P<0.05$ and $T=1.48$, $P>0.05$ for the N and F distances respectively).

In the conditions with change in target size, the integrated EMG activity of the TAi increased with the target size within 188 to 245 ms after the hand movement onset ($T=3.05$, $P<0.05$ and $T=3.80$, $P<0.01$ for the N and F distances respectively). That of the DAi also increased within 152 to 209 ms after the hand movement onset, but only for the N distance ($T=3.2$, $P<0.05$ and $T=0.48$, $P>0.05$ for the N and F distances respectively).

In the conditions with at least a change in target distance, the integrated EMG activity of the TAi increased with the target size within 128 to 156 ms after the hand movement onset ($T=4.15$, $P<0.01$ and $T=7.09$, $P<0.01$ for the N and F distances respectively).That of the DAi also increased within 135 and 159 ms after the hand movement onset, but only for the F distance ($T=0.52$, $P>0.05$ and $T=4.44$, $P<0.01$ for the N and F distances respectively).

Interestingly, these results clearly demonstrated that the integrated EMG activity of the TAi 50 ms after movement initiation or correction significantly increased in all the experimental conditions. 50 ms after movement initiation and correction, the integrated EMG activity of the DAi increased only for the near distance when there was no or solely a target size perturbation. In the conditions with at least a distance perturbation, the DAi integrated EMG activity increased significantly only when the first target was big.

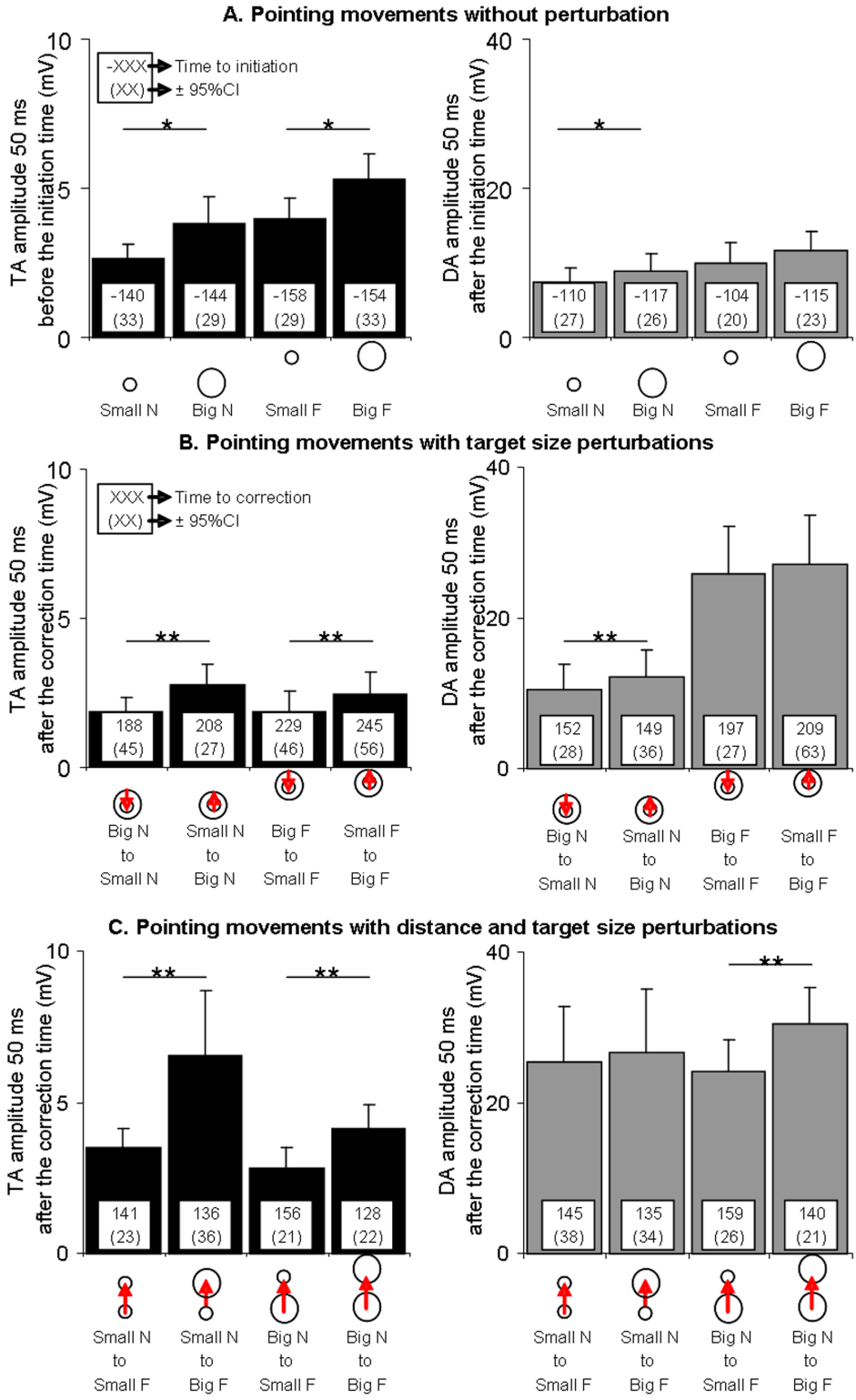

Figure 21 *Amplitude of the TAi and DAi activities 50 ms after the initiation or the correction times. The integrated EMG activity 50 ms after the initiation time in the pointing movements without perturbation is reported in the upper panel. Similarly, the amplitude of the integrated EMG activity in the TAi (black bars) and the DAi (grey bars) after the correction time for the pointing movements with target size perturbations and the pointing movements with distance and target size perturbations are reported in the middle and the lower panels, respectively. In each bar was reported the mean value (± 95%CI) of the initiation time or the correction time. Statistical analyses were conducted using a Student test in order to reveal the effect of the target size on the amplitude of the TAi and DAi EMG activities 50 ms after the initiation or the correction times.*

3.4. DISCUSSION

In this study we investigated whether corrective actions while pointing are ballistic, or if feedback may be used to guide the movement after the perturbation. Depending on the condition, the target would either change location, size, location and size, or remain unchanged. If corrective movements are ballistic, the variability should be proportional to the size of the target. If corrective movements rely on feedback, then the terminal variability should be independent of the target size, although the approach should take longer.

Our main results showed that as soon as a perturbation was triggered during the movement we observed a lengthening of the MT, but the speed-accuracy trade-off was maintained. Interestingly, however, the final spatial precision was identical for most conditions, in particular when the target size only was varied and the target remained at a small distance from the starting point. As a whole these results suggest that the corrective movements are not purely ballistic but rather that some powerful feedback processes may be involved in coping with an implicit speed-accuracy trade-off, since the terminal variability is similar in all conditions.

4.a Unperturbed movements: the target size influences motor programming before movement initiation. The feedforward components of the speed-accuracy trade-off.

We observed that the integrated EMG activities of the TAi and DAi were proportional to the target size about 140 ms before movement initiation. It has already been shown that target size may influence motor programming in goal-directed movement. For instance, Fitts and Peterson (1964) and Sidaway et al. (1995) demonstrated that reaction times were inversely proportional to target size. More recently, Bonnetblanc et al. (2004) demonstrated that anticipatory postural adjustments were influenced by target size when goal-directed movements were performed from an upright standing posture. In this latter case, the authors observed modulation in the EMG magnitude of

the TAi until 200 ms before the hand movement onset. In all these studies however, the target size was fixed a priori and there was no incertitude about the target location or size. By contrast, in our experiment, the target size and location were not specified before the go-signal. This reinforces the idea that target size may influence the initial programming phase of the pointing movement and suggests that it may be processed earlier in the planning phase. This finding is thus in accordance with the hypothesis that the speed-accuracy trade-off may be controlled in a feedforward manner. Interestingly however, this effect was observed despite the fact that the terminal variability of the endpoint remained identical in all conditions, suggesting that when the speed-accuracy trade-off is unexpectedly modified, terminal feedbacks are used to monitor and control the hand displacement.

4.b Perturbed movements: unexpected changes in the speed-accuracy trade-off induce implicit modulations of the endpoint velocity independently of the terminal variability.

As soon as a perturbation was triggered during the movement, we observed a lengthening of the MT despite the fact that the speed-accuracy trade-off was maintained. Interestingly, however, the final spatial precision was identical in most conditions. The corrective motor sequence remained more stereotyped when at least the target distance was modified. By contrast, motor corrections were observed later and in different orders when the target size only varied at the far distance. Finally, we observed an effect of the target size on the EMG activity of the tibialis anterior more than 140 ms before the hand movement onset in unperturbed movements, less than 140 ms after the target distance at least was modified on the EMG activity of the tibialis anterior, and around 150 ms after the target size only was varied on the EMG activity of the deltoid anterior.

These results strongly suggest that the endpoint velocity is modulated after the perturbation. Interestingly, however, as these corrections are late and non-stereotyped when the target size only is changed, they seem to rely on visual

feedback and slower guidance processes, like for instance those observed in manual pursuit. By contrast, when the target location is modified, these corrections appear sooner for the far distance and are much more stereotyped, suggesting that lower or more automatic processes are involved (Saijo et al. 2005, Gomi et al. 2008, Fautrelle et al. 2010a). Clearly, when the target size varied, subjects did not need to re-program their ballistic movement to reach the second target of identical location. They rather modulated the endpoint velocity to cope with the implicit requirements of the speed-accuracy trade-off. This is in agreement with a central coding of hand velocity. This hypothesis was put forward by a number of behavioral studies conducted primarily in the 1980s. A representative reference of such studies is that of Milner et al. (1986). However, the most direct support for this hypothesis has been provided by neurophysiological recordings in monkeys. For example, Schwartz (1993) observed that within a given time series of population vectors computed from the activity of motor cortical neurons, their lengths and directions varied in a consistent relationship to the tangential velocity of a drawing movement. This finding was also specifically formulated for reaching movements (Moran and Schwartz 1999). In addition, Stark et al. 2007 demonstrated that neurons related to velocity were far more common than neurons related to any other parameter. These results were obtained for neurons recorded in the primary motor (M1) and dorsal premotor (PMd) cortices. This type of finding has been extended to other types of neural signals as well, such as MEG. Jerbi et al. (2007) found significant phase locking between slow (2 to 5 Hz) oscillatory activity in the contralateral primary motor cortex and time-varying hand speed.

Finally, in an interesting investigation of the speed-accuracy trade-off in a PET parametric study, Winstein et al. (1997) observed that as the index of difficulty of a task decreased, significant increases in regional cerebral blood flow (rCBF) were evident in the anterior cerebellum, left middle occipital

gyrus, and right ventral premotor area. Functionally, these areas were associated with pointing conditions in which the demands of motor execution were high and precise trajectory planning was minimal. By contrast, as the pointing task difficulty (ID) increased, rCBF increased in areas associated with the planning of more complex movements requiring greater visuomotor processing. In particular, when more precise targeting was required, a cortical-subcortical loop composed of the controlateral motor cortex, intraparietal sulcus and caudate was activated. As a whole, this study revealed that two different networks were involved when the required precision varied, despite the fact that the behavioral task remained the same. In our experiment, as the target size could be drastically modified, an important constraint may be that the CNS has to switch from one network to the other. This constraint may be downplayed by specifying the final variability a priori, which was nonetheless attained at the expense of the endpoint velocity. The speed-accuracy trade-off we still observed here may be an implicit constraint involving basic representation and modulation of the endpoint velocity. It reveals a breakdown of the perception-action coupling.

ACKNOWLEDGEMENTS

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4. CATCHING FALLING OBJECTS: THE ROLE OF THE CEREBELLUM IN PROCESSING SENSORY-MOTOR ERRORS AND IN UPDATING FEEDFORWARD COMMANDS. AN FMRI STUDY.

Lilian Fautrelle, Cédric Pichat, Fréderic Ricolfi, Carole Peyrin, François Bonnetblanc

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4.1 INTRODUCTION

When we are catching falling or thrown objects with our hand and the object can be seen, electromyographic activations occur in the arm in advance of the estimated time to contact and before feedback processes are able to compensate a posteriori for the perturbation (Lacquaniti and Maioli 1989a, b). This classical observation proves that the brain is able to exert some level of feedforward control over any movement we perform. More specifically, these so-called anticipatory postural adjustments (APA) are fine-tuned according to the weight of the object and illustrate the brain's ability to anticipate and predict the upcoming motor perturbation and sensory outcomes before they occur. It has been shown that this prediction capacity is severely impaired in cerebellar patients, as APAs are cancelled before perturbation onset (Babin-Ratté et al. 1999, Lang and Bastian 1999, 2001, Nowak et al. 2002, 2007).

Predicting the sensory consequences of a gesture is necessary for on-line control. The difference between the brain's predicted outcome of the behavior (or efferent copy) and the observed outcome is called the sensory-motor error. This error allows motor corrections to be triggered more rapidly by compensating for biophysical transduction, transmission and processing delays (Desmurget and Grafton 2000).

Another important function of this sensory-motor error is to drive motor adaptations that occur on a trial by trial basis during the completion of repetitive actions (Tseng et al. 2007). This process is used to update feedforward commands and calibrate internal models or representations of the dynamics of our own body or of our physical interaction with the environment (Wolpert and Miall 1996). It is assumed that the cerebellum stores a motor memory in the form of internal models and is a key structure in updating these internal models (Marr 1969, Blomfield and Marr 1970, Kawato et al. 1987, Johansson and Cole 1992, Wolpert and Miall 1996,

Kawato and Wolpert 1998, Wolpert and Kawato 1998, Wolpert et al. 1998, Johansson 1998, Ito 2000, Blackmore et al. 2001).

In most experiments, the cerebellum-dependent adaptation is investigated by inducing systematic sensory-motor conflicts (Bock 1992, Shadmher and Mussa-Ivaldi 1994, Martin et al. 1996, Krakauer et al. 2000, Morton and Bastian 2004, 2006), for instance discrepancies between vision and proprioception (Tseng et al. 2007) or between vestibular and non vestibular sensory graviceptor (Dharani 2005). In the case of a simple change in the dynamic of the environment, and when the system is not fed by a constant error (unpredictable event), it has also been suggested that the predicted state and/or motor command is constantly updated using past experiences (Bhushan and Shadmehr 1999, Donchin et al. 2003, Pasalar et al. 2006). In a process similar to pure motor adaptation, the cerebellum generates a discrepancy signal between the predicted sensory consequences as compared to peripheral feedback, and the sensory prediction error is iteratively modified (Bastian 2006). This entire process may be the origin of permanent updating of feedforward commands and more particularly of anticipatory postural adjustments. Both functions are summed-up in figure 22. In other words, the cerebellum is presumably the location where the efference copy is transformed to a sensory prediction that is compared to the sensory input. The discrepancy signal (sensory prediction error) is believed to be the output of the cerebellum. The sensory prediction error influence adaptation of the forward model (in the cerebellum), online corrections (Tseng et al 2007, through cortex), and probably changes of the inverse model (also cortical).

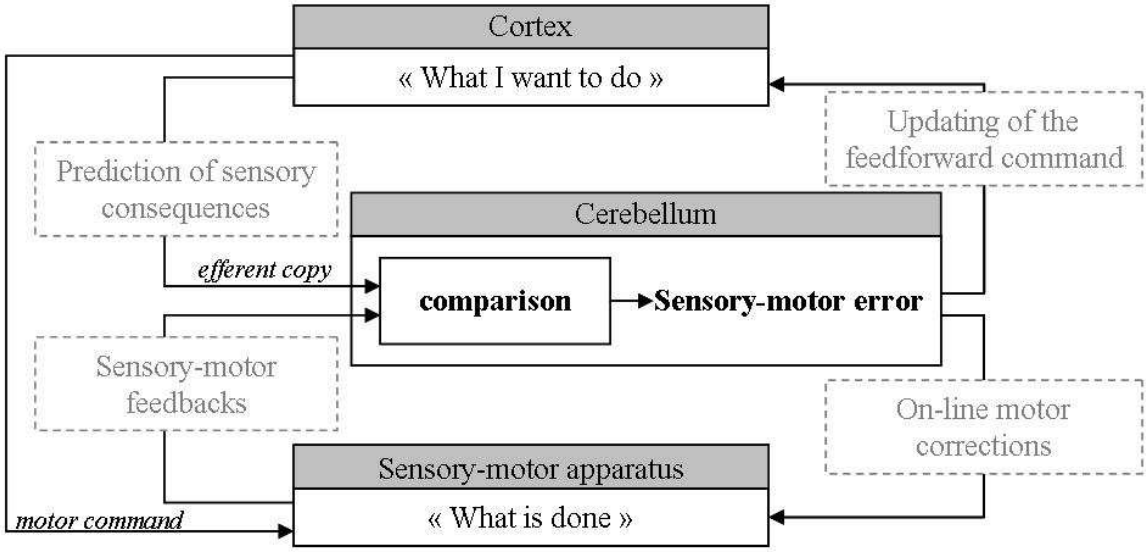

Figure 22 *The motor flexibility (Johansson 1998, Desmurget and Grafton 2000, Bastian 2008). The motor control needs to continuously adapt to changes by comparing differences between the brain's predicted outcome of a certain behavior ("What I want to do") and the real produced outcome ("What is done"). This discrepancy signal triggers a sensory-motor error that allows updating feedforward motor command or producing on line-motor corrections. In the literature, it is assumed that the cerebellum is a key structure to ensure such processes.*

To further investigate the hypothesis which holds that unexpected and variables errors are processed in the cerebellum to update feedforward commands when repetitively catching a ball, we used a block design fMRI experiment in which balls looked exactly the same but the level of incertitude (i.e. prediction) about their weight varied. In certain conditions, the weight of the ball was predictable, in others, it was not. By contrasting functional imaging signal obtained in conditions in which it was possible and impossible to predict the weight of the ball, we aimed to highlight sensory-motor error processing which we expected to be more marked in the conditions without prediction (less accurate feedforward process or more important feedback corrections, i.e. more important sensory-motor error) with respect to conditions with prediction (more accurate feedforward process or less important feedback corrections, ie less important sensory-motor error). In this vein and according to the Bayesian framework it has been demonstrated that the nervous system adapts more when its state estimate is more uncertain (Wei and Körding 2010). We hypothesized that we would solicit a cerebellar network that drives the processing of sensory-motor errors that may update feedforward commands. In addition, before catching an object with the hand, vision allows for the critical estimation of time to contact (Lacquaniti and Maioli 1989). In order to determine whether cerebellar networks involved in the updating of sensory motor errors are dependent on visual cues, we suppressed sight in a final condition without prediction of the ball weight. In addition, in this latter "blind" condition, we also hypothesized that prediction of sensory consequences would be less accurate in comparison to the condition in which vision was not removed, and that in this case, sensory-motor errors would be compensated by feedback processes in a greater extent. In other words, when sight is suppressed, the prediction of sensory consequences may also be impaired due to poorest sensory estimations that may be cumulated with impaired updating of forward modeling.

4.2 MATERIALS AND METHODS

4.2.a Participants

Sixteen healthy participants [all males, 27.9 ± 4.7 years old, 180.75 ± 5.6 cm, and 76.5 ± 7.6 kg] volunteered for the experiment. All participants had normal or corrected to normal vision (lenses) and none of them had a previous history of neuromuscular or neurological disorders. All subjects were right handed as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). The entire experiment conformed to the Declaration of Helsinki and informed consent was obtained from all participants according to the guidelines of the clinical ethic committee of the University of Burgundy.

4.2.b Experimental Design and fMRI paradigm

A block design paradigm was used that alternated periods of rest and a motor task. It resulted in functional imaging signal of the right-hand repetitive ball catching task as contrasted to the rest periods in the four different catching conditions.

Participants were lying on their back in the scanner and the upper right limb was elevated by five centimeters so that the right hand was not in contact with anything during the ball catching sessions. A double-mirror mounted on the MRI head coil was adjusted to allow the participants to clearly see (with no inversion) the 25 cm vertical trajectory of the falling balls as well as their right hand.

During the rest period, participants were instructed to remain quiet and motionless and to keep their eyes open without thinking of anything in particular. Participants were observed during this period to check that no movement was performed. During the ball catching period, participants were simply instructed to catch falling balls with their right hand. For each recording session, 10 scans at rest were followed by 10 scans during which the

catching task was performed and this alternation of rest and catching periods was repeated four times in one session, for a total of 80 scans for each experimental condition (4x10 scans at rest and 4x10 scans of ball catching). Each subject participated in four different sessions in which the condition of the repetitive falling balls differed. In each experimental condition, ten balls fell during the ten scans. In the first experimental condition (light ball condition), participants were required to catch light balls (6.5 cm in diameter, weighing 30 g, and black). In the second experimental condition (heavy ball condition), participants were required to catch heavy balls (6.5 cm in diameter, weighing 300 g, and black in color). In the third condition (random condition), 5 light balls and 5 heavy balls were randomly dropped. Note that the light and heavy balls looked the same and differed only in their mass, so that participants could not know if the falling ball was heavy or light before catching it. In addition, to determine whether cerebellar networks involved in the updating of sensory motor errors are dependent on visual cues, we blindfolded our subjects in a final condition without prediction of the ball weight. In this condition (blind condition), participants had their eyes blindfolded and either light or heavy balls were randomly dropped. Consequently, the subjects were not able to anticipate the time to contact of the falling ball with their hand. The orders of the session were totally randomized from one subject to another. Before each block a few practice trials were performed to recall the balls weight in advance. In a similar paradigm, Lacquaniti and Maioli (1989b) observed no adaptation on EMG traces in a condition with vision and a single trial adaptation was observed in no-vision condition. As such 10 trials seem sufficient to make the condition with constant ball weight predictable.

The task was very simple. The balls were released by the experimenter from a 25 cm height at the vertical of the hand. Subjects grasp the ball with their fingers when receiving it with no displacement of the arm. The movement

was authorized one degree of freedom at the level of the wrist (horizontal rotation) but many more at the level of the hand. As such subjects performed the task very easily in all the conditions and always succeeded to catch it with no particular noticeable difficulty.

Among the potential limitations of this paradigm, one may suggest that some adaptation occurred on a trial by trial basis within the constant weight conditions. This effect illustrates a decrease of the sensory-motor error and allows highlighting even more the cerebellar networks when contrasting the random and no-vision conditions with the light and heavy conditions.

One may also suggest that feedback (e.g. a different manipulation of the ball due to an inaccurate prediction of the motor perturbation) and/or proactive strategies (e.g. subjects adopt a stiffness strategy to cope with the variability of the ball weight) may be different between conditions. However, even if true, the sensory-motor errors would increase in these cases. And contrasting the random and no-vision conditions with the light and heavy conditions would highlight even more the cerebellar networks we sought to observe.

In the same vein, the randomness may be insufficient (only two balls were used) and there may be also a possibility that subjects adapted a plan to deal with the uncertainty at the beginning of the first random block and stick to that plan (for instance a more passive reaction, with less anticipation movements). However, in both cases, it would play against our hypothesis and would limit the size and detection of the sensory-motor errors and the associated contrasts between the random and fixed conditions. Additionally, these a priori changes in the motor strategies would exhibit different levels of activation in M1. Indeed, this is sustained by Dai et al. (2001) who demonstrated both in an isometric and a dynamic task that the level of activation in M1 was proportional to the force produced. Because the balls weights were very different in our task (30 vs. 300g) changes in motor strategies would be observable. For instance, this is typically illustrated as a

classical effect in some fMRI studies in which parasite activations can be observed in the ipsilateral motor area when the urgency button is slightly hold in the non working hand.

In other words, the weights of the balls were very different (30g vs. 300g) in order to determine clearly using functional imaging signals whether subjects adopted a conscious motor strategy before catching the balls in the conditions without predictions. We hypothesized that if subjects had average their motor strategy before catching the balls we would have clearly observed different level of activation in motor areas between the conditions with and without prediction. In addition, they were also asked to perform the catching task naturally with a relaxed hand.

After debriefing, subjects were asked whether they were able to predict the ball weight in the random and blind conditions. All subjects confirmed that they were unable which suggested that sensory-motor errors are greater in these two conditions. They also confirmed that they did not used different strategies between all the blocks and performed the task without conscious motor strategies between all blocks but with a relaxed hand.

In the present task, error signals were very difficult to measure efficiently for several reasons. Indeed, the movement was very limited, very usual and natural. Due to its nature, error signals are probably minored in this type of task. As such, it limits the capabilities to detect and record potential biases during the sensory-motor transformations. In addition, the hand offers many possibilities (as a system with many degrees of freedom) to compensate for the errors of catching and there is probably too few trials to observe an error when averaging the data. This latter aspect limits the possibilities to systematically measure an error. However, a reasonable assumption would be that in the conditions with constant weight (light or heavy) the probability to make an error of ball weight is inferior to that in the random or blind conditions. As such behavioral differences may be very subtle. Any supposed

similarities between these two sets of behavioral conditions would in fact play against our hypothesis and diminish the contrast observed between these two sets of conditions.

Our method is a constrained choice to try to exhibited networks associated with processing of sensory-motor errors in complex (several degrees of freedom) and very usual movements in which errors may be difficult to observe behaviorally and with no experimental modification of the sensory to motor mapping. Our method thus contrasts with most common paradigms used in this case (e.g. saccadic adaptation, prismatic adaptation, force field adaptation, etc).

4.2.c MRI acquisition

Whole-brain fMRI was performed using EPI on a 3 T Magnetom Trio system (Siemens AG, Munich, Germany), equipped with a standard head coil configuration. The imaging volume was oriented parallel to the bicommissural (AC– PC) plane. First a T1-weighted high-resolution three-dimensional volume (repetition time = 1700 ms, echo time = 2.93 ms, flip angle=90°; 144 adjacent axial slices, 1.09mm thickness; in-plane voxel size=1×1×1mm) was acquired. Second, functional volumes composed of forty 3-mm adjacent, interlaced horizontal slices were acquired using a gradient Echoplanar T2*-weighted EPI sequence (repetition time = 3050 ms, echo time = 45 ms, flip angle = 90°, matrix sizes = 64x64x40, voxel sizes = 3x3x3 mm). Each participant performed 4 consecutive block fMRI sessions devoted to each experimental condition. In each functional session, 80 scans were acquired (i.e. a total of 320 scans per participant). The averaged inter-trial interval was 3s. The total duration of each functional scan was 4'36".

4.2.d MRI data processing

Data were analyzed using the general linear model for block design as implemented in SPM5 (Wellcome Department of Imaging Neuroscience, London, UK). Individual scans were time corrected; T1-weighted anatomical

volume was co-registered to mean images created by the realignment procedure and was normalized to the MNI space using an affine registration which was followed by estimating nonlinear deformations, whereby the deformations was defined by a linear combination of three dimensional discrete cosine transform (DCT) basis functions, as mentioned by Ashburner and Friston (1999). The anatomical normalization parameters were subsequently used for the normalization of functional volumes. Finally, each functional volume was smoothed by an 8-mm FWHM (Full Width at Half Maximum) Gaussian kernel. Time series for each voxel were high-pass filtered (1/128 Hz cutoff) to remove low frequency noise and signal drift.

After pre-processing, statistical analysis was first performed on functional images for each participant and each session individually. For each participant, the ball catching and rest periods in the four conditions (light ball, heavy ball, random and blind) were modeled as eight regressors convolved with a canonical hemodynamic response function (HRF). Movement parameters derived from realignment corrections for each session were also entered in the design matrix as additional regressors of no interest. The general linear model was used to generate parameter estimates of activity at each voxel, for each condition, and each participant. Statistical parametric maps were generated from linear contrasts between the HRF parameter estimates for the different experimental conditions.

At the individual level, we first assessed the whole network of cerebral areas involved in the processing of each ball catching condition by contrasting the ball catching blocks with the rest blocks in each session. We then highlighted brain correlates associated with the processing of sensory motor errors by contrasting [2 random conditions > (light ball + heavy ball)] conditions, and [2 random blind > (light ball + heavy ball)] conditions on the other hand. We next performed a group analysis and applied sample t-tests to all contrasts. Clusters of activated voxels were then identified, based on the intensity of the

individual response ($p < 0.05$, FWE corrected for multiple comparisons, $T > 7.49$ for contrasts calculated relative to the rest period and $p < 0.001$ uncorrected, $T > 3.73$ for contrasts between conditions of interest). An extended threshold of 20 voxels was determined empirically and then used for all contrasts. Moreover, the regions highlighted in both contrasts of interest were defined as regions of interest (ROI) in order to confirm that mean ROI parameter estimates were significantly different in light ball compared to random and blind conditions separately, and in heavy ball compared to random and blind conditions separately. In this way, mean ROI parameter estimates were compared between the studied conditions using t-tests. Brain regions were reported according to the stereotaxic atlas of Talairach and Tournoux (1988).

4.3 RESULTS

In order to determine whether the cerebellum was involved in the processing of sensory motor errors, we first identified all the cerebral networks activated in the catching task in each experimental condition (light ball, heavy ball, random and blind conditions). Secondly, to verify the involvement of the cerebellum in sensory motor error, we contrasted images obtained in the conditions in which prediction was impossible (random and blind conditions) with those in which prediction of the ball weight was possible (light ball and heavy ball conditions). Such contrasts allowed us to isolate feedback processes from feedforward processes linked to the prediction of the upcoming mechanical perturbation.

4.3.a Motor tasks contrasted with rest periods revealed similar networks in the right posterior cerebellum and in the left primary motor cortex in all conditions.

The first step was to identify the activations corresponding to the motor task in the four experimental conditions (namely light ball, heavy ball, random, and blind conditions versus rest, $p < 0.05$ corrected). Similar neural networks were recruited in all conditions. The two largest clusters of activation were found in the right posterior cerebellum (lobule V, Schmahmann et al. 1999) and in the left primary motor cortex extending to the left primary somatosensory cortex (BA 3, 4) (cf. Figure 23). However, in the random and the blind conditions, additional neural networks including the supplementary motor area (SMA), the premotor cortex, and the left posterior cerebellum were also activated. Finally, significant additional activations of the insula, the superior temporal and supramarginal gyrus, and the thalamus were also noted in the blind condition only (see Table 4).

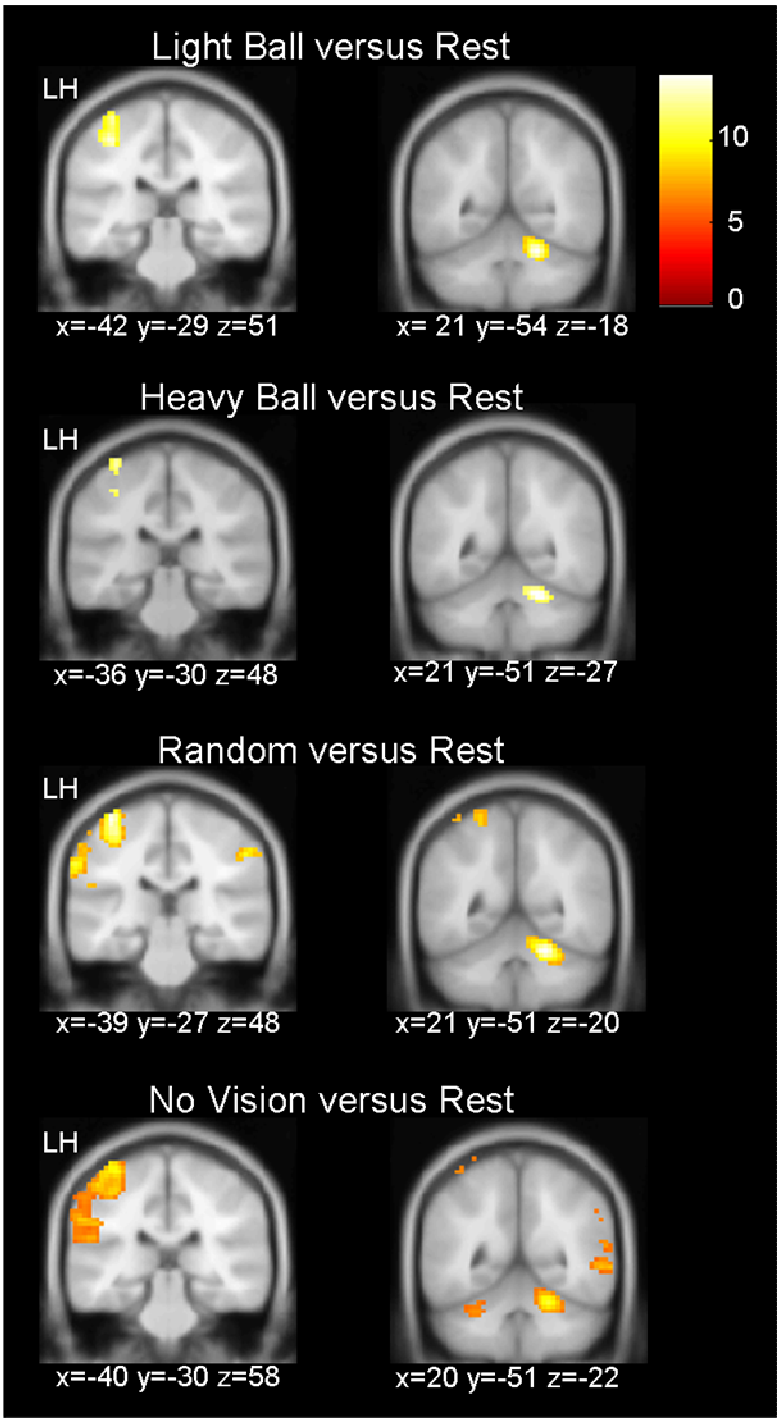

Figure 23 *Significant activations in the four experimental conditions (light ball, heavy ball, random and blind conditions versus rest, $p < 0.05$ corrected for multiple comparisons) when the motor task period was contrasted with the rest period. The two largest clusters of activation were found in the right posterior cerebellum and in the left primary motor cortex in each condition.*

Contrast	Region	H	BA	*k*	x	y	z	T
Light Ball > Rest	right posterior cerebellum (Lobule V)	R		111	21	-53	-18	14.15
	primary sensory or motor cortex	L	2/3	196	-42	-29	51	11.26
	[primary motor cortex]	L	4		-45	-32	62	11.14
Heavy Ball > Rest	right posterior cerebellum (Lobule V)	R		49	21	-51	-27	9.46
	primary sensory motor cortex	L	2/3	55	-36	-30	48	9.27
	[primary motor cortex]	L	4		-36	-38	40	9.11
Random > Rest	primary sensory cortex	L	3	683	-39	-27	48	14.87
	[primary motor cortex]	L	4		-39	-23	62	14.43
	right posterior cerebellum (Lobule V)	R		427	21	-50	-18	14.70
	primary sensory motor cortex	R	1/2	159	65	-30	40	11.94
	occipito-temporal cortex	L	19/39	46	-50	-64	9	10.60
	premotor cortex and SMA	L	6	23	-42	-2	11	10.36
	left posterior cerebellum (Lobule VI)	L		42	-30	-56	-17	10.12
Blind > Rest	primary sensory cortex	L	3/4/6	855	-56	-19	20	18.47
	[primary motor cortex]	L			-39	-38	60	17.72
	[SMA]	L			-39	-20	62	14.85
	right posterior cerebellum (Lobule V)	R		261	21	-50	-18	13.56
	insula	L		85	-42	-5	14	13.12
	superior temporal gyrus	R	21/22	116	56	-52	3	12.63
	supramarginal gyrus	R	40	110	59	-39	32	11.31
	left posterior cerebellum (Lobule VI)	L		72	-30	-53	-20	10.27
	thalamus	L		47	-18	-20	15	9.30

Table 4 *Cerebral regions specifically activated during ball catching in the four experimental conditions ($p < 0.05$ corrected for multiple comparisons). For each cluster, the region showing the maximum T value is listed first, followed by the others belonging to the cluster [between brackets]. The cerebellum lobules are reported according to Schmahmann et al. (1999). The Talairach coordinates (x, y, z), the corresponding Brodman Area (BA) the laterality of the hemisphere (H; L = left hemisphere; R = right hemisphere) and the number of voxels in the cluster (k) are reported. Voxel size: 3x3x3 mm.*

4.3.b Activation in the right and left cerebellum increased with task uncertainty

The second step was to determine the neural network involved in the processing of sensory-motor errors by contrasting [2 random > (light ball + heavy ball)] conditions, and [2 blind > (light ball + heavy ball) conditions] ($p < 0.001$ uncorrected). In these contrasts, the same number of identical stimuli on both sides of the subtraction was maintained. For the sake of clarity, they are named "random" and "blind" contrasts respectively in the following. The significant clusters which were found were thus not due to a different level of tactile and proprioceptive feedback but to the task uncertainty. The results identified the right and left cerebellum and the right thalamus in both contrasts. More precisely, left cerebellum (lobule VI) and right thalamus networks shared some overlap for the random and the blind contrasts.

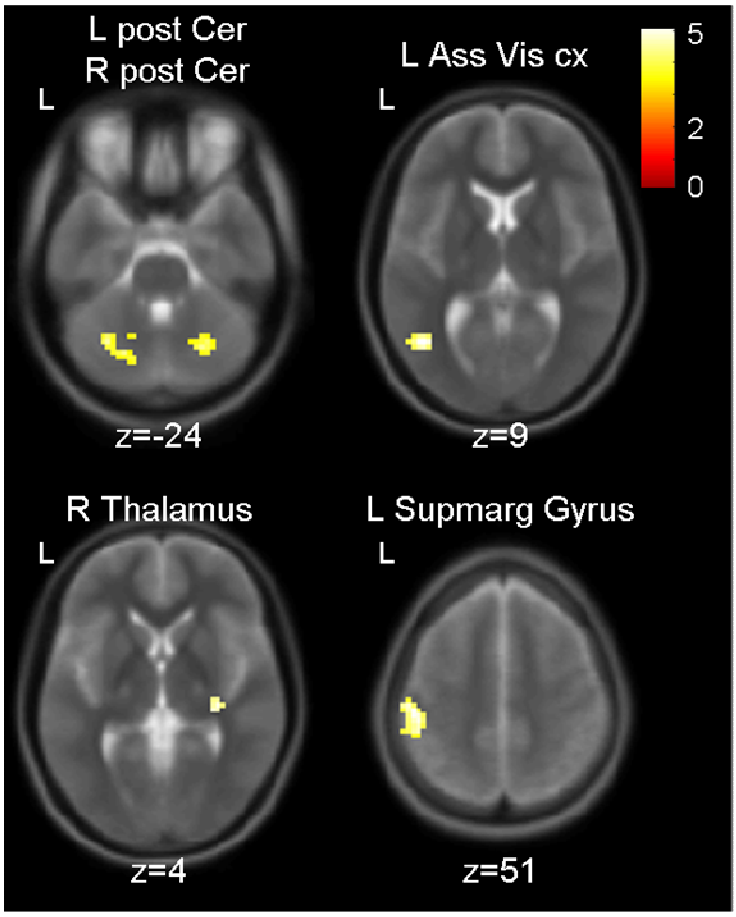

Figure 24 *Significant activations in the [2 random > (light ball + heavy ball)] contrast (P<0.001, uncorrected). L=Left. R=Right. post Cer = Left posterior portion of the cerebellum. Ass Vis cx = Associative visual cortex. SupMarg Gyrus = Supramarginal Gyrus.*

In the right cerebellum, activation networks were differently centered. The right posterior cerebellum (24x, -65y, -24z, lobule VI) was indeed significantly activated in the random condition whereas the anterior portion of the right cerebellum (24x, -39y, -23z, lobule IV) was activated when vision was removed (blind condition; cf. Figure 24 and 25). However, none significant activation was observed when the blind and random condition were contrasted together. Note that in the random condition, 5/33 of the significant voxels were observed in the anterior portion of the right cerebellum.

Additional and specific networks were noted for each contrast (see Table 5). In the random contrast, the associative visual cortex and the left supramarginal gyrus were highlighted. The blind contrast revealed the functional contribution of the right frontal gyrus, the anterior prefrontal cortex in both hemispheres and the left primary somatosensory cortex (see Table 5). Note that the inverse contrasts did not show any significant activation.

Finally, all the regions highlighted by these two contrasts were defined as regions of interest (ROI). Mean ROI parameter estimates were extracted from the ROI clusters and the values were submitted to t-tests in order to compare the light ball and the heavy ball conditions separately, with the random and the blind conditions. At this point, it is important to underline that ROI analyses serve to verify whether observed networks were activated independently of the ball weight. Results revealed that all ROI activities defined in Table 5 increased significantly in the random in comparison to the light (All $t < -2.79$, $p < 0.014$) and heavy ball conditions (All $t < -3.41$, $p < 0.004$). Similarly, ROI activities increased significantly in the blind condition in comparison to the light (All $t < -2.32$, $p < 0.03$) and heavy ball conditions (All $t < -2.24$, $p < 0.04$). In addition, no significant difference was found when light ball and heavy ball conditions were compared for both contrasts.

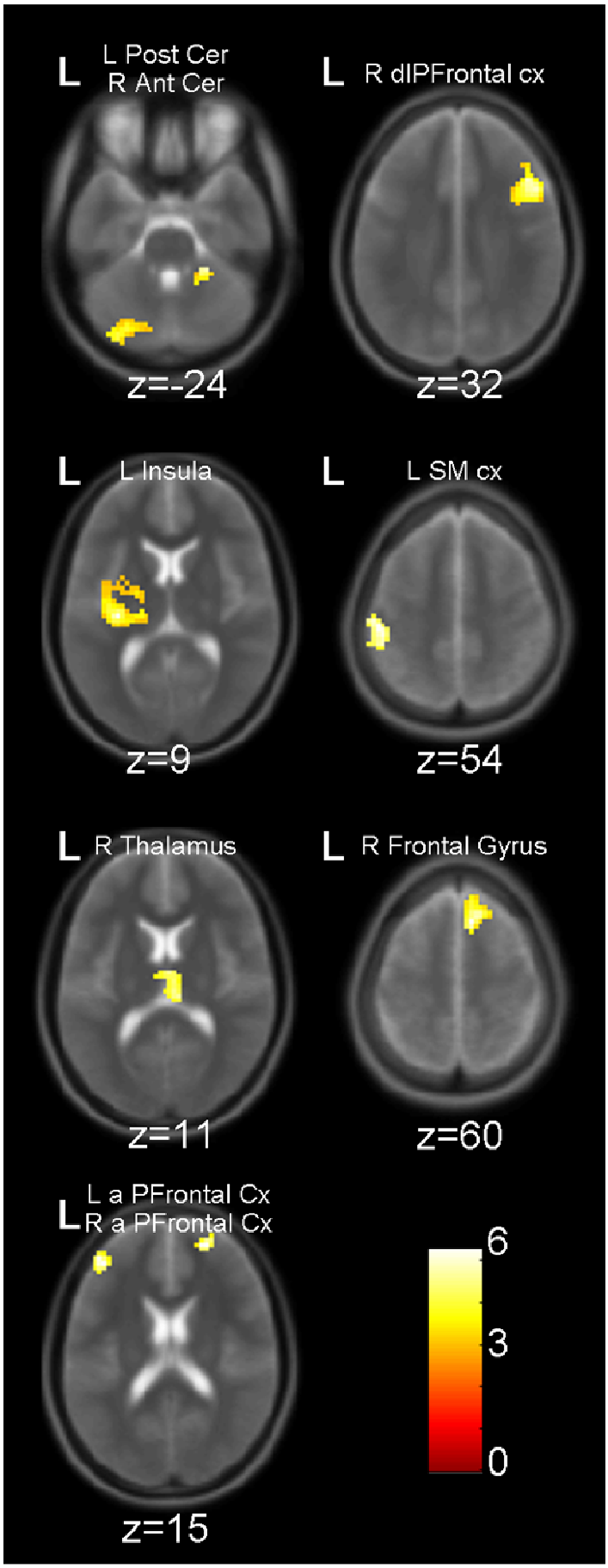

Figure 25 *Significant activations in the [2 blind > (light ball + heavy ball)] contrast (P<0.001, uncorrected). L = Left. R = Right. post Cer = Left posterior portion of the cerebellum. Ant Cer = Anterior portion of the cerebellum. A PFrontal Cx = anterior prefrontal cortex. dlPFrontal cx= dorsolatéral prefrontal cortex. SM cx = primary sensory motor cortex.*

Contrast	Region	H	BA	*k*	x	y	z	T
[2*random > (light ball + heavy ball)]	right posterior cerebellum (Lobule VI)	R		33	24	-65	-24	5.46
	occipito-temporal cortex	L	19/39	40	-45	-61	9	5.13
	left posterior cerebellum (Lobule VI)	L		52	-30	-62	-22	4.90
	supramarginal gyrus	L	40	25	-48	-32	51	4.63
	thalamus	R		23	30	-26	4	4.52
[2*blind > (light ball + heavy ball)]	insula	L		817	-33	-20	9	6.93
	[premotor cortex and SMA]	L			-56	4	22	6.09
	dorsolateral prefrontal cortex	R	9	188	50	16	32	6.62
	frontal gyrus	R	8	143	9	18	60	6.54
	right anterior cerebellum (Lobule IV)	R		29	24	-39	-23	6.13
	anterior prefrontal cortex	R	10	83	24	53	14	5.98
	anterior prefrontal cortex	L	10	47	-42	42	15	5.75
	left posterior cerebellum (Lobule VI)	L		79	-21	-77	-26	5.49
	thalamus	R		120	3	-18	12	5.45
	primary sensory motor cortex	L	1/2	110	-48	-29	57	5.33

Table 5 *Cerebral regions specifically activated to process the sensory motor errors ($p < 0.001$ uncorrected). For each cluster, the region showing the maximum T value is listed first, followed by the others belonging to the cluster [between brackets]. The cerebellum lobules are reported according to Schmahmann et al. (1999). The Talairach coordinates (x, y, z), the corresponding Brodman Area (BA) the laterality of the hemisphere (H; L = left hemisphere; R = right hemisphere) and the number of voxels in the cluster (k) are reported. Voxel size: 3x3x3 mm.*

4.4 DISCUSSION

Our aim here was to identify the main cerebellar structures involved in the processing of sensory-motor errors when catching a falling object. By contrasting functional imaging signals obtained in conditions in which it was possible and impossible to predict the weight of the ball, we aimed to highlight sensory-motor error processing which we expected to be more marked in the conditions without prediction (less accurate feedforward process or more important feedback corrections, i.e. more important sensory-motor error) with respect to conditions with prediction (more accurate feedforward process or less important feedback corrections, i.e. less important sensory-motor error).

In order to determine whether networks activated in the catching task were similar to those generally reported in the literature, we first assessed the whole network of cerebral areas involved in the processing of each ball catching condition by contrasting the ball catching blocks with the rest blocks obtained at each session. We found common activations in left motor and sensory areas and in the right cerebellum for all conditions. Additional activations were observed in the random and blind conditions. Importantly, when subjects were blindfolded, the time to contact could not be estimated and we may have expected some differences between the activations observed in the random vs. blind condition. Interestingly, however, we also observed similar activations within the cerebellum between the two conditions suggesting that the sensory-motor processing shared some common networks independently of visual cues. These common activations were similar to those generally obtained for similar tasks in the literature (Field and Wann 2005, Senot et al. 2008, Bedard and Sanes 2009).

When we contrasted conditions of greater uncertainty about the ball weight with conditions of no uncertainty, our main results clearly demonstrated that when the ball is caught with the right hand without possible prediction about

its weight, two networks in both the right and left cerebellum are highlighted. Interestingly, when we performed these contrasts, we did not notice any activation at the level of the primary motor cortices. Nor did we observe different levels of activation in the primary sensory cortex (post central gyrus) when we contrasted the random condition (with sight) with the light and heavy ball conditions. In contrast, this level was different when we contrasted the blind condition with the light and heavy ball conditions, suggesting that the manipulation of the ball induced slightly different reafferences (Table 5).

The subtraction of the baseline activity from the activity in the blind condition extracted activity related to the estimation of the weight and the time to contact, while the subtraction of the baseline activity from the activity in the random condition extracted activity related to the estimation of the weight only. This may explain greater activations in the sensory cortex for the blind condition which suggests greater manipulation of the ball when caught with the hand. Interestingly, however, despite these disparities there seem to be some overlap within the cerebellum between activations in the random vs. blind conditions.

None significant activation was observed when the blind and random conditions were contrasted together. Clusters of the right cerebellum networks were aligned on the same antero-posterior axis, so in the same horizontal plane. Activations were respectively centered in a more posterior (24x, -65y, -24z) and in a more anterior portion (24x, -39y, -23z) of the right cerebellum (see Fig 26). Using PET, Desmurget et al. (1998) demonstrated that in humans, the medioposterior cerebellum was involved in the control of saccadic adaptation. In their study, they reported a network whose coordinates (1.5x, -62y, -18z) might involve some overlap with the more posterior one we obtained (note that their y and z coordinates were quite similar to ours). In their study, they demonstrated increased activity in the medioposterior cerebellum after adaptation compared to random target presentation. One

may suggest that this result is opposite to our, however, in saccadic adaptation a systematic target jump is made during the saccadic blind period. In consequence, a systematic bias and sensory-motor error is introduced unconsciously on a trial by trial basis. In our experiment, sensory-motor errors are conscious and variable between trials but more important in the condition without prediction. As a whole, this comparison suggests that at this level, the cerebellum may be involved in the processing of sensory-motor errors for different effectors and in updating the associated feedforward commands whatever the error is systematic and unconscious or variable and conscious. Alternatively, in the study of Desmurget et al. (1999) a new internal model was probably built, following a constant perturbation. In this case, cerebellar activations may indicate a new internal model that could not be consolidated during the random perturbation.

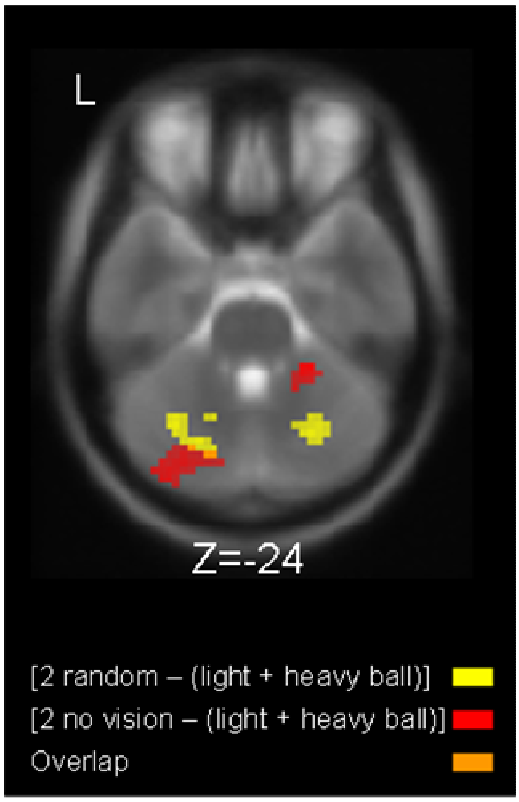

Figure 26 *Cerebellar networks significantly activated in [2 random > (light ball + heavy ball)] (in yellow) and in [2 blind > (light ball + heavy ball)] (in red). Voxels common to both contrasts appear in orange.*

By contrast, in our experiment, the difference in cerebellar activations may rather be proportional to the error and not necessarily to the modification of the internal model. We could not thus disambiguate whether the presented errors should lead to changes of internal model or to initiation of on-line corrections. In our study, we investigated the cerebellar structures that are involved in the processing of sensory-motor errors. This error signal is computed as the difference between what is predicted and real sensory feedbacks (see figure 22). As such this error may trigger on-line motor corrections and/or update feedforward commands. However, these responses seem to originate from the same source and identical sensory-motor error processing. In this vein, Diedrichsen et al. 2005 demonstrated that execution errors (assigned to the movement) were systematically associated with feedforward correction on the next trial in a pointing task. This is the kind of error that may occur in our experimental design. In accordance with our result, they also observed, that errors were associated with cerebellar activation in lobule IV and V whatever the perturbation (i.e. mechanical perturbation, visual feedback perturbation, or target displacement) and even if there was no behavioral adaptation during the task, but only feedback on-line corrections. In addition, Tseng et al. (2007) demonstrated that adaptation to visuo-motor perturbation depends on the cerebellum and is driven by the mismatch between expected and actual sensory feedbacks independently of the occurrence of on-line corrections.

In a ball catching task, to adapt to ball weight changes, anticipatory muscles activities must be modified and timed to occur before the impact (Bennett et al. 1994 and Lang and Bastian 1999). Cerebellar subjects adapted slowly or not at all to modifications of the ball weight for light to heavy or heavy to light balls. Finally, Lang and Bastian (2001) showed that cerebellar patients remained slow or unable to adapt to the change of the ball weight even with on-line information. Altogether it confirmed the idea that the processing of

the sensory-motor error is computed in the same cerebellar circuits despite different behavioral effects and different types of errors, independently of the occurrence of on-line corrections.

Some studies have shown that cerebellar activity specifically reflects the operations of internal models in the prediction of dynamic constraints during movement control (Imamizu et al. 2000, Kawato et al. 2003, Diedrichsen et al. 2005). At the cellular level, the role of Purkinje cells has been evoked to explain cerebellar plasticity that occurs during learning and motor adaptation. More particularly, it has been suggested that Purkinje cells could modify the gain of motor commands in many adaptive mechanisms by comparing signals conveyed by parallel fibers and a teaching signal conveyed by climbing fibers (Ito 1993, 2002, Boyden et al. 2004, De Zeeuw and Yeo 2005). This process could involve the cerebellum in updating sensory prediction based on error detection between true reafferences and the prediction itself (Ramnani 2006).

Interestingly, in a quite similar experimental design as our, Schmitz et al. (2005) investigated brain activations in a task in which subjects had to lift an object whose mass could be unexpectedly varied. Recognizing the role of cerebellum in anticipatory control and prediction of sensory consequences, they hypothesized that if cerebellar activations were reflecting rapid grip force corrections during conditions without predictions, strongest activations should have been observed in this case. However, they did not observed activations in the cerebellum when the conditions without and with prediction of the object weight were contrasted. This result is in contradiction with our and with neuroimaging studies that have revealed the presence of activity in the human cerebellum related to error signals (Ramnani et al. 2000, Imamizu et al. 2000, Diedrichsen et al. 2005). Schmitz et al. suggested that depending on whether the weight was lighter or heavier than expected, the corrections were not the same and should have probably not activated the same areas. Because both events were mixed they could not made the distinction. Another

explanation could occur from the fact that in their experiment the ratio between the heavy and the light object was not important enough (230 and 830g, i.e. × 3.6 vs. 30 and 300g, i.e. × 10).

We also observed one network in the left cerebellum that was centered roughly on the same location independently of the manipulation of sight (-30x, -62y, -22z and -21x, -77y, -26z for the random and blind conditions, respectively). These activations within the right posterior cerebellum may involve the flocculo nodular lobe. This structure, under the influence of vestibular signals, is known to send motor commands to axial antigravity muscles and extensors (with bilateral projections). These activations suggest that the effects of the perturbation associated with the ball catching task were bilateral and may also trigger some postural responses in the left side. In this case, different and more axial feedforward motor commands may be involved, as catching the ball may imply greater perturbation of the axial and proximal muscular control. This will be readily accepted if we consider the idea that the human hand manipulates many objects of different weights every day from a standing or sitting position, but that catching an object while lying on one's back is much less frequent and may unusually challenge axial movements. In any case, these left cerebellar activations also suggest that the left cerebellum could be involved in the processing of sensory-motor errors and maybe in the updating of feedforward commands.

A possible limitation of our study could be that the predicted changes in error magnitude would not be associated with changes in prediction error, as the internal model used will be different in the random conditions compared to the blocked conditions. However, this interpretation is limited for at least two reasons that are linked together. First, it suggests that different controllers are involved each time the dynamics is modified despite the movement kinematics remains roughly the same. This raised an important problem of storage, as many controllers would be differentiated and stored in the brain

and especially in the cerebellum. Second and related to the previous remark, this interpretation is not compatible with the role that plays the cerebellum in the adaptation to the environment dynamics. Indeed, the cerebellum rather adapts the same controller to various dynamical constraints (Wolpert et al. 1998 for a review).

Interestingly, when subjects were blindfolded ([2 blind - (light ball + heavy ball)] contrast), we also observed right activations in the thalamus and the prefrontal cortex when we contrasted the conditions without and with prediction. It is known that the prefrontal cortex sends projections to the cerebellum via the cortico-olivo-cerebellar pathways and the inferior olive and reciprocally that the cerebellum sends projections back to the prefrontal cortex via the cerebellar nuclei and the thalamus. This is rather in contradiction with the traditional view that considers the cerebellum and its canonical circuitry as a strictly motor structure providing error correction during motor adaptation. However, Ramnani (2006) has suggested that the cerebellum may compute some predictive cognitive consequences of cognitive operations, and that the error between predicted and actual cognitive outcomes is used to refine future predictions. In our task, the prefrontal cortex may be involved in the cognitive operation that assigns probabilities for each of the ball weights. This structure may thus influence motor error signals according to the conscious prediction of the ball weight. This network was mainly exhibited in the blind contrast maybe because subjects could not estimate visually the time to contact and might rely more importantly to cognitive predictions (rather than vision) in relation to sensory predictions. Note that small activations in the thalamus were also noticeable for the random contrast that might not reach the prefrontal cortex. Nevertheless, this motor and cognitive network that seems to link the cerebellum, the thalamus and the prefrontal cortex was observed only in the right hemisphere, suggesting that adaptations to perturbations were more challenging for the left

or axial part of the body (via the flocculo-nodular lobe) although the ball was caught with the right hand. In the blind condition, we also observed left activations within the insula, the premotor and supplementary motor areas. Premotor and supplementary areas are known to be involved when the motor sequence becomes more difficult (Roland et al. 1980). These structures may be more engaged in the task when vision is suppressed. Similarly, the insula has been shown to store an internal model of gravity which is involved in the representation of visual gravitational motion (Indovina et al. 2005, Maffei et al. 2010). The fact that we observed greater activations when sight was suppressed may suggest that the representation of gravity is challenged in this situation.

Finally, when we contrasted the random condition (with sight) with the light and heavy ball conditions, we observed activations in the left occipito-temporal cortex. This area is known to be involved in visual attention (Barnes et al. 2000). It may be that when ball weight varied unexpectedly, subjects engaged more attentional resources to try to optimize their catching.

In conclusion, in a situation of repetitive catching of a falling ball when the possibility of prediction about ball weight is manipulated, our results showed that both the right and left cerebellum is engaged to process sensory-motor errors and to update feedforward motor commands, perhaps on a trial by trial basis. In addition, when subjects were blindfolded, we observed a more anterior network in the right cerebellum and we identified a cerebellar-thalamo-prefrontral network that may be involved in cognitive prediction (rather than sensory prediction) about the ball weight.

4.5 ACKNOWLEDGEMENTS

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4. DISCUSSION GENERALE

4.1 RAPPEL DES OBJECTIFS

Le système sensori-moteur humain est capable de s'ajuster rapidement aux changements de l'environnement. Ces processus de correction sont réalisés grâce à la génération d'un signal d'erreur basé sur la différence entre les prédictions des conséquences sensorielles d'une action comparées aux retours sensoriels réels (Hoff et Arbib 1992, 1993, Babin-Ratté et al. 1999, Lang and Bastian 1999, 2001, Desmurget et Grafton 2000, Bonnetblanc 2008). Ces corrections interviennent sur des échelles temporelles courtes via (i) des corrections motrices en ligne, ou (ii) l'actualisation hors ligne et itérative des commandes motrices d'un essai à l'autre (e.g. adaptation motrice). Comme ces deux grands processus se déroulent sur des durées courtes et qu'un certain nombre d'hypothèses suggère qu'ils seraient issus du même calcul d'erreur, nous les avons regroupés ensemble au sein de ce travail expérimental dans le but d'améliorer notre compréhension de la flexibilité du contrôle moteur. Plus particulièrement, les mouvements de pointages étudiés dans la littérature sont réalisés à partir d'une position initiale assise qui implique seulement un mouvement du bras effecteur (Jeannerod 1986, Crenna et Frigo 1991, Ma et Feldman 1995). Cependant, dans des conditions plus naturelles, le mouvement développé peut être plus complexe : en effet, la situation initiale et la tâche à réaliser peuvent nécessiter l'implication d'un plus grand nombre de degrés de liberté et donc le contrôle d'un plus grand nombre de muscles. C'est pourquoi nous nous sommes intéressés dans ce travail à la compréhension de la flexibilité du contrôle moteur lorsqu'elle est mise en jeu dans les mouvements complexes.

Dans ce sens, quatre axes principaux ont été soulevés à partir de la littérature scientifique et ont guidés notre contribution expérimentale. Tout d'abord, nous avons cherché à évaluer si l'homme était capable de générer des

corrections motrices rapides de l'ordre de la centaine de millisecondes. Dans le même temps, nous avons cherché à déterminer les niveaux anatomiques auxquels les corrections motrices pouvaient être éventuellement observées lors de la réalisation d'un mouvement dirigé en posture érigée. Par la suite, nous nous sommes interrogés sur le mode d'organisation de la commande musculaire générée pour la correction motrice. Le système nerveux est-il capable d'établir des synergies musculaires, c'est-à-dire des liens fonctionnels complexes entre les activations musculaires générées, lors de corrections motrices rapides ? Troisièmement, nous avons cherché à évaluer comment se comportaient les processus de corrections motrices en ligne lorsqu'un mouvement dirigé était soumis à une modification du conflit « vitesse/précision » pendant son exécution. Dans ce cas particulier, la cible à atteindre ne change pas seulement de localisation mais aussi de taille. Cette modification des stimuli n'est pas observée couramment dans notre environnement où la taille des objets physiques reste constante. Hors nous savons depuis Woodworth (1899) que la taille d'un objet contraint de manière importante l'exécution d'un mouvement dirigé. Enfin, nous avons cherché à mettre en évidence les corrélats neuro-anatomiques des centres cérébraux impliqués dans le calcul du signal d'erreur sensori-moteur qui est à la source de la flexibilité motrice.

4.2 RAPPEL DES PRINCIPAUX RESULTATS

La première étude de ces travaux expérimentaux démontre clairement qu'à partir de la position debout, suite à un saut de cible, des corrections motrices très rapides peuvent être envoyées sur les muscles des bras (DAi) et sur les muscles des jambes (TAi). En effet, tous les sujets testés ont déclenché des activités EMG de correction en 100 ms ou moins dans le deltoïde antérieur après le saut de cible. Au niveau du tibialis antérieur, 4 sujets sur 7 ont présenté des corrections motrices en moins de 100 ms.

La seconde étude nous renseigne dans un premier temps sur la modalité de recrutement des muscles lors de la génération d'une correction motrice suite à un saut de cible dans un mouvement dirigé complexe impliquant les jambes, le tronc et le bras pour atteindre la cible. Plus particulièrement, cette étude confirme dans un premier temps que lors de l'initiation d'un mouvement planifié, des corrélations significatives lient les occurrences des débuts des activités musculaires de certains muscles entre eux, et ce, indépendamment de leur localisation anatomique ou de leur position dans la séquence motrice. Dans un second temps, cette étude établit clairement que lors de la génération de corrections motrices en ligne, des corrélations significatives lient les occurrences des débuts des activités musculaires de nombreux muscles entre eux. De manière similaire à celles reportées lors de l'initiation de l'action, ces corrélations sont indépendantes de la localisation anatomique des muscles ou de leur rang temporel dans la séquence motrice générée. Enfin, en comparant les synergies musculaires mises en jeu lors de l'initiation du mouvement et des corrections motrices en ligne, cette étude montre que les séquences motrices employées dans ces deux cas sont significativement différentes et que le couplage musculaire est plus important dans les corrections motrices comparé aux phases d'initiations du mouvement. De plus, lors de la génération de corrections motrice en ligne, les corrélations couplent de nombreux muscles des jambes avec des muscles du tronc et du bras. Au contraire, lors de l'initiation, la majorité des corrélations est focalisée au niveau du membre inférieur. Contrairement à ce qui a été démontré par l'étude de tâches motrices moins complexes, nos résultats n'établissent aucune logique anatomique de recrutement musculaire de type proximo-distale (Jeannerod 1986) ou jambe-tronc-bras (Stapley et al. 1998, 1999, Adamovich et al. 2001, Bonnetblanc et al. 2004, Bonnetblanc 2008).

Dans la troisième expérimentation de ce travail, le conflit « vitesse/précision » est modifié pendant la réalisation du mouvement de manière à étudier l'impact

d'un changement de l'indice de difficulté du mouvement de pointage sur les corrections motrices. Pour cela, nous avons induit expérimentalement des changements non seulement de la localisation mais également de la taille de la cible pendant que le sujet réalisait le mouvement de pointage. Les résultats de cette étude établissent que la durée du mouvement augmente significativement lorsqu'une modification de la taille ou de la localisation spatiale de la cible apparaît pendant le mouvement. Néanmoins, la variabilité terminale de la position finale du doigt ne diffère pas significativement dans ces conditions. En d'autres termes, ces résultats démontrent que la vitesse de la main au cours du mouvement peut être modulée en fonction de la taille et de la distance de la cible terminale pendant la génération du plan moteur ou lors de la phase finale d'approche de la cible et ce, indépendamment de la variabilité de la position terminale de la main. De tels résultats suggèrent que lorsque le conflit « vitesse/précision » est modifié pendant la réalisation d'un mouvement complexe dirigé, une représentation de la vitesse de la main basée sur les retours sensori-moteurs semblent être utilisée par le cerveau pour générer et contrôler le déplacement manuel. D'une manière plus polémique, nous pourrions affirmer ici qu'un traitement intermédiaire est impliqué dans le contrôle des mouvements de la main plutôt qu'un couplage perception/action, bien que les mouvements restent rapides et avec des délais de correction compris entre 180 et 350 ms sur la cinématique de la main.

Enfin, dans une dernière étude, nous nous sommes intéressés aux corrélats neuro-anatomiques des aires corticales impliquées dans les processus de calculs de l'erreur sensori-motrice. En effet, de nombreuses études ont clairement avancé l'hypothèse qu'un signal d'erreur était à la base de la capacité de flexibilité du contrôle moteur (Johansson 1998, Desmurget et Grafton 2000, Bastian 2008). Dans ce but, nous avons conduit un protocole en imagerie par résonnance magnétique fonctionnelle pendant lequel les sujets réalisaient une tâche de rattrapés répétés de balles dont l'incertitude de la

masse variait suivant les conditions expérimentales. Nos résultats démontrent dans les conditions sans prédiction des activations significatives bilatérales dans le cervelet, et plus particulièrement dans les lobules IV, V, et VI (Schmahmann et al. 1999). Lorsque les sujets n'ont pas la possibilité de prédire la masse de la balle qu'ils vont saisir, le cervelet semble engagé de manière bilatérale dans les processus de calcul de l'erreur sensori-motrice et dans la mise à jour de la commande motrice suivante, probablement sur une base d'essai par essai (Desmurget et Grafton 2000, Bastian 2008). De plus, lorsque les sujets sont expérimentalement privés de leur vision, nos résultats identifient un réseau cortical supplémentaire impliquant le thalamus et les cortex préfrontaux bilatéraux, possiblement impliqué dans des processus de prédictions cognitives pour palier à l'impossibilité dans cette condition de prédire la masse de la balle mais aussi le moment de contact de la balle avec la main.

En résumé ce travail établit les caractéristiques de la flexibilité motrice suivantes : à partir de la position debout, lors de la réalisation de mouvements complexes rapides et suite à un saut de cible réalisé dans des conditions simples (seulement deux cibles potentielles, une seule et unique direction de saut), des corrections motrices très rapides peuvent être envoyées en moins de 100 ms dans des muscles du bras et de la jambe sur la base d'informations visuelles. De plus, le SNC est capable d'utiliser des synergies musculaires lorsqu'il génère des corrections motrices. Ces synergies musculaires ne semblent pas suivre d'ordre de recrutement anatomique et sont différentes de celles utilisées lors de l'exécution d'un plan moteur initial pour une tâche très similaire. De manière additionnelle, lorsque l'indice de difficulté de la tâche est modifié au cours de la tâche, la durée du mouvement s'allonge mais la variabilité de la précision terminale reste inchangée. Ceci indiquerait que les retours sensori-moteurs basés sur une représentation de la vitesse de la main

semblent être utilisés par le cerveau pour générer et contrôler le déplacement manuel. Enfin, les lobules IV, V, et VI du cervelet participeraient de manière bilatérale au calcul de l'erreur sensori-motrice lors d'une tâche motrice et vraisemblablement aux processus d'actualisation de la commande motrice probablement essai par essai.

4.3 100 MS : EST-CE LA DUREE MOYENNE MINIMALE DES LATENCES DE CORRECTION MOTRICE CHEZ L'HOMME ?

Si ce travail nous a permis de mettre en avant certaines caractéristiques de la flexibilité motrice dans les mouvements complexes dirigés, il soulève également un certain nombre de nouvelles questions. Le délai moyen de 100 ms reporté dans notre première étude est-il le délai minimum pouvant séparer un stimulus et une contraction musculaire ? De notre point de vue, trois éléments permettraient de réduire encore ces latences : diminuer la complexité de la tâche, vérifier que d'autres muscles ne corrigent pas avant le TAi et le DAi (notamment certains muscles profonds impliqués dans les réponses d'orientations sous influence directe des faisceaux vestibulo et tecto-spinaux), et augmenter la quantité et les origines des retours sensoriels (influences multi-sensorielles).

4.3.a La complexité de la tâche

Tout d'abord, bien qu'ayant souhaité rendre le plus simple possible notre manipulendum expérimental dans la première expérience, celui-ci comporte quand même des contraintes a priori qui peuvent limiter la rapidité des corrections motrices. Nous avons vu que la diminution de la taille de la cible finale et plus particulièrement l'augmentation de la précision requises par un mouvement volontaire dirigé réduit la vitesse d'exécution de celui-ci (Woodworth 1899, Fitts 1954). Or notre manipulendum requiert des mouvements de pointage du doigt sur des cibles de 10 mm2. Augmenter significativement la taille des cibles ou diminuer la contrainte de précision permettrait très vraisemblablement d'augmenter encore la vitesse du

mouvement. Paillard (1996) mentionne qu'à la manière d'un phénomène d'urgence, plus le temps pour corriger est court, et plus les corrections motrices sont rapides. De ce fait, nous nous posons la question de savoir si l'utilisation de situations plus écologiques nous permettrait d'observer des activations musculaires plus rapides suite à l'apparition d'un stimulus visuel (une étude est en cours sur le sujet).

4.3.b La pertinence des enregistrements EMG

Dans nos trois premières expérimentations, nous avons utilisé des enregistrements EMG de surface sur 13 à 16 muscles. Dans la première étude, seulement 8 muscles ont montré des modifications significatives suite au saut de cible. Le type d'enregistrement EMG, ainsi que les muscles enregistrés peuvent représenter une limite dans l'estimation des latences minimales entre un stimulus et une activation musculaire. En effet, l'EMG de surface ne permet pas l'accès aux muscles profonds. Or, les études du réflexe de fixation visuelle sur un stimulus lumineux stationnaire ou en mouvement (Hess et al. 1946) ont montré, chez le singe, un recrutement très précoce (60 ms) des muscles profonds de la nuque grâce à des enregistrements EMG invasifs (Corneil et al. 2004, 2008, Chapman et Corneil 2011). Chez l'homme, il serait intéressant de déterminer les latences des corrections motrices dans les muscles du cou ainsi que leur niveau de coordination avec les autres muscles impliqués dans la séquence motrice de correction.

4.3.c Fusion multi-sensorielles : un moyen de réduire les délais de correction motrice ?

Enfin, comme la majorité des études de la littérature, nous avons étudié la rapidité de la flexibilité suite à un saut de cible (Pélisson et al. 1986, Goodale et al. 1986, Hoff et Arbib 1992, 1993, Prablanc et Martin 1992, Desmurget et al 1999, Desmurget et Grafton 2000, Desmurget et al. 2001, Sarlegna et Blouin 2010). Que ces sauts de cible soient détectés de manière consciente ou non, les propriétés du système sensori-moteur sont dans de tels cas étudiées à

partir de stimuli purement et exclusivement visuels. Or, il est connu que les afférences non seulement visuelles mais également proprioceptives (Pipereit et al. 2006), tactiles (Chapman et Beauchamp 2006), vestibulaires (Fitzpatrick et Day 2004, Carvalho et al. 2011), ou auditives (Bernstein et al. 1970, Niemi et Näätänen 1981, Jepma et al. 2009 Fischer et al. 2011) peuvent avoir un impact sur la commande motrice. Par exemple, Pipereit et al. (2006) démontrent que dans le cas d'un mouvement de pointage soumis à une perturbation environnementale mécanique, une perturbation des informations proprioceptives induit une diminution significative de l'efficacité des processus d'adaptation. En revanche, dans cette étude, le biais des informations proprioceptives n'a pas d'impact sur l'adaptation à une perturbation environnementale purement visuelle. D'après ces auteurs ces résultats suggèrent que les mécanismes sous-jacents de l'adaptation visuelle et de l'adaptation proprioceptive sont en partie distincts. De ce fait, nous pouvons nous demander si une sollicitation multi sensorielles, et donc le recrutement de plusieurs processus différents, ne pourraient pas permettre de diminuer les latences des corrections motrices.

4.4 Corrections motrices rapides : boucles corticales de bas ou de hauts niveaux ?

Dans le contrôle moteur, la possibilité de réaliser des ajustements rapides pendant des mouvements complexes dirigés face à des modifications de l'environnement est une capacité primordiale de notre SNC. Développer les connaissances sur le fonctionnement et les voies nerveuses impliquées dans de tels processus est un enjeu important dans le champ des neurosciences. Les valeurs des latences séparant un stimulus visuel et une réponse nerveuse reportées par les études électrophysiologiques sont en contradiction avec celles reportées par les études comportementales. D'un côté, il est clairement établi que dans un contexte simple, des corrections motrices peuvent être déclenchées rapidement après une perturbation visuelle (Goodale et al. 1986,

Pélisson et al. 1986, Prablanc et Martin 1992, Day et Lyon 2000, Gaveau et al. 2003, Schepens et Drew 2003, Corneil et al. 2004, Saijo et al. 2005, Resvani et Corneil 2008, Gomi 2008, Corneil et al. 2010, Perfiliev et al. 2010, Pruszynski et al. 2010, Brendan et Corneil 2011). Dans notre première étude, les latences reportées de 100 ms en moyenne, notamment dans les muscles de la jambe, sont plus courtes que celles mentionnées dans les boucles traditionnelles du traitement de l'information visuelle. Dans ce premier cas, les boucles nerveuses sollicitées pourraient être plus courtes que les boucles traditionnelles et impliquer un nombre de neurones moins important. Cette hypothèse issue des travaux comportementaux trouve un argument neurophysiologique dans les travaux relatifs au colliculus supérieur et à l'existence des voies tecto et reticulo-spinales (Illert et al.1978, Werner 1993, Dorris et al. 1997, Stuphorn et al. 1999, 2000). D'un autre côté, lorsque la tâche expérimentale devient plus complexe, nous pouvons noter une augmentation des délais de correction. Dans la seconde et la troisième étude de ce travail, la tâche motrice est plus complexe que dans la première expérimentation. Comparativement à la première tâche, le nombre de degrés de liberté à contrôler est plus grand dans la seconde étude et l'indice de difficulté de la tâche est plus variable dans la troisième étude. En effet, dans la troisième étude, même si le mouvement de pointage peut s'avérer plus facile lors de l'allumage d'une cible de grande taille, l'incertitude évènementielle d'une perturbation est plus importante et le stimulus de perturbation lui-même est très inhabituel. Dans notre vie de tous les jours, il est très rare qu'un objet change brusquement de taille.

Les résultats des études deux et trois présentent des latences de correction plus longues que celles établies dans la première étude (de l'ordre de 160 ms et de 140 ms respectivement sur le muscle du TAi dans les études 2 et 3). Saijo et al. (2005) complexifient la tâche en demandant au sujet un pointage sur la cible opposée à la cible allumée pendant le saut de cible. Dans un tel cas, ces

auteurs reportent également une augmentation des délais de correction. Lors de situations plus complexes, les boucles de bas niveaux ne semblent pas capables d'assurer pleinement la correction motrice et des boucles de plus haut niveaux pourraient prendre le relais et être la l'origine de la flexibilité motrice. De manière encore plus intéressante, Saijo et al (2005) reportent dans le cas d'une anti-réaction que les sujets ne sont pas capables de corriger tout de suite à l'opposé de la cible allumée, mais que le début de la correction se fait en direction de celle-ci. C'est seulement 70 ms plus tard que le sujet se dirige dans la direction opposée à la cible allumée. Ce résultat tend à corroborer le modèle de Gomi (2008) à multiples niveaux et la cohabitation de boucles de bas et hauts niveaux dans les processus de flexibilité motrice.

4.5 Quelles ouvertures pour nos futurs travaux psychophysiques ?

Pour déterminer de manière certaine quelles boucles sont impliquées dans les corrections motrices générées dans nos trois première études, il est envisageable de réaliser des protocoles similaires en stimulant le cortex pariétal controlatéral par stimulation magnétique transcrânienne (SMT). La SMT utilisée en impulsion simple permet de créer une lésion réversible temporaire de la zone stimulée. Le cortex pariétal est une structure qui joue un rôle fondamental dans l'intégration des informations visuelles pour l'action et dans les processus de transformations nécessaires permettant la mise en relation entre des entrées sensorielles et la commande motrice adéquate (Duhamel et al. 1997, Desmurget et al. 1999, Andersen et Buneo 2002, Battaglia-Mayer et al. 2003). Avec la réalisation du premier protocole additionné d'une SMT sur le cortex pariétal controlatéral au moment du saut de cible, il sera donc possible de déterminer plus précisément les voies neuronales responsables de la correction motrice. En effet, si les temps de correction motrice restent aussi rapides que dans notre première étude, nous pourrons attribuer la production de ces corrections à des boucles sous-corticales. Inversement, si le temps de correction motrice augmente significativement lors de la stimulation du cortex

pariétal, nous pourrons alors mettre en avant l'implication des centres supérieurs dans la génération des corrections motrices rapides.

4.6 Proprietes fonctionnelles du reseau cerebelleux actif dans le calcul de l'erreur sensori-motrice ?

La quatrième étude de ce travail expérimental suggère que les lobules IV, V, et VI du cervelet participent de manière bilatérale au calcul de l'erreur sensori-motrice lors d'action répétée et vraisemblablement aux processus d'actualisation itératifs de la commande motrice. Bien que le réseau cérébelleux ait été démasqué, cette étude ne nous a pas permis d'étudier l'évolution de l'activité de ces aires lors d'une augmentation de l'incertitude. Dans la condition non vision, la complexité de la tâche augmente, notamment par l'impossibilité pour les sujets de prédire le temps de contact de leur main avec la balle. Dans notre expérimentation IRMf, les retours sensoriels nécessaires pour établir le signal d'erreur sont majoritairement les retours proprioceptifs et tactiles. Schlerf et al. (2010) établissent que le lobule VI du cervelet est grandement impliqué dans les mouvements complexes de la main. Il serait intéressant de tester si les réseaux cérébelleux impliqués dans les processus de calcul de l'erreur sensori-motrice sont indépendants du type de retour sensoriel utilisé ou du type d'effecteur impliqué dans la tâche expérimentale.

4.7 CONCLUSIONS ET PERSPECTIVES

Pour conclure, ce travail de thèse a permis de mettre en lumière des réseaux cérébelleux impliqués dans le processus de calcul de l'erreur sensori-motrice. Cette erreur apparaît lorsque les retours sensoriels réels ne correspondent pas aux prévisions établies par le cerveau. Il est fort probable que le SNC actualise de manière hors ligne et itérative les commandes motrices suivantes à partir de ce signal d'erreur. Toujours à partir de ce signal d'erreur sensori-moteur, le SNC est également capable de générer des corrections motrices en ligne si le temps imparti est suffisant. Ces corrections motrices, lors de la réalisation d'un mouvement complexe dans un contexte simple, peuvent apparaître de manière très rapide en une centaine de millisecondes seulement. Lors d'une tâche ou d'un contexte encore plus complexe, le SNC est capable d'utiliser des synergies motrices élaborées pour palier aux modifications environnementales inopinées. Néanmoins, de nombreuses questions restent encore en suspens concernant les propriétés et les caractéristiques des processus de flexibilité du contrôle moteur dans les mouvements dirigés. Le signal d'erreur et les substrats neuronaux impliqués dans sa génération sont-ils dépendants du contexte ou de l'effecteur utilisé? Cent millisecondes est-elle la durée minimale moyenne des latences des corrections musculaires chez l'homme ?

Si des boucles sous-corticales sont mises en jeu lors des processus de corrections motrices rapides, quelle est et où se trouve la représentation du schéma corporel dans ces cas là ?

D'autres expérimentations restent encore à être produites pour comprendre plus en détails les processus de flexibilité motrice dans les mouvements complexes dirigés.

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6. ANNEXES

6.1 UPRIGHT POINTING TO CONSCIOUS DOUBLE-STEP STIMULI: VERY EARLY CORRECTIONS REVEALED BY UPPER TO LOWER LIMBS EMGS

Progress in Motor Control, Marseille, France, 2009

6.2 MUSCULAR SYNERGIES DURING MOTOR CORRECTIONS: INVESTIGATION OF THE LATENCIES OF MUSCLE ACTIVITIES

International Society of Electrophysiology and Kinesiology, Aalborg, Denmark, 2010

6.3 CATCHING FALLING OBJECTS: THE ROLE OF THE CEREBELLUM IN PROCESSING SENSORY-MOTOR ERRORS AND IN UPDATING FEEDFORWARD COMMANDS. AN FMRI STUDY

Organization for Human Brain Mapping, Québec, Canada, 2011

Upright pointing to conscious double-step stimuli: very early corrections revealed by upper to lower limbs EMGs.

Lilian Fautrelle, Claude Prablanc, Bastien Berret, Yves Ballay, Thierry Pozzo, François Bonnetblanc*
lilian.fautrelle@u-bourgogne.fr

1. Background

How fast can we correct a planned movement when an unexpected event makes this planning inadequate?

⇨ Classical double step studies: minimum kinematic delays currently attributed to cortical processes = centred around **120-140 ms** (Prablanc and Martin 1992)

⇨ More recently, using EMG, very short corrections are likely to be processed at a subcortical level (Gomi, 2008) as shown by both neurophysiological (Aldermark, 1987) and clinical (Day and Brown 2001) approaches.

⇨ Finally, despite the many studies on double step pointing or reaching paradigms, the corrections delays from arm to lower limb remain little explored, especially while standing.

2. Task & Procedures

Subject Parameters

7 right handed adults (all males, age = [20-26]; mean = 23 years old, height [175-183]; mean = 179.7 m) performed pointing movements as fast and as accurately as possible with their right index.

Pointing Task

5 pointing conditions:

1) near: single step; from the start switch to the first target.

2) far: single step; from the start switch to the second target.

3) t0: double-step with a target jump at hand movement onset.

4) t0+50ms: double-step with a target jump 50 ms after hand movement onset.

5) t<0* : double-step with a target jump 120 ms after the first visual stimulus.

Randomisation: 20 blocks of 11 trials

[(4 x near) + (4 x far) + (t0) + (t0+50ms) + (t<0 *)]

** for sake of clarity, data of this experimental condition are not presented*

Recordings

Kinematics (120 Hz): Filtered with a Butterworth 4th order, dual-pass algorithm (10 Hz cut-off frequency). Statistical analyses performed using repeated measures ANOVAs. Post-hoc anlyses, Bonferroni's test when necessary.

EMGs: Fs: 960 Hz. Bandpass filtered [20-400Hz] full-wave rectified and filtered using an averaging moving-window algorithm (window size = 25 ms).

EMGs Analyse

⇨ Trials were averaged for each target location and stationary or perturbed condition and signals were synchronized on hand movement onset.

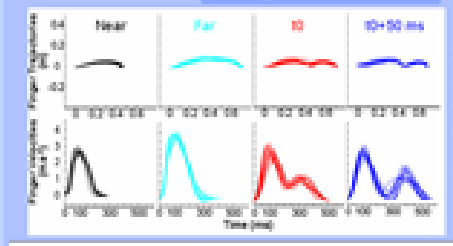
⇨ EMG for each muscle were integrated per 10 ms window (iEMG) from -250 ms before the perturbation (target jump) to 800 ms after.

⇨ For each muscle, iEMG values between the perturbed and the near target condition were compared for each window using t-tests (time to EMG modulation within a 10 ms interval).

⇨ We chose as a measure of the perturbation reaction time, the first instant for which the P-value was lower than 0.05 for a 50 ms minimum duration.

3. Results

Finger Kinematics

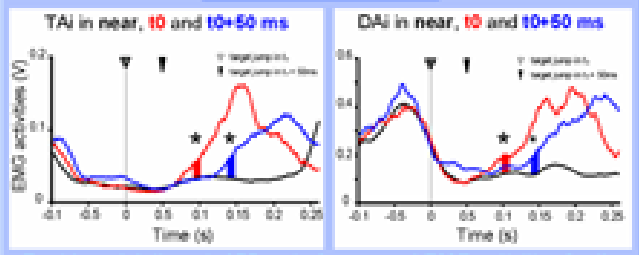


Twenty finger trajectories (upper panel) and velocity profiles (lower panel) of a typical subject in the four experimental conditions.

	Near	Far	t0	t0+50ms		
Finger End Point Area (cm²)	0.20 ± 0.01	0.20 ± 0.02	0.20 ± 0.01	0.20 ± 0.02	F(4, 24) = 0.23	P = 0.97
Movement Time (ms)	287 ± 23	379 ± 31	339 ± 17	370 ± 19	F(4, 24) = 39.28	P < 0.001
Hand Reaction Time (ms)	352 ± 19	353 ± 20	356 ± 23	357 ± 27	F(4, 24) = 0.101	P = 0.99
Acceleration Duration (ms)	126 ± 21	168 ± 29	127 ± 20	122 ± 30	F(4, 24) = 12.88	P < 0.001
Mean Velocity (m.s⁻¹)	1.7 ± 0.2	2.0 ± 0.2	1.6 ± 0.2	1.3 ± 0.2	F(4, 24) = 36.14	P < 0.001
Peak Velocity (m.s⁻¹)	2.9 ± 0.2	3.7 ± 0.2	2.9 ± 0.2	2.7 ± 0.3	F(4, 24) = 4.04	P < 0.001

Finger kinematics parameters averaged (± SD) for the 7 subjects

EMG Activities



Rapid modulations (<100 ms) of averaged EMG activities for the TAi and the DAi, for one subject, for two target jump timings.

	Muscles	TAi	SOLi	PSi	DAi	DPi	BBi
Subjects	Conditions	Individual subject analyses					
A	t0	[150;160]	[140;150]	[100;110]	**[80;90]**	[90;100]	[90;100]
	t0+50ms	[130;140]	[110;120]	[90;100]	**[80;90]**	[90;100]	[90;100]
B	t0	[120;130]	[170;180]	[130;140]	**[90;100]**	[140;150]	[120;130]
	t0+50ms	[150;160]	[110;120]	[120;130]	**[120;130]**	[150;160]	[120;130]
C	t0	**[90;100]**	[190;200]	[120;130]	**[80;90]**	[150;160]	[160;170]
	t0+50ms	**[100;110]**	[150;160]	[120;130]	**[80;90]**	[150;160]	[160;170]
D	t0	**[90;100]**	[140;150]	[100;110]	**[80;90]**	[150;160]	[90;100]
	t0+50ms	**[90;100]**	ns	[110;120]	**[90;100]**	[130;140]	[120;130]
E	t0	**[90;100]**	ns	[120;130]	**[90;100]**	[170;180]	[110;120]
	t0+50ms	**[90;100]**	ns	[110;120]	**[90;100]**	[150;160]	[120;130]
F	t0	**[90;100]**	[130;140]	[120;130]	**[70;80]**	[210;220]	[130;140]
	t0+50ms	**[80;90]**	[130;140]	[150;160]	**[70;80]**	[210;220]	[110;120]
G	t0	[110;120]	ns	[110;120]	**[80;90]**	[130;140]	[100;110]
	t0+50ms	[120;130]	ns	[120;130]	**[100;110]**	[130;140]	[120;130]
		All subjects' analyses					
ALL	t0	**[110;120]**	[150;160]	[130;140]	**[80;90]**	[150;160]	[120;130]
	t0+50ms	**[110;120]**	[130;140]	[110;120]	**[90;100]**	[150;160]	[110;120]

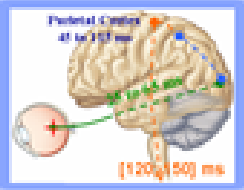
First temporal interval (10 ms) computed on the integrated EMG data for which a significant effect of the forward target jump was observed.

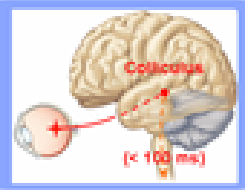
4.Discussion

Very fast motor corrections can be triggered both at arm and leg levels within 100 ms, when pointing to a suddenly displaced visual target from an upright standing position.

Part of the networks identified by the PET functional neuroanatomy involves the posterior parietal cortex and the cerebellum (Desmurget et al, 1999).

Our results suggest that there are likely additional fast subcortico-spinal corrective loops, putatively the superior colliculus (Gomi, 2008).





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Muscular synergies during motor corrections: investigation of the latencies of muscle activities

L. Fautrelle[12], Y. Ballay[12], F. Bonnetblanc[12]
[1] INSERM, U887, Motricité Plasticité, Dijon, FRANCE
[2] Université de Bourgogne
lilian.fautrelle@u-bourgogne.fr

1. Introduction

Muscle synergies has been widely investigated, mainly by means of principal component analyses (PCA) in the case of unperturbed movements [1, 2].

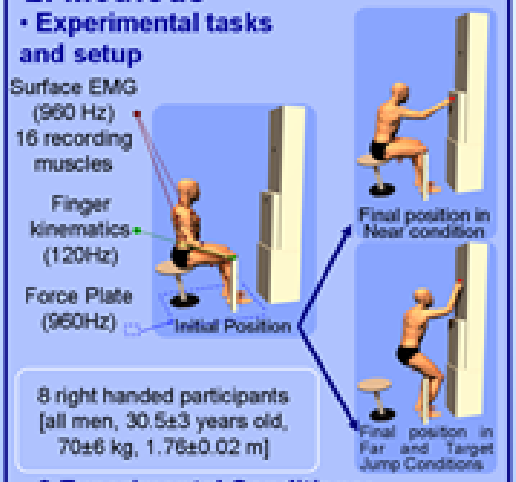
However, reaching movements can be altered at any time if the target location is changed during their execution. In this case, PCA does not precisely measure the latencies of muscles activities.

Consequently, the aim of this study is:

- **to develop a simple method to investigate how a random target jump toward a single location induced motor corrections in the whole musculature during a complex pointing movement.**
- **to investigate the latencies of muscular activities and the way they are correlated between certain muscles to stress the muscular synergies involved in the movement.**

2. Methods

• Experimental tasks and setup



8 right handed participants [all men, 30.5±3 years old, 70±6 kg, 1.76±0.02 m]

• 3 Experimental Conditions:

-**Near** : the near target was suddenly lit and remained lit throughout the movement (9/21).

-**Far**: the far target was suddenly lit and remained lit throughout the movement (9/21).

-**Target Jump**: the near target was initially lit and upon hand movement onset, was turned off and the far target was immediately turned on. (3/21)

-126 trials, 6 blocks of 21 trials, pseudo randomized

-Movements are performed as far as possible

•Data Analyses:

Correction Time: detected by a comparison at each value using t-tests between the Near and the Target Jump conditions [3].

Initiation Time: detected by a comparison at each value using t-tests between the baseline and the Near condition.

Synergetic organization: correlation coefficients were computed between values obtained for each subject and each muscle, for the 120 possible combinations (16 muscles x 15/2).

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3. Results

①EMG activities show a significant increasing 200ms in average after the target jump

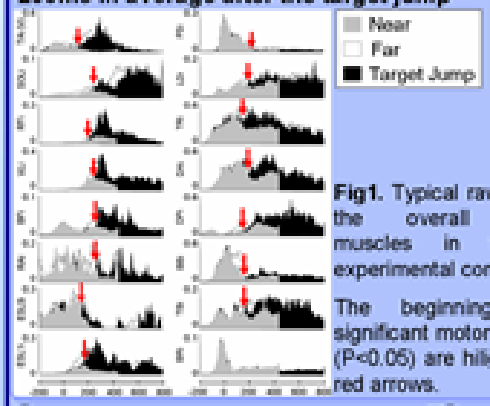


Fig1. Typical raw data from the overall recording muscles in the three experimental conditions.

The beginning of the significant motor corrections ($P<0.05$) are hilight with the red arrows.

Muscles Abbreviations

Tibialis Anterior: **TAi**
Soleus: **SOLi**
Rectus Femoris: **RFi**
Vastus Lateralis: **VLi**
Biceps Femoris: **BFi**
Rectus Abdominis: **RAi**
Erector Spinae at L5: **ESL5i**
Erector Spinae at L1: **ESL1i**
Pectoralis: **PSi**
Latissimus Dorsi: **LDi**
Trapezoid: **TRi**
Deltoidus Anterior: **DAi**
Deltoidus Posterior: **DPi**
Biceps Brachii: **BBi**
Triceps Brachii: **TBi**
Bracho Radialis: **BRi**

②Order of muscles recruitment are significantly different between the initiation and the correction.

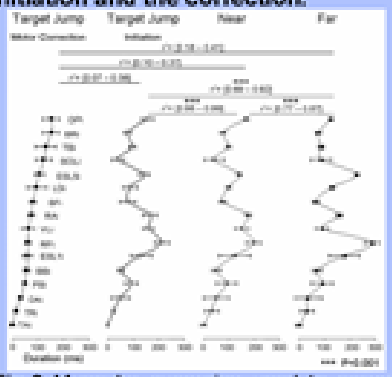


Fig.2 Muscular synergies used to correct (first column) or to initiate (second, third and fourth columns) the pointing movements.
The origin (0) of the temporal axis correspond to the first muscular activities.

③ More pairs of muscles are correlated during the motor correction than during the initiation.

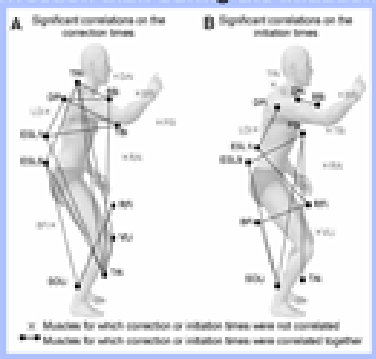


Fig.3 Significant correlations computed on correction times and initiation times.
A black line between two muscles represents a significant correlation ($P<0.05$).

4. Discussion

This study thus provides a simple method to investigate the latencies of muscular activities and the way they are correlated between certain muscles to stress the muscular synergies involved in the movement.

It suggests behavioural evidences that at the level of the Primary Motor Cortice (M1), muscles appear to be controlled as a coupled functional system, rather than individually and separately, according to the electrophysiological data obtained during brain mapping (4).

Catching falling objects: the role of the cerebellum in processing sensory-motor errors and in updating feeforward commands. An fMRI study.

L. Fautrelle[1,2], C. Pichat[4], F. Ricolfi[1,3], C. Peyrin[4], F. Bonnetblanc[1,2]

[1] INSERM, U887, Motricité Plasticité, Dijon; [2] Université de Bourgogne; [3] Service de Neuroradiologie, Hôpital Général, CHU de Dijon; [4] LPNC, CNRS UMR5105, Grenoble

lilian.fautrelle@u-bourgogne.fr

1. Introduction

•Human motor system continuously adapts to changes in their environment.

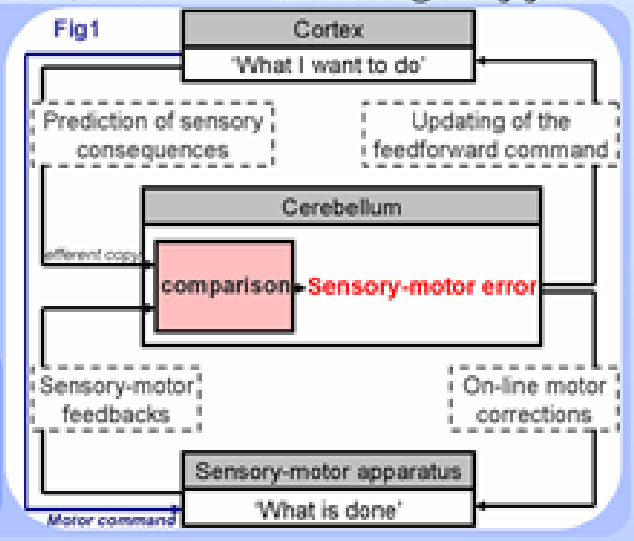
•To generate motor adaptations, central nervous system have to compare differences between the brain's predicted outcome of a certain behavior and the observed outcome (please see fig1) [1 2].

•Such a discrepancy signal is called sensory-motor error [1].

•It is assumed that cerebellum is a key structure in the processing of sensory-motor errors and in updating feeforward commands (please see fig1) [3 4].

Aim of this study: determine the main cerebellar structures involve in the processing of sensory-motor errors and in updating feedforward commands during a simple motor task.

Fig1



2. Materials & Methods

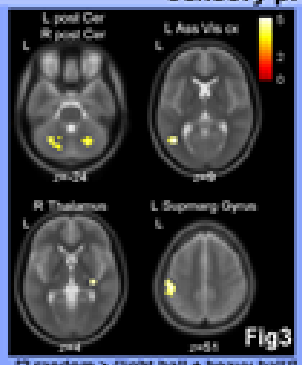
- **Subjects**
  - 16 healthy right handed participants
  - all males 27.9 ± 4.7 years old, 180.75 ± 5.6 cm, and 76.5 ± 7.6 kg
- **MRI acquisitions:**
  - EPI on a 3T MAGNETOM Trio (Siemens)
  - Repetition Time = 3050 ms
  - Echo Time = 45 ms
  - Voxel sizes = 3x3x3 mm
- **4 block sessions per subjects:**

Fig2

- **Experimental task**
  - •Subjects lying on their back
  - •A double-mirror allowed the subjects to see their right hand and the vertical trajectory of the falling balls (please see fig2).
- **•4 experimental conditions**
  - •Light balls (Ø = 6.5cm, 30g)
  - • Heavy balls (Ø = 6.5cm, 300g)
  - • Random (light or heavy balls)
  - • No vision (random and blindfolded subjects)

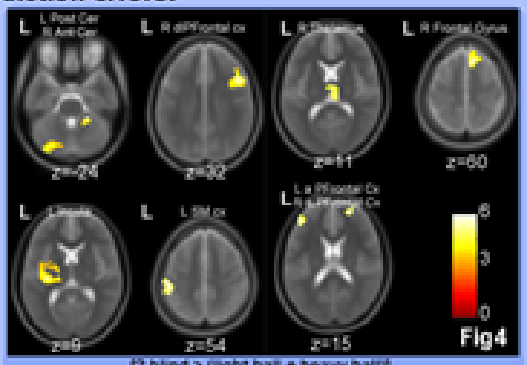
•Light and Heavy balls looked the same: participants could not know if the falling ball was heavy or light before catching it.

3. Results Cerebral regions specifically activated to process the sensory prediction errors:



[2 random > (light ball + heavy ball)]

P<0.001, uncorrected. L=Left, R=Right, post Cer=Left posterior portion of the cerebellum. Ass Vis cx=Associative visual cortex. SupMarg Gyrus=Supramarginal Gyrus.



[2 blind > (light ball + heavy ball)]

P<0.001, uncorrected. L=Left, R=Right, post Cer=Left posterior portion of the cerebellum. Ant Cer=Anterior portion of the cerebellum. A PFrontal Cx=anterior prefrontal cortex. dlPFrontal cx=dorsolateral prefrontal cortex. SM cx=primary sensory motor cortex.

Contrast	Region	H	BA	k	x	y	z	T
[2*random > (light ball + heavy ball)]	right posterior cerebellum (Lobule VI)	R		33	24	-65	-24	5.46
	occipito-temporal cortex	L	19/39	40	-45	-61	9	5.13
	left posterior cerebellum (Lobule VI)	L		52	-30	-62	-22	4.99
	supramarginal gyrus	L	40	25	-48	-32	51	4.63
	thalamus	R		23	30	-28	4	4.52
[2*blind > (light ball + heavy ball)]	insula	L		817	-33	-20	9	6.93
	[premotor cortex and SMA]	L			-56	4	22	6.09
	dorsolateral prefrontal cortex	R	9	188	50	16	32	6.62
	frontal gyrus	R	8	143	9	18	60	6.54
	right anterior cerebellum (Lobule IV)	R		29	24	-39	-23	6.13
	anterior prefrontal cortex	R	10	83	24	53	14	5.98
	anterior prefrontal cortex	L	10	47	-42	42	15	5.75
	left posterior cerebellum (Lobule VI)	L		79	-21	-77	-26	5.49
	thalamus	R		120	3	-18	12	5.45
	primary sensory motor cortex	L	1/2	110	-48	-29	57	5.33

For each cluster ($p < 0.001$ uncorrected), the region showing the maximum T value is listed first, followed by the others belonging to the cluster [between brackets]. The cerebellum lobules are reported according to [5]. (x, y, z) = Talairach coordinates; BA = Brodman Area; H: L=left R=right hemisphere; k = number of voxels in the cluster

Voxel size: 3x3x3 mm

5.Conclusions & Discussion

When repetitively catching falling balls with no possibility to predict the ball weight, our results showed that both the right and left cerebellum is engaged to process sensory-motor errors and to update feedforward motor commands, perhaps on a trial by trial basis.

In addition, when subjects were blindfolded, we observed a more anterior network in the right cerebellum and we identified a cerebellar-thalamo-prefrontal network that may be involved in cognitive prediction (rather than sensory prediction) about the ball weight.

6. References

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