Université de Montréal

Étude des processus inhibiteurs de la mémoire de travail dans le vieillissement normal et la démence de type Alzheimer

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Cette thèse intitulée:

Étude des processus inhibiteurs de la mémoire de travail dans le vieillissement normal et dans la démence de type Alzheimer

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Sommaire

La neuropsychologie du vieillissement s'intéresse entre autres à la différenciation cognitive entre les personnes âgées présentant un processus normal de vieillissement et celles présentant un processus pathologique, tel une démence. En raison de sa prévalence élevée, la démence de type Alzheimer fait l'objet de plusieurs études qui ont comme objectif commun de mettre en évidence des différences quantitatives et qualitatives avec le vieillissement cognitif normal. Le but de la présente thèse est de contribuer à cette caractérisation neuropsychologique du vieillissement normal et pathologique en ce qui a trait aux processus inhibiteurs de la mémoire de travail.

La première partie de la thèse porte sur le vieillissement normal et vise à mieux comprendre le fonctionnement de l'administrateur central, la composante attentionnelle de la mémoire de travail, chez les sujets âgés. Dans une perspective de fractionnement de l'administrateur central, nous nous intéresserons à ses capacités d'inhibition que nous opposerons à ses capacités de manipulation. Ces deux fonctions sont évaluées en égalisant à travers les groupes les niveaux de base de maintien. Le premier article de la thèse présente les résultats obtenus chez des sujets jeunes et âgés à une tâche de mémoire de travail sollicitant l'inhibition. Les sujets ont complété une tâche d'empan visuel de chiffres, pendant laquelle ils entendaient différents bruits devant être inhibés (*"irrelevant speech effect"* - ISE). Nos résultats dans deux expériences indiquent que les sujets âgés ne montrent aucune difficulté particulière à inhiber des distracteurs phonologiques lorsqu'ils doivent effectuer simultanément une tâche de mémoire de travail. Le second article rapporte les capacités de manipulation dans le vieillissement normal. Dans une tâche de rappel alphabétique, les sujets devaient rappeler une liste de mots qu'ils

devaient préalablement replacer mentalement dans leur ordre alphabétique. Nous avons montré que cette tâche sollicite l'administrateur central de la mémoire de travail, puisque chez des sujets jeunes, elle est affectée par une double-tâche. Or, trois expériences ont montré que les sujets âgés avaient une performance comparable à celle des sujets jeunes sur cette tâche. Ces différentes expérimentations montrent donc une absence d'effet lié à l'âge sur les tâches d'administrateur central mesurant l'inhibition phonologique et la manipulation. Ces résultats remettent en question l'hypothèse d'un trouble massif de l'administrateur central dans le vieillissement normal.

La mise en évidence de fonctions cognitives préservées par l'effet du vieillissement normal pourrait contribuer à la caractérisation de la maladie d'Alzheimer dans la mesure où elle permet l'observation de dissociations neuropsychologiques entre les deux groupes. La seconde partie de la thèse s'intéresse à l'étude des processus attentionnels en mémoire de travail dans la démence de type Alzheimer. Le troisième article porte sur les capacités de manipulation et d'inhibition en mémoire de travail dans la maladie d'Alzheimer. L'utilisation de la tâche d'ISE et de rappel alphabétique a permis de montrer une préservation de l'inhibition de distracteurs phonologiques chez la plupart des patients Alzheimer, mais aussi une atteinte sévère des capacités de manipulation. Le quatrième article évalue de façon plus détaillée différents aspects liés à l'inhibition. Par l'utilisation de la tâche d'amorçage négatif, nous avons montré certains déficits chez les patients Alzheimer, qui sont qualitativement différents de ceux des personnes âges saines. Ils montrent ainsi une facilitation dans la condition d'inhibition de retour à la tâche d'amorçage négatif. De plus, les patients montrent une atteinte accrue de l'habituation à cette même tâche, ainsi que de l'inhibition sémantique, au test de Hayling. La sensibilité à l'interférence par contre, telle que mesurée par le Stroop, est augmentée dans le vieillissement normal mais non dans la maladie d'Alzheimer. Les résultats montrent des atteintes spécifiques à la maladie d'Alzheimer et les dissociations observées appuient l'hypothèse du fractionnement de l'administrateur central de la mémoire de travail.

Table des matières

Liste des figures

Introduction

Article n° 1

Article n° 2

Liste des tableaux

Article n° 1

Article n° 2

Article n° 4

Liste des abréviations

AC:	Administrateur central
AN:	Amorçage négatif (negative priming)
DTA:	Démence de Type Alzheimer
ISE:	Irrelevant speech effect
MdeT:	Mémoire de travail

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Chapitre I:

INTRODUCTION

La caractérisation du fonctionnement cognitif dans le vieillissement normal et pathologique est une problématique importante en neuropsychologie. Le vieillissement cérébral normal entraîne certaines dysfonctions cognitives, lesquelles sont difficilement distinguables de celles associées à un début de vieillissement pathologique, tel la maladie d'Alzheimer. Il est donc essentiel de préciser les atteintes spécifiques au processus pathologique de vieillissement et de mettre en évidence ses aspects qualitativement différents des atteintes reliées au vieillissement normal afin d'augmenter la validité du diagnostic de la maladie. Le premier objectif de cette thèse est d'ordre clinique puisqu'il consiste à contribuer à la caractérisation neuropsychologique du vieillissement normal et pathologique. Le second objectif est théorique et consiste en la précision des modèles cognitifs de l'inhibition et de la mémoire de travail.

Cette thèse est présentée sous forme de quatre articles. L'introduction a pour but d'exposer les éléments de la littérature nécessaire à la compréhension des articles, de les situer dans un contexte plus général et d'en préciser le fil directeur. Pour cela, le modèle théorique de référence de la mémoire de travail et ses différentes composantes seront d'abord présentés (Section 1) avec une attention particulière portée à la composante administrateur central. Ensuite, la Section 2 exposera la notion d'inhibition. Par la suite, nous présenterons certaines des données portant sur le substrat neuroanatomique de l'administrateur central et de l'inhibition (Section 3). Une section présentera les atteintes de l'administrateur central et de l'inhibition observées dans le vieillissement normal et exposera une théorie explicative du vieillissement normal faisant appel au déclin des processus inhibiteurs (Section 4). Enfin, la dernière section de l'Introduction abordera ces différents aspects tels qu'évalués chez des patients souffrant de démence de type Alzheimer.

1. La Mémoire de Travail

La mémoire de travail (MdeT) est conçue comme un système temporaire de maintien et de traitement de l'information. Elle est sollicitée dans toute tâche cognitive exigeant simultanément le maintien et la manipulation de matériel, comme par exemple le calcul mental, la résolution de problèmes et la compréhension du langage. L'évaluation classique de la MdeT consiste en une mesure d'*empan*: le sujet doit restituer une série d'items dans leur ordre de présentation, c'est-à-dire effectuer un *rappel sériel immédiat*. La série d'items la plus longue ainsi rappelée correspond à l'empan du sujet. La MdeT est un système à capacité limitée (Miller, 1956) et se distingue donc de la mémoire à long terme, dont la capacité est vaste et qui emmagasine des traces permanentes. Le modèle de Baddeley et Hitch (1974; Baddeley, 1986), élaboré pour rendre compte des effets expérimentaux reliés à l'empan, se veut actuellement une des références théoriques les plus influentes dans ce domaine.

Selon ce modèle, la MdeT est composée de trois principaux sous-systèmes (voir Figure 1)

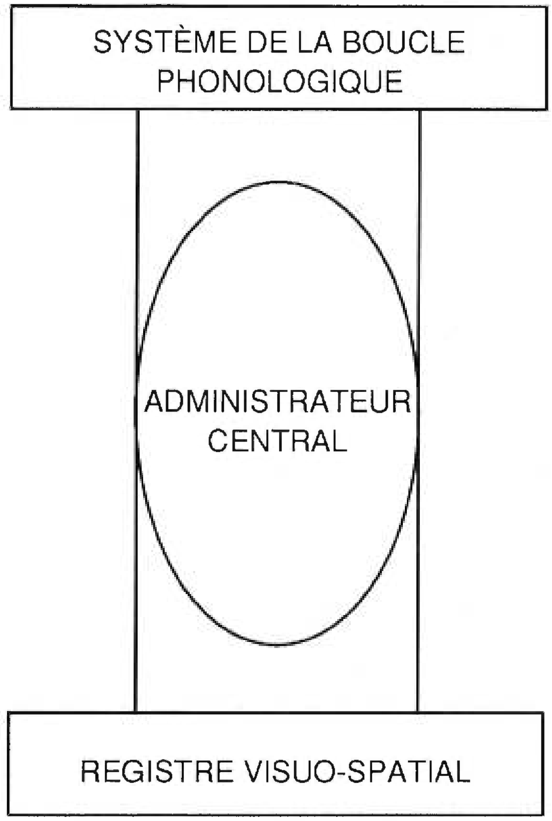

Figure 1. Modèle théorique de la mémoire de travail selon Baddeley (1986).

La *boucle phonologique* est responsable du maintien des informations verbales (chiffres, lettres, mots) et la *voie visuo-spatiale*, de celui des informations non verbales, visuelles et spatiales. L'*administrateur central* quant à lui, coordonne le fonctionnement de ces deux systèmes esclaves et est responsable de la gestion attentionnelle en MdeT. Dans les prochaines sections, nous décrirons le fonctionnement de la boucle phonologique et de l'administrateur central, les deux composantes autour desquelles s'articulent les hypothèses liées à ce travail.

1.1 La boucle phonologique

Deux principaux sous-systèmes composent la boucle phonologique (voir Figure 2). Le *registre phonologique* (ou *système de stockage phonologique*) maintient les informations verbales sous un code phonologique, pour une durée de quelques secondes. Lorsque la tâche en cours l'exige, le matériel peut être maintenu plus longuement par auto-répétition. L'auto-répétition est effectuée par la *procédure de répétition subvocale*. Cette dernière est aussi responsable du transfert de l'information verbale présentée en modalité visuelle au registre phonologique. En effet, les informations présentées auditivement parviennent obligatoirement et directement au registre phonologique et y sont maintenues sous un code phonologique. Cependant, les informations acheminées par la modalité visuelle n'accéderaient au registre phonologique que par la procédure de répétition subvocale (voir Figure 2).

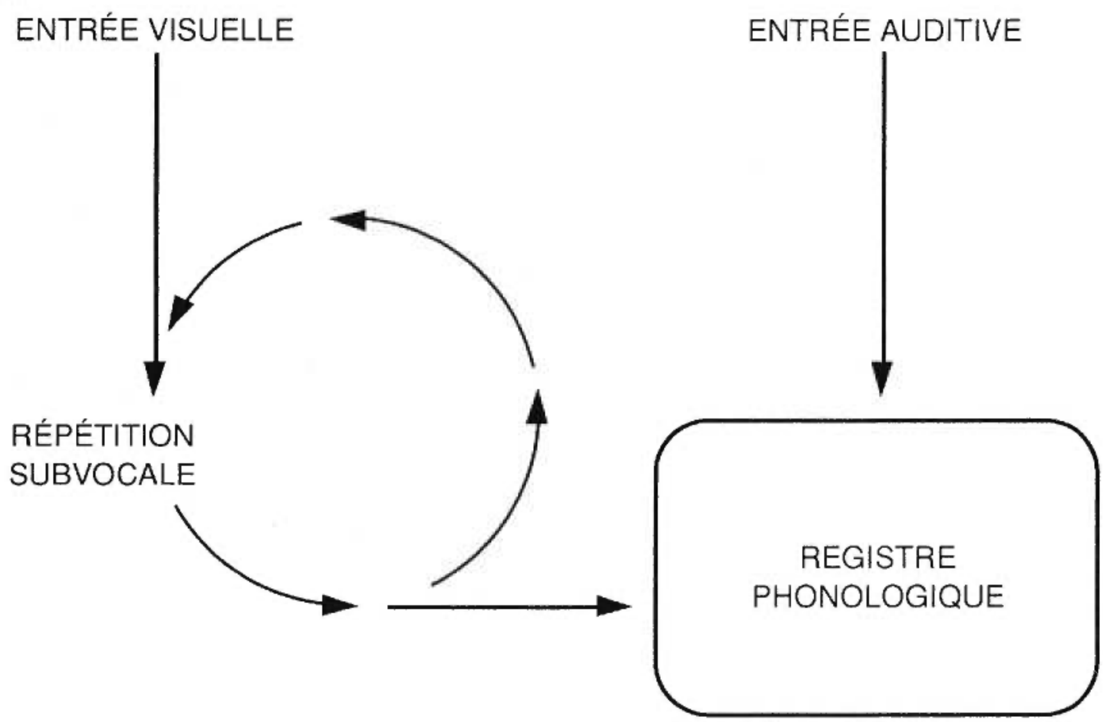

Figure 2. Modèle théorique de la boucle phonologique selon Baddeley (1986).

Cette organisation de la boucle phonologique repose sur l'observation d'effets robustes mis en évidence sous certaines conditions expérimentales. Ces effets sont d'ailleurs utilisés en neuropsychologie pour évaluer le fonctionnement de la boucle phonologique chez les patients cérébrolésés. L'*effet de similarité phonologique*, caractérisé par un rappel sériel immédiat inférieur pour des items ayant la même sonorité (par exemple: b-v-d) comparativement à des items ne la partageant pas (par exemple: k-f-j), est expliqué par une interférence accrue lors de la récupération lorsque les codes phonologiques des items sont proches (Baddeley, 1966; Conrad & Hull, 1964). L'observation de l'effet de similarité phonologique chez un individu signifie qu'il utilise son registre phonologique pour mémoriser. L'effet disparaît sous suppression articulatoire (répétition continue d'un segment verbal non-pertinent, comme par exemple "bla") lorsque les items sont présentés dans la modalité visuelle. L'interprétation de ce phénomène est que la suppression articulatoire occupe la procédure de répétition subvocale et bloque ainsi l'accès au registre phonologique pour les items lus. D'ailleurs, en présentation auditive, la suppression articulatoire n'annule pas l'effet de similarité phonologique puisque l'entrée par la modalité auditive conduit à un accès direct au registre phonologique (voir Figure 2).

Par ailleurs, l'*effet de longueur du mot* définit le meilleur rappel pour des mots courts (par exemple: pain-jupe-sac) que pour des mots longs (par exemple: bibliothèque, médicament, anniversaire) (Baddeley, Thomson & Buchanan, 1975). Les mots courts, pouvant être articulés plus rapidement, seraient auto-répétés et maintenus plus efficacement. L'effet de longueur du mot réflèterait donc le fonctionnement de la procédure de répétition subvocale. D'ailleurs, sous suppression articulatoire, l'effet de longueur du mot est annulé et ce, dans les deux modalités (voir Figure 2).

1.2 L'administrateur central

La majorité des travaux portant sur la MdeT se sont intéressés aux systèmes esclaves, soit la voie visuo-spatiale et tout particulièrement la boucle phonologique. Par conséquent, l'administrateur central (AC) est une composante dont on connaît moins bien le fonctionnement (Baddeley, 1996). Paradoxalement, Baddeley attribue à l'AC des fonctions qui apparaissent essentielles non seulement à la MdeT, mais aussi à l'ensemble du système cognitif. Selon Baddeley, le *système de supervision attentionnel* (*"supervisory attentional system"* - SAS) du modèle du contrôle de l'action de Norman & Shallice (1986) pourrait refléter le fonctionnement de l'AC. Ce modèle sera décrit dans le second article de la thèse, mais rappelons que le SAS est responsable de la modulation du comportement. Dans les situations routinières, les schémas appropriés sont activés et la résolution des conflits simples se fait de façon semi-automatique. Par contre, dans les situations nouvelles, dangereuses, complexes, l'action doit être contrôlée par le SAS, qui modifie les niveaux d'activation des schémas (ou des sous-schémas) de façon à ce que l'action adéquate soit réalisée.

Récemment, certains auteurs ont tenté de mieux comprendre le fonctionnement de l'AC et en ont proposé le fractionnement (Stuss, Shallice, Alexander & Picton, 1995; Baddeley, 1996). Le fractionnement de l'AC en sous-composantes plus restreintes le rendrait évidemment plus opérationnalisable. Burgess & Shallice (1994), par l'utilisation et la recension de plusieurs tâches effectuées auprès de patients porteurs de lésions frontales, suggèrent la dissociation des fonctions exécutives. De la même façon, Stuss et al. (1995) appuient le fractionnement du SAS, ou de l'AC, et proposent même des fonctions précises, chacune étant associées à des épreuves neuropsychologiques reconnues en clinique. Ainsi, des fonctions de mise à jour, de gestion de l'attention, de flexibilité et d'inhibition ont entre autres été proposées.

Dans une perspective de fractionnement de l'AC, nos travaux s'intéressent à une de ces fonctions, soit l'*inhibition*. De plus, nous comparerons l'inhibition aux capacités de *manipulation* de la MdeT. La manipulation est définie comme l'action de modifier activement et consciemment le format de l'information maintenue dans la MdeT avant de la rappeler. Par définition, la MdeT est non seulement un simple système de maintien passif mais aussi de manipulation active des informations (Baddeley, 1986). Dans diverses situations cognitives, le matériel encodé en MdeT doit donc être modifié et manipulé avant d'être rappelé, ou avant de poursuivre son traitement. Par ailleurs, l'inhibition joue un rôle important dans l'attention sélective en permettant aux stimuli non-pertinents de ne pas perturber la performance du sujet. Selon Baddeley (1996), le contrôle des stimulations non-pertinentes dépend largement de l'AC présumément par ses fonctions inhibitrices. Selon Hasher & Zacks (1988), une atteinte des processus inhibiteurs (notamment dans le vieillissement normal, voir Section 4.2) occasionnerait une surcharge d'éléments en MdeT. Cette surcharge diminuerait l'efficacité de la MdeT et aurait par conséquence diverses répercussions négatives sur le fonctionnement cognitif des sujets. Pour d'autres auteurs (Engle, 1995), l'inhibition n'est pas conçue comme une fonction isolée, mais est plutôt le produit du contrôle des ressources attentionnelles. Une telle conception ne va cependant pas nécessairement à l'encontre de la proposition selon laquelle l'inhibition serait une fonction de l'AC, puisque selon

Baddeley (1986), l'AC serait responsable de la gestion des ressources attentionnelles en mémoire de travail (Baddeley, 1986). Enfin, l'inhibition représente une élément essentiel du fonctionnement du SAS dans le modèle du contrôle de l'action de Shallice (Norman & Shallice, 1986; Stuss et al, 1995) en intervenant directement dans la modulation des schémas lors de situations nouvelles et complexes. Or depuis quelques années, l'inhibition a fait l'objet d'un nombre important de travaux chez le sujet normal dans le contexte des études sur l'attention sélective. Ces travaux ont permis de circonscrire le fonctionnement et le rôle de l'inhibition et seront résumés dans la prochaine section.

2. Les processus inhibiteurs

L'inhibition est définie comme étant un processus cognitif qui permet la suppression active de l'information distractrice (Hamm & Hasher, 1992). Pour la plupart des auteurs, elle est conçue comme l'une des deux composantes de l'attention sélective: l'*activation* (ou *amplification*) traite les informations pertinentes à la tâche en cours, tandis que l'*inhibition* supprime les informations non-pertinentes. Ces deux systèmes agiraient de façon simultanée et parallèle, afin d'assurer une sélection attentionnelle efficace.

L'inhibition a été l'objet de plusieurs écrits en psychologie cognitive (cf. Dempster & Brainerd, 1995, pour une revue historique). Depuis quelques années, l'intérêt envers l'inhibition est croissant et ce, dans divers domaines de la cognition, tels le langage (Gernsbacher & Faust, 1991; Arbuckle & Gold, 1993), l'attention

(Tipper, 1985), la mémoire à long terme (Gérard, Zacks, Hasher, & Ravandsky, 1991), et la MdeT (Hasher & Zacks, 1988).

2.1 La tâche d'effet d'écoute inattentive et la procédure d'amorçage négatif comme mesure de l'inhibition

La tâche d'effet d'écoute inattentive (*"irrelevant speech effect"* - ISE) consiste en un rappel sériel immédiat de chiffres présentés visuellement, simultanément à l'inhibition de bruits distracteurs (Salamé & Baddeley, 1982). Typiquement, la performance de mémoire est affectée par la présence de bruits verbaux et est laissée intacte lorsque ces derniers sont non verbaux. De plus, l'intensité, l'amplitude ou le contenu sémantique des bruits ne modifie aucunement l'effet. D'après le modèle de de Baddeley (1986), les bruits verbaux et les items verbaux à mémoriser interféreraient au sein du registre phonologique de la MdeT, entraînant une chute du rappel. Cette tâche n'a cependant jamais été administrée à des sujets âgés, ou à des populations cliniques montrant un déficit inhibiteur. Selon nous, un déficit d'inhibition devrait entraîner un effet d'écoute inattentive accru chez les sujets.

La procédure d'*amorçage négatif* (AN) (ou *"negative priming"*) est reconnue comme étant la méthode classique d'évaluation de l'inhibition. Considérant que la sélection attentionnelle s'effectue simultanément via les systèmes d'activation et d'inhibition, une mesure isolée des processus inhibiteurs s'avère extrêmement difficile au plan méthodologique. Or le paradigme d'AN permet d'isoler l'inhibition d'un stimulus de son activation. Dans le paradigme d'AN, le sujet voit apparaître deux stimuli à l'écran d'un ordinateur (soit des lettres, des mots, ou des images). Un essai est toujours composé de deux présentations, soit l'amorce (ou *"prime"*) et le test (ou *"probe"*), chacun étant composé de deux stimuli (voir Figure images). Un essai est toujours composé de deux présentations, soit l'amorce (ou *"prime"*) et le test (ou *"probe"*), chacun étant composé de deux stimuli (voir Figure 3). L'un des stimuli est présenté en rouge (cible) et l'autre en vert (distracteur). La tâche du sujet consiste à dénommer le stimulus rouge le plus rapidement possible tout en ignorant le vert.

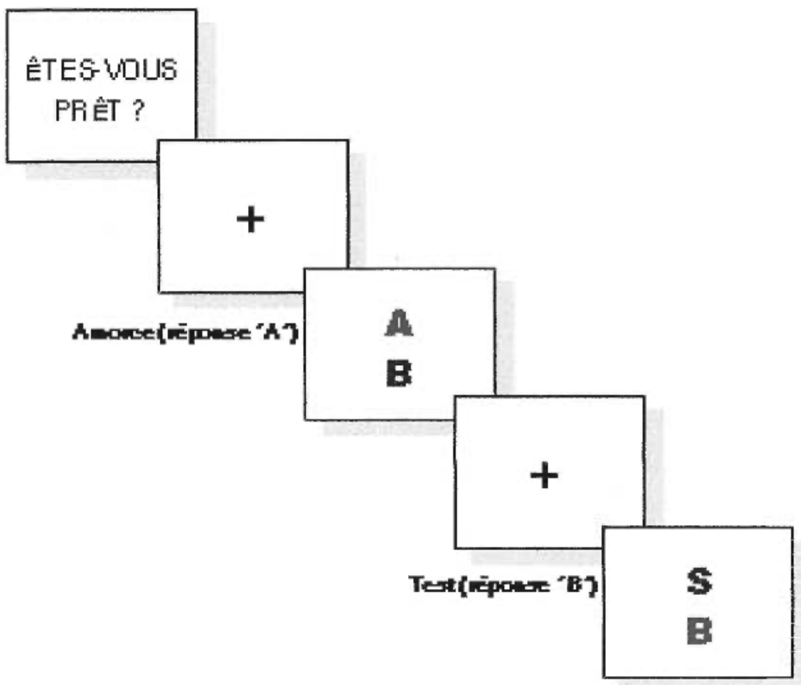

Figure 3. Procédure expérimentale de la tâche d'amorçage négatif (les lettres en rouge représentent les cibles et celles en vert, les distracteurs).

Dans la condition contrôle, les stimuli sont différents et n'entretiennent aucun lien entre eux. Dans la condition d'inhibition par contre, le stimulus ayant servi de distracteur à l'amorce (vert) devient la cible au test (rouge). Le temps de réaction associé à la condition d'inhibition est significativement plus élevé que celui associé à la condition contrôle (voir Figure 4).

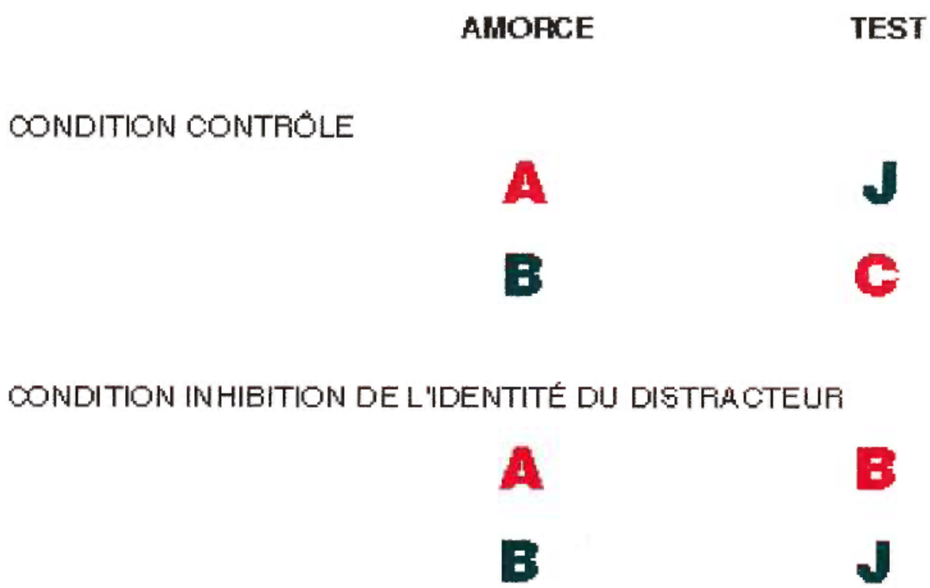

Figure 4. Exemple des conditions expérimentales utilisées dans la tâche d'amorçage négatif (les lettres en rouge représentent les cibles et celles en vert, les distracteurs).

L'interprétation de cet effet est que le distracteur doit être activement inhibé afin d'effectuer la sélection dans l'amorce. Lorsque ce distracteur devient la cible à la présentation subséquente, l'inhibition résiduelle portée sur ce dernier ralentit le développement de l'activation nécessaire à sa dénomination, d'où l'augmentation du temps de dénomination. Cette augmentation du temps de dénomination est reconnue comme étant le marqueur attentionnel de l'inhibition et son absence est généralement interprétée comme signalant un déficit des processus inhibiteurs (Connelly & Hasher, 1993; Kane et al., 1994; Stoltzfus et al., 1993; Tipper, 1991). L'AN permet donc de quantifier précisément l'inhibition dirigée vers un distracteur en particulier et même de contrôler certaines variables méthodologiques pour étudier l'inhibition sous différentes conditions. Ce paradigme a aussi significativement

2.2 Interprétations alternatives des effects d'amorçage négatif

L'interprétation de l'effet d'AN décrite plus haut dans le contexte de *l'inhibition sélective* (Tipper, 1985) est actuellement la principale dans la littérature. Cependant, elle est contestée par certains auteurs, qui suggèrent deux hypothèses alternatives. L'hypothèse de *l'incompatibilité de traits* (Park & Kanwisher, 1994) avance que le ralentissement observé dans la condition d'inhibition apparaît lorsque la cible du test diffère du stimulus ayant occupé sa position spatiale à la présentation précédente (amorce) et ce, indépendamment du fait que ce stimulus ait été cible ou distracteur. Un conflit entre les codes attribués aux stimuli dans les présentations successives et non une inhibition dirigée vers le stimulus distracteur de l'amorce serait responsable de l'effet. La deuxième hypothèse alternative est celle de la *récupération épisodique* (Neill & Valdes, 1992). Selon cette hypothèse, la présentation du test induit une récupération automatique de l'épisode précédent (amorce), qui peut contenir de l'information sur l'identité, la position spatiale et le statut (i.e. cible ou distracteur) du stimulus et sa réponse. Un conflit entre les codes attribués à la présentation antérieure (amorce) et ceux attribués aux mêmes stimuli à la présentation subséquente (test) obligent une résolution, ce qui augmente le temps de traitement. Bien que pertinentes, ces deux dernières hypothèses reçoivent moins d'appui dans la littérature (pour une revue voir Fox, 1995). D'ailleurs, il a entre autres été montré que de courts intervalles entre la présentation des stimuli (*"stimulus onset asynchrony"* - SOA) peuvent entraîner de la facilitation, contrairement à des SOA plus longs, qui entraînent de l'amorçage négatif (Yee, 1991). L'inhibition nécessiterait donc un certain temps pour se développer et se manifester. Si l'amorçage négatif était causé par une incompatibilité entre les traits ou les codes en mémoire, le SOA ne devrait pas influencer l'apparition d'inhibition. En effet, une incompatibilité devrait se manifester tôt, peu importe le SOA utilisé.

Par ailleurs, d'autres questionnements théoriques portent sur l'objet de l'inhibition, sa flexibilité, son niveau d'opération, sa persistence, ou sa fonction précise (pour une revue, voir Fox, 1995). Plusieurs auteurs étudient l'AN et les différentes variables méthodologiques l'influençant dans le but d'améliorer la compréhension de ce phénomène empirique chez le sujet normal. Néanmoins, la plupart s'entendent pour proposer qu'elle mesure les fonctions inhibitrices en attention sélective. C'est dans ce contexte que la procédure d'AN sera utilisée ici, c'est-à-dire comme tâche d'inhibition classique nous permettant d'étudier l'effet du vieillissement sur les processus inhibiteurs.

2.3 La fonction de l'inhibition et sa relation avec l'interférence

Tel que décrit précédemment, les processus inhibiteurs jouent donc un rôle majeur dans la cognition. Cependant, la fonction précise de l'inhibition demeure toujours un sujet d'investigation. Dans la littérature, deux hypothèses ont été émises à ce sujet.

L'hypothèse la plus ancienne, la *pré-sélection*, avance que la fonction de l'inhibition serait d'agir pendant la sélection des stimuli, afin de réduire l'interférence causée par la présence de distracteurs (Tipper, 1985; Tipper & Baylis, 1987). Dans ce cas, la fonction de l'inhibition, parallèle à celle des processus d'activation, serait de permettre une meilleure sélection attentionnelle en supprimant les informations distractrices. Simultanément à la question théorique de la fonction de l'inhibition est donc inévitablement soulevée celle concernant le lien existant entre les processus d'inhibition et le concept d'interférence. Pour les auteurs appuyant cette première hypothèse, l'inhibition et l'interférence sont reliées et covarient: meilleure est l'inhibition, moins forte est l'interférence. Selon ce point de vue, l'effet d'AN et la mesure de l'interférence devraient être corrélés puisqu'ils seraient tous deux sous-tendus par l'inhibition.

Par ailleurs, la seconde hypothèse suggère une fonction différente de l'inhibition, soit celle de supprimer les stimuli préalablement identifiés comme distracteurs lors de la sélection, afin que ces derniers ne soient pas réactivés et ne puissent interférer avec la tâche en cours (Stoltzfus et al., 1993; Tipper, Weaver, Cameron, Brehaut & Bastedo, 1991). Conséquemment, l'inhibition n'agirait pas pendant la sélection, tel que suggéré par la première hypothèse, mais plutôt *post-sélection*. Selon ce point de vue, l'inhibition et l'interférence ne sont donc pas conçus comme étant des phénomènes corrélés. La fonction de l'inhibition serait de permettre le flot continu de la pensée, du discours et du comportement, en inhibant des représentations déjà activées et/ou traitées et perturbant la tâche en cours. Certains auteurs ont même proposé une distinction théorique et empirique entre l'inhibition et l'interférence. L'*interférence* réfèrerait à la mesure de la diminution de performance associée à la présence et à la compétition de plusieurs informations distractrices (Harnishfeger, 1995). Elle diffèrerait de l'*inhibition*, dans la mesure où cette dernière serait dirigée directement vers un ou plusieurs stimuli identifiés comme distracteurs afin de supprimer leur activation. L'interférence pour sa part s'observerait en présence de plusieurs informations perçues simultanément et affectant le temps de traitement de l'information cible. En ce sens, l'interférence pourrait, contrairement à l'inhibition, être mise en évidence avec des stimuli encore non activés et n'ayant pas nécessairement de représentations.

Il existe donc deux points de vue différents sur le lieu ou la fonction de l'inhibition et par le fait même, sur la relation entre les concepts d'inhibition et d'interférence. Malgré tout, la distinction entre ces deux concepts reste extrêmement vague et finalement relativement ténue. Néanmoins, dans le cadre des travaux présentés ici, un effort a été fait pour utiliser des tâches ou des conditions expérimentales qui permettent une mesure indépendante de l'interférence et de l'inhibition afin de vérifier si elles sont atteintes de façon concommitante chez nos sujets.

3. Substrats neuroanatomiques de l'administrateur central et de l'inhibition

Nous avons présenté l'AC comme un système indépendant au sein de la MdeT et l'inhibition comme une fonction de l'AC. L'existence de systèmes indépendants et distincts l'un de l'autre implique aussi que leur substrat neuroanatomique soit distinct. Des arguments émanant de la neuropsychologie appuient l'autonomie de ces systèmes. Par exemple, la boucle phonologique et la répétition subvocale peuvent être endommagées de façon isolée lors d'un dommage cérébral (Vallar & Baddeley, 1984; Belleville et al, 1992). La composante AC pourrait aussi être atteinte par un dommage cérébral sans que les systèmes esclaves ne le soient (Van der Linden, 1992; Morris, 1986; Belleville et al, 1996). La présence de telles dissociations appuie l'hypothèse selon laquelle ces systèmes sont indépendants.

Certaines études ont tenté de localiser neuroanatomiquement par différentes techniques d'imagerie (Pet-scan) et par l'étude de patients cérébrolésés, les différents sous-systèmes de la MdeT. Par exemple, le registre phonologique serait localisé au niveau du gyrus supramarginal gauche, tandis que la procédure de répétition subvocale serait associée à l'aire de Broca (Paulesu, Frith, & Frackowiak, 1993). La localisation de l'AC est moins claire. Néanmoins, des hypothèses concernant le cortex pré-frontal (Baddeley, 1986, 1990; Shallice, 1988; Stuss & Benson, 1986), et le cortex frontal dorsolatéral bilatéral (D'Esposito et al., 1995) ont été émises sur la base d'études de patients cérébrolésés et d'études d'imagerie. D'autres auteurs proposent que l'atteinte de l'administrateur central serait observée suite à des lésions touchant à la fois le cortex pré-frontal, pariétal et temporal (pour discussion voir Morris, 1994). Certains auteurs ont suggéré que l'inhibition serait sous le contrôle des lobes pré-frontaux (Stuss & Benson, 1986; Moscovitch & Winocur, 1996; Shallice, 1988). Cette hypothèse biologique permet de circonscrire les populations cliniques à risque de montrer un déficit de l'inhibition. Ainsi, les performances des personnes âgées sont fréquemment interprétées comme résultant d'un déclin des fonctions frontales (Duncan, 1993; Moscovitch & Winocur, 1996; West, 1996). Cette hypothèse est compatible avec une atteinte de l'AC et de l'inhibition dans le vieillissement.

4. Administrateur central et inhibition dans le vieillissement normal

4.1 L'administrateur central

Plusieurs travaux ont porté sur l'effet du vieillissement normal sur le fonctionnement de la MdeT (Craik, 1977; Feyereisen & Van der Linden, 1992; Foos, 1989; Light & Anderson, 1985; Salthouse, 1990; 1994; Wright, 1981). La plupart des premières études dans ce domaine utilisaient toutefois des tâches relativement grossières, telles l'empan, qui ne permettaient pas de déterminer quelles composantes de la MdeT étaient atteintes. Des travaux plus récents ont procédé à l'évaluation spécifique de chaque sous-composante de la MdeT et ont permis de dresser une première esquisse de la nature du dysfonctionnement lié à l'âge. Ainsi, les systèmes esclaves semblent préservés des effets du vieillissement normal car les personnes âgées montrent des effets normaux de similarité phonologique et de longueur du mot (Belleville et al., 1996; Morris, 1984). Toutefois, une gestion attentionnelle moins efficace, une difficulté dans la coordination des tâches et une allocation déficitaire des ressources attentionnelles seraient observées chez le sujet âgé, suggérant une atteinte de l'AC (Baddeley, 1986; Gick & Craik, 1986; Van der Linden et al., 1994). Ainsi, certains auteurs ont montré des difficultés dans la mise à jour du contenu de la MdeT, une fonction qui serait sous le contrôle de l'AC (Van der Linden et al., 1994). Par la mise à jour, l'AC élimine de la MdeT les items devenus non pertinents afin de pouvoir traiter plus efficacement les items pertinents. De plus, certaines études montrent un déficit chez les sujets âgés lorsque ces derniers doivent manipuler les informations maintenues en MdeT (Craik, 1986; Dobbs & Rule, 1989; Wright, 1981). Par contre, d'autres études ne montrent pas de déficit de l'AC chez les sujets âgés (Baddeley, Logie, Bressi, Della Sala & Spinnler, 1986; Salthouse, 1992; Della Sala & Logie, 1993). Par exemple, l'utilisation d'une tâche d'attention divisée impliquant une épreuve d'empan de chiffres simultanément à une poursuite visuo-motrice permet de montrer une performance équivalente entre les sujets jeunes et âgés (Baddeley et al., 1986).

Les données suggérant un trouble de l'AC dans le vieillissement normal apparaissent donc contradictoires. Or, ces résultats discordants pourraient éventuellement s'expliquer par une différence méthodologique importante entre les études. En effet, les travaux dans ce domaine cherchent généralement à mettre en évidence une interaction entre le facteur âge et un facteur expérimental (par exemple le fait qu'une tâche soit réalisée en attention complète ou en attention divisée). Or, ces études observent généralement aussi un effet principal de l'âge. Cet effet principal pourrait être responsable de l'interaction (Salthouse, 1985; Loftus, 1978). Un tel problème peut survenir pour plusieurs raisons. D'abord, on ne connaît généralement pas la forme de la fonction entre une variable et un comportement. Par conséquent, une variable indépendante peut avoir un effet différent chez les jeunes et les âgés parce que chaque groupe se situe à un niveau différent de la fonction. À titre d'exemple, il est possible que la division attentionnelle ait davantage d'impact sur une capacité de mémoire faible que sur une capacité de mémoire plus forte et ce, sans égard à l'âge. De plus, la présence d'un effet plancher chez des sujets âgés ou d'un effet plafond chez les jeunes pourrait être la cause d'une interaction menant à l'interprétation d'un déficit chez les sujets âgés. Ces interactions ne relèvent pas de la variable expérimentale, mais plutôt d'un artefact lié à la mesure même.

Salthouse et al. (1995) envisagent plusieurs solutions à ce problème dont aucune n'est exempte de risque. Il n'en demeure pas moins qu'il s'agit d'un facteur important à considérer dans l'étude du vieillissement, puisque des effets principaux de l'âge sont presque toujours observés. Nous proposons ici de faire appel à l'égalisation individuelle des niveaux de performance pour contourner le problème liés à l'interprétation des interactions (Salthouse et al., 1995). Plus précisément, la procédure d'égalisation consiste en une correction méthodologique des mesures de performance pour des groupes de sujets présentant des différences cognitives de base, qui sont additionnelles et différentes de celles mesurées par la variable expérimentale. Par exemple, dans une tâche de mémoire utilisant une condition contrôle (niveau de base) et une condition expérimentale, cette procédure mènera à modifier la tâche afin d'éliminer la différence de groupe observée dans la condition de base (e.g. modifier la longueur des listes à rappeler ou le temps de présentation des stimuli, etc.). Ainsi, la difficulté de la tâche initiale est rendue équivalente pour chacun des sujets par un ajustement individuel. La mesure de la variable expérimentale ajoutée réflètera donc plus justement l'interaction entre l'appartenance au groupe et cette variable.

Un déficit à une tâche de MdeT peut être interprétée de façon plus juste lorsqu'il se situe dans un contexte où les niveaux de base ont été égalisés car il permet de s'assurer qu'il ne résulte pas d'artéfact méthodologique. Malheureusement, très peu d'études ont envisagé un contrôle des différences dans les niveaux de base. Or, il est intéressant de noter que les études ne rapportant pas d'effet du vieillissement normal sur l'AC de la MdeT ont justement égalisé les performances de base des sujets jeunes et âgés (notamment, Baddeley, Logie, Bressi et al., 1986; Salthouse, 1992). Par exemple, Baddeley et collaborateurs ont évalué le rappel sériel immédiat en attention complète ou de façon concurrente à une tâche de poursuite visuelle. Pour cela, ils ont adapté individuellement pour chaque sujet la longueur des listes à retenir (selon l'empan du sujet) et la vitesse de la cible à poursuivre (correspondant à un seuil de réussite pré-déterminé). Dans ces conditions, les personnes âgées étaient aussi efficientes que les sujets jeunes dans la conditions d'attention divisée. L'existence d'un déficit des fonctions de l'AC dans le vieillissement normal reste donc à être confirmée en utilisant des procédures qui éliminent autant que possible les effets reliés à des différences de niveau de base.

Dans l'étude du vieillissemnt cognitif, un facteur important à considérer est celui de la vitesse de traitement de l'information. En effet, les personnes âgées sont reconnues comme ayant une vitesse réduite et certains ont proposé que cette réduction sous-tend plusieurs des troubles cognitifs liés au vieillissement normal (Salthouse, 1985; 1991). Il devient conséquemment important de pouvoir départager les différences liées à l'âge provenant de la vitesse de celles provenant de la variable mesurée. En ce qui concerne l'AC, certains auteurs (Fisk & Warr, 1996) avancent que le fait de contrôler l'effet associée à la vitesse de traitement permet d'éliminer celui de l'AC. Les différences observées à des tâches d'AC dans le viellissement seraient donc primairement attribuables à la réduction de la vitesse d'activation de l'information en MdeT des personnes âgées. Cependant, plusieurs questionnements demeurent suite à ces études. Premièrement, la plupart des auteurs n'utilisent que très peu de tâches d'AC. Comme l'AC est une composante qui est conçue comme fractionnable, la réalisation d'une seule tâche ne saurait refléter adéquatement le fonctionnement de l'AC. De plus, certaines études utilisent, comme tâche mesurant le facteur vitesse, des tâches qui sollicitent non seulement la vitesse mais aussi la MdeT (e.g. substitution de symboles de Weschler). La covariance entre les deux tâches devient donc évidente, puisque les deux mesurent possiblement la MdeT. Le choix des tâches expérimentales est donc d'une extrême importance dans ce type d'études, qui restent encore à répliquer.

4.2 L'inhibition dans le vieillissement normal: Le modèle de Hasher & Zacks (1988)

L'inhibition est une des fonctions de l'AC qui pourrait être atteinte dans le vieillissement normal. Afin de rendre compte des déficits cognitifs observés chez les sujets âgés, Hasher & Zacks (1988) ont en effet proposé un modèle explicatif du vieillissement normal reposant sur un dysfonctionnement des processus d'inhibition liés à la MdeT. Selon ce modèle, les processus inhibiteurs seraient déficitaires chez la personne âgée. Ceci aurait comme conséquence d'affecter la sélection des informations. Certaines informations non-pertinentes qui auraient dû être inhibées auraient alors accès à la MdeT et perturberaient le traitement et le rappel des informations pertinentes. Par exemple, une conversation se déroulant entre deux personnes présentes dans l'environnement d'un individu âgé pourrait perturber le traitement et la compréhension de ce qu'il lit, les bruits verbaux étant moins bien inhibés. Il en serait de même des stimuli internes, par exemple les associations ou le langage intérieur pourraient ralentir la compréhension d'un texte ou nuire à sa mémorisation. Selon ce point de vue, les déficits de la MdeT observés dans le vieillissement normal pourraient être causés par un déficit des processus inhibiteurs.

Hasher, Zacks et leurs collaborateurs utilisent depuis plusieurs années la procédure d'AN dans leurs travaux afin d'appuyer leur hypothèse (Connelly & Hasher, 1993; Connelly et al., 1991; Gerard et al., 1991; Hartman & Hasher, 1991; Hasher et al., 1991; Kane et al., 1994; Stoltzfus et al, 1993). L'utilisation de l'AN comme procédure expérimentale permet de contourner un problème d'interprétation majeur et fréquent dans la littérature sur le vieillissement cognitif. La population âgée est reconnue pour montrer un ralentissement général de la vitesse de traitement de l'information (Salthouse, 1991), ce qui limite souvent l'interprétation des données en neuropsychologie du vieillissement. Comme l'absence d'effet d'AN se définit comme un temps de réaction plus rapide (i.e. aucun ralentissement observé), elle ne saurait être interprétée comme la conséquence d'un ralentissement global de la vitesse de traitement. Conséquemment, cette procédure expérimentale s'avère fort intéressante pour l'étude du vieillissement. Or plusieurs études ont observé une absence d'AN chez les sujets agés (Connelly & Hasher, 1993; Connelly et al., 1991; Gerard et al., 1991; Hartman & Hasher, 1991; Hasher et al., 1991; Kane et al., 1994; Stoltzfus et al, 1993). Plus précisément, ces derniers ne montraient pas de ralentissement de la réponse dans les conditions d'inhibition et ce, malgré la manipulation de différentes variables, telles le temps de présentation et le délai entre la réponse et la présentation subséquente (*"response-stimulus interval"* - RSI). Ce résultat est classiquement interprété comme un déficit des processus inhibiteurs et appuie l'hypothèse selon laquelle l'absence d'inhibition réduirait l'efficacité de la MdeT des personnes âgées.

Le modèle du vieillissement cognitif proposé par Hasher & Zacks se veut une explication des troubles de la MdeT et suggère une relation étroite entre inhibition et MdeT. Or, il ne définit pas de façon précise les liens existant entre les deux concepts. Pourtant, ce pont nous apparaît essentiel. D'une part, l'inhibition pourrait être une des composantes de l'AC comme le suggèrent Stuss et al. (1995). De plus, l'AC pourrait être touché dans le vieillissement normal. Malheureusement, dans la littérature actuelle, aucune des tâches utilisées pour évaluer l'inhibition dans le vieillissement normal ne fait directement appel à la MdeT. Un des buts de notre travail sera de combler cette lacune en utilisant entre autre une tâche mesurant directement l'inhibition de stimuli non-pertinents lors de l'exécution d'une tâche de mémoire de travail.

5. Administrateur central et inhibition dans la démence de type Alzheimer

La démence de type Alzheimer (DTA) est une maladie dégénérative liée au vieillissement et affectant différentes fonctions cognitives telles l'attention, la mémoire et le langage. Sa prévalence est relativement élevée dans la population âgée, soit de 1 à 5,8% selon les études (Puel, Démonet, Ousset & Rascol, 1991). Pour ces raisons, la DTA fait l'objet de plusieurs études en neuropsychologie et en neurosciences. Au plan neuroanatomique et neurochimique, la DTA entraîne certaines modifications identifiables à l'analyse histopathologique. Les cerveaux de patients DTA contiennent des plaques séniles, des dégénérescences neurofibrillaires et des dégénérescences granuo-vacuolaires. Ces anomalies histologiques sont retrouvées principalement dans les régions hippocampique et paralimbique, dans les aires associatives, dont le cortex pré-frontal (Donnet, Foncin & Habib, 1991; Puel, Démonet, Ousset & Rascol, 1991). La perte neuronale entraîne inévitablement une diminution du nombre de synapses (De Kosky & Scheffe, 1990) et une connectivité moindre chez ces patients. Par ailleurs, la DTA est hétérogène au plan neurologique et certains sous-groupes de la maladie ont même été proposés (Habib, Joanette & Puel, 1991). Il n'existe à ce jour aucun marqueur biologique de la DTA. Du vivant du sujet, le diagnostic se fait par la mise en évidence d'une atteinte cognitive compatible avec une DTA et ne pouvant être expliquée par aucune autre maladie. Dans ce contexte, l'évaluation neuropsychologique du patient est déterminante.

Au plan cognitif, la DTA entraîne différents troubles cognitifs dont une atteinte de la MdeT (pour une revue, voir Belleville, Crépeau, Caza & Rouleau, 1995). Les patients DTA montrent en effet une diminution de leur empan et ce, quel que soit le type de matériel utilisé pour le mesurer (des lettres, des mots, des chiffres ou des positions spatiales; Belleville et al, 1995). Selon Morris & Baddeley (1988) le trouble de MdeT dans la DTA résulterait d'un dysfonctionnement isolé de l'AC. D'une part, Morris (1986) a montré des effets normaux de similarité phonologique et de longueur de mots chez un groupe de patients DTA suggérant que la boucle phonologique est fonctionelle. D'autre part, les patients DTA montrent des performances réduites aux tâches évaluant l'AC. Par exemple, dans une épreuve de Brown-Peterson, les sujets doivent rappeler des trigrammes après un délai temporel variant de 0 à 30 secondes. Ce délai peut être comblé par une tâche interférente (e.g. par l'ajout d'une tâche de comptage ou calcul à l'intérieur du délai), ou demeurer vide. Les patients DTA sont reconnus pour montrer une perte accrue dans la condition interférente de cette tâche (Belleville et al., 1996; Morris, 1986). De plus, les DTA montrent une diminution de la performance dans des paradigmes de double tâche (Baddeley et al., 1986; 1991), dans lesquelles ils doivent diviser leur attention entre deux tâches simultanées. Au niveau de l'inhibition, seulement deux études sont relevées dans la littérature à notre connaissance (Sullivan, Faust, & Balota, 1995; Simone & Baylis, 1997). Ces auteurs ont d'ailleurs montré, à l'aide du paradigme d'amorçage négatif mais en utilisant une méthodologie qui diffère de la nôtre, une atteinte de l'inhibition chez les patients DTA.

Une même hypothèse explicative est donc fournie pour expliquer la DTA et le vieillissement normal, soit un déficit de l'AC. La différence entre les deux groupes est essentiellement quantitative, la DTA occasionnant un trouble plus sévère de l'AC que le vieillissement normal. Or, le neuropsychologue clinicien souhaite pouvoir distinguer les manifestations cognitives reliées à une DTA de celles associées à un processus normal du vieillissement et l'existence de différences essentiellement quantitatives entre les deux manifestations complique cette démarche. Cet état de fait pourrait s'expliquer par différents facteurs. Premièrement, le déficit est parfois attribué par défaut: on postule une diminution de l'AC lorsque les systèmes esclaves sont fonctionnels. De plus, il est possible que l'atteinte de l'AC dans le vieillissement normal résulte d'un manque de contrôle méthodologique des niveaux de base. Enfin, l'AC est encore mal décrit théoriquement et ne peut être évalué empiriquement que par un nombre relativement restreint de tâches. Un manque de pouvoir discriminatif des tâches disponibles pourrait expliquer qu'elles ne parviennent pas à différencier le vieillissement normal du vieillissement pathologique.

Le fractionnement de l'AC pourrait permettre d'identifier des atteintes spécifiques et qualitativement différentes chez ces patients. Les études de l'AC dans la DTA se sont jusqu'à maintenant principalement intéressées à l'attention divisée. Pourtant, l'étude des différents processus inhibiteurs pourrait s'avérer intéressante. Les processus inhibiteurs jouent un rôle dans de nombreuses tâches et sont reliés à plusieurs fonctions cognitives tel la lecture, la compréhension et la mémoire. De plus, les plaintes des patients DTA et leur profil neuropsychologique suggèrent des difficultés d'inhibition. Par exemple, les nombreuses intrusions que ces patients commettent dans les tâches cliniques ou dans les tâches de mémoire pourraient être causées par un trouble des processus inhibiteurs (e.g. Belleville et al., 1992).

Le domaine théorique de la mémoire de travail et de l'inhibition reste donc avec de nombreuses interrogations, tant au plan de la modélisation de l'AC que de son lien avec les processus inhibiteurs. Selon nous, l'étude de patients âgés pourrait contribuer à une meilleure compréhension de ces fonctions cognitives. D'une part, la littérature relève peu d'études utilisant des tâches d'AC et d'inhibition auprès de sujets âgés et de patients cérébrolésés ; il sera donc intéressant d'explorer comment ces processus peuvent être atteints par la pathologie. D'autre part, nos travaux sont guidés par un intérêt clinique, puisque les études sur l'efficacité de l'AC et de l'inhibition dans la DTA sont très peu nombreuses. Une meilleure compréhension théorique de ces fonctions et de leur contribution au profil neuropsychologique de ces patients pourrait permettre d'en améliorer le diagnostic.

6. Objectifs généraux de la thèse

La présente thèse vise trois principaux objectifs. Le premier est de documenter le fonctionnement de l'AC dans le vieillissement normal en contrôlant pour les différences de niveau de base existant entre les sujets jeunes et âgés. Nous évaluerons les capacités d'inhibition en utilisant une tâche qui fait clairement appel à la MdeT. Nous comparerons ces capacités d'inhibition à une autre fonction de l'AC, soit la capacité de manipulation du contenu de la MdeT. Notre second objectif est de vérifier l'atteinte des mêmes composantes dans la DTA. Une meilleure connaissance de l'effet du vieillissement normal sur l'inhibition permettrait en effet une description plus précise du déficit spécifiquement lié à la DTA. Enfin, comme la majorité des études en neuropsychologie cognitive, les résultats obtenus auprès de populations cliniques pourraient améliorer notre connaissance du fonctionnement cognitif normal. Notamment, nous souhaitons contribuer à la question du fractionnement de l'AC en vérifiant si l'inhibition et la manipulation peuvent être dissociées. Ensuite, nous souhaitons pouvoir contribuer aux modèles théoriques de l'inhibition et de l'interférence.

Pour remplir ces objectifs, quatre articles sont proposés. Le premier article (*The Irrelevant Speech Effect and aging: An assessment of inhibitory processes in working memory*) porte sur l'étude des processus inhibiteurs dans le vieillissement normal avec une tâche faisant appel à la mémoire de travail, soit le rappel sériel immédiat. Par le biais de l'*effet d'écoute inattentive* (*"irrelevant speech effect"*), nous étudierons l'inhibition de distracteurs verbaux présentés auditivement lors d'une tâche de rappel de chiffres présentés visuellement. Le second article (*Effect of normal aging on the manipulation of information in working memory*) discutera de l'effet du vieillissement normal sur les fonctions de manipulation en mémoire de travail. Le troisième article (*Inhibition and manipulation capacities of working memory: Dissociation in patients with dementia of Alzheimer type*) évaluera la performance de patients DTA, de contrôles âgés et de sujets jeunes à la tâche d'inhibition phonologique et à la tâche de manipulation. Le quatrième article (*Exploration of multiple inhibitory systems and interference in dementia of Alzheimer type*) étudiera différents processus inhibiteurs ainsi que l'interférence dans la DTA et le vieillissement normal en utilisant notamment la procédure d'AN.

Chapitre II:

SECTION EXPÉRIMENTALE

Article n° 1

Irrelevant speech effect in aging: An assessment of inhibitory processes in working memory

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Abstract

The purpose of this study was to assess whether older adults can inhibit irrelevant auditory information while performing a span task. In Experiment 1, young and older participants recalled seven visually presented digits while subject to three types of irrelevant noise: white noise (non-verbal), and familiar and non-familiar language (verbal). A baseline measure was obtained in silence. The effect of each noise was also assessed under articulatory suppression (AS). In Experiment 2, the number of digits to recall was adjusted to participants' individual span. Results show a clear irrelevant speech effect (ISE), that is, recall declines in the presence of familiar and non-familiar verbal noise, but is unaffected by white noise. AS negates ISE. Most important, ISE does not interact with age: older adults have no more difficulty inhibiting irrelevant auditory information than do young adults. These results are discussed relative to current theories of inhibition in aging.

Introduction

Current empirically based models suggest that information selection involves inhibition mechanisms that actively suppress concurrent distractors (Kane, Hasher, Stoltzfus, Zacks, & Connelly, 1994; Hasher & Zacks, 1988; Navon, 1989a, 1989b; Neumann, 1987; Tipper, 1985, 1992). A major function attributed to these inhibitory processes is to prevent irrelevant material from accessing working memory and to deactivate any such material that enters the system notwithstanding. Recently, it has been proposed that these inhibitory mechanisms may be impaired in normal aging (Connelly & Hasher, 1993; Kane et al., 1994; Hasher, Stoltzfus, Zacks, & Rypma, 1991; Hasher & Zacks, 1988; McDowd & Filion, 1992) and that various intellectual deficits exhibited by older people may be due to such impairment. These problems include difficulty understanding and remembering both rapidly presented information (Stine, Wingfield, & Poon, 1986) and syntactic structures that make heavy demands on working memory (Kemper, 1988), long-term retrieval deficits (Gérard, Zacks, Hasher, & Radvansky, 1991), distractibility in reading (Connelly, Hasher, & Zacks, 1991) and increased off-target verbosity, that is, speech lacking in focus or coherence (Arbuckle & Pushkar Gold, 1993).

The inhibition-deficit hypothesis relies largely on studies that have assessed inhibition through *negative priming* (Neill, 1977; Tipper, 1985). In this procedure, participants are presented two letters of the alphabet simultaneously, one, red (the target) and the other, green (the distractor). Their task is to name the red letter as fast as possible. Results show that response time increases when the letter serving as the distractor in one trial (priming) is used as the target in the very next trial (probe). The explanation for this suppression effect is that the distractor-now-target is actively inhibited: When a distractor becomes the target in the subsequent trial, its selection is delayed because of residual inhibition. A weakening of this suppression effect has been observed repeatedly in experiments involving older people, providing empirical evidence for an inhibition deficit (Connelly & Hasher, 1993; Hasher et al., 1991; Tipper, 1991). According to Hasher and Zacks' (1988), this deficit results in irrelevant material occupying working memory and interfering with its contents.

Working memory is involved in the temporary retention and processing of information (Baddeley & Hitch, 1974; Baddeley, 1986). It relies on the coordinated functioning of various subcomponents. The *central executive* controls and distributes limited attentional resources to specialized slave systems responsible for maintaining information in particular codes. One of these is the *phonological loop*, which retains verbal information. It includes a *phonological store* where verbal information is held in a phonological code. The phonological store is time-limited and a *rehearsal procedure* is used to prevent material there from decaying. This procedure is also used to transfer written input into the phonological store. Thus, whereas auditory information is believed to have direct access to the phonological store, verbal material presented in the visual modality must be articulated subvocally for it to be retained there. In other words, both auditory and visual verbal input have access to the phonological store, the former, directly and the latter, through rehearsal (see Figure 1).

The relationship between working memory and inhibition has been assessed by means of the *irrelevant speech effect* (ISE) paradigm, also referred to as the *unattended speech effect* paradigm (Salamé & Baddeley, 1982). In this procedure, participants must recall immediately short sequences of visually presented digits while trying to ignore irrelevant background noise. According to Hasher and Zacks (1988), this is a scenario where inhibitory mechanisms should intervene to deny irrelevant information access to working memory. The ISE was first demonstrated by Colle and Welsh (1976). In their study, English speakers were shown eight consonants; after a 10-s delay, they were asked to perform a serial recall. An irrelevant text in a non-familiar language (German) was presented auditorily during encoding, delay and recall. Participants were instructed to ignore the text while memorizing consonants. Results showed decreased memory performance associated with the presence of irrelevant speech. Salamé and Baddeley (1982, 1989) replicated this finding using an immediate-recall procedure with no delay.

Certain evidence reported in studies using young adults suggests that the ISE occurs at the level of the phonological store of working memory (but see Jones, 1993, for an alternative explanation). First, ISE is unrelated to the acoustic qualities of stimuli, be it intensity (Colle, 1980; Salamé & Baddeley, 1987) or amplitude (Salamé & Baddeley, 1987; 1989). Second, it is unrelated to the semantic content of verbal noise; several authors have shown that familiar and foreign languages disturb recall equally (Colle & Welsh, 1976; Salamé & Baddeley, 1982). Finally, recall is affected by auditory stimuli that include a verbal component, as is the case with speech or songs, but remains intact when the auditory background is non-verbal, as is the case with white noise (Colle & Welsh, 1976; Salamé & Baddeley, 1982, 1987).

This pattern of results is compatible with the structure of the phonological loop as described above (Baddeley, 1986, 1990). An auditory verbal background interferes with the retention of visually presented digits because under normal conditions both types of material have access to the phonological store and, therefore, one may impede the other. Denying visual information access to the phonological store should, in theory, preclude appearance of the ISE. This has been demonstrated in young adults (Salamé & Baddeley, 1982) through the technique of articulatory suppression (AS). In this procedure, participants are asked to repeat continuously a word segment such as *the* or *bla* while presented material in the visual modality. AS occupies the rehearsal procedure and prevents the transfer of written input to the phonological store, thereby neutralizing the ISE (see Figure 1).

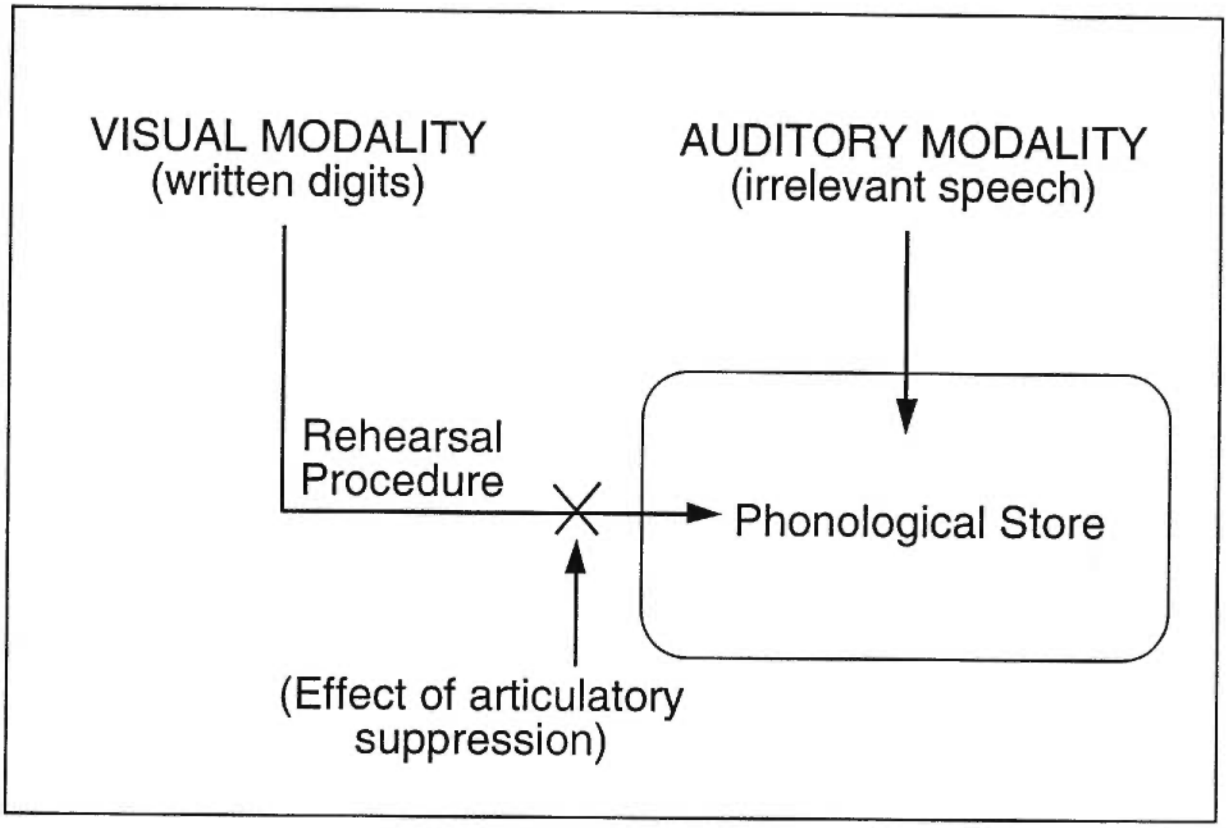

Figure 1. The working memory model: Irrelevant speech directly accesses the phonological store. Written digits are transferred only through the rehearsal procedure. Articulatory suppression precludes the use of rehearsal thus preventing digits from being retained in the phonological store.

The main goal of this study was to assess whether the inhibition deficit considered by some to be characteristic of normal aging extends to the ability of older people to suppress auditory distractors when performing a working-memory task. A major motive for the study was the frequent complaint of older people regarding their increased distractibility in the presence of background noises. In the ISE paradigm, participants are instructed to ignore distracting noises and to focus their attention solely on memorizing digits. This is essential in order to achieve optimal performance on the task. Participants necessarily employ inhibition processes to perform the task, particularly ones involving verbal material to produce maximum phonological interference. Given that the ISE occurs within the phonological store, a phonological deficit or a decrease in the capacity of the phonological store should, in theory, also result in an abnormal ISE. This however, cannot account for the diminished performance of older people on the task as their phonological storage capacity is entirely normal (Belleville, Peretz, & Malenfant, 1996).

A secondary purpose of the study was to propose a new way of assessing inhibitory processes with a view to broadening the existing array of inhibition tasks and contributing to test the generability of the age-related inhibition deficit. To this end, the immediate recall of lists of visually presented digits was measured in young and older French-speaking adults subject to verbal and non-verbal background noise. French and Romanian versions of a text (familiar and foreign languages, respectively) were used as verbal distracting material. White noise was used as a non-verbal distractor. These noise conditions were compared against a baseline condition where participants performed in silence. In addition, the effect of AS on ISE was assessed. This variable was included to determine the validity of our experimental paradigm. It was important to demonstrate that the effects were comparable to those previously reported in normal young adults. Furthermore, the use of AS would serve to confirm that the observed ISE actually occurs within the phonological store of working memory.

On the strength of the findings reported in previous studies, we predicted the presence of an ISE, that is, recall should remain unaffected by the presence of non-verbal noise but should decrease in the presence of verbal backgrounds. However, AS should negate this ISE. Although both groups of participants were expected to exhibit an ISE, the effect should be larger in older adults owing to their inhibition impairment. In other words, older adults should be more impaired by speech noises than young adults, given that the situation requires the heavy intervention of inhibitory processes.

Experiment 1

METHODS

Participants

Thirty-two French-speaking adults, 16 young and 16 old, took part in the experiment. The young adults (5 males and 11 females) ranged in age from 18 to 24 years (M = 21.1) and had a mean of 13.7 years of schooling (SD = 2.3). The older adults (7 males and 9 females) ranged in age from 65 to 91 years (M = 76.4) and had a mean of 9.4 years of schooling (SD = 3.36). The difference in formal education between young and older participants was significant, $t(15) = 4.2589$, $p < .001$, but corresponds to the increase in average educational level in Quebec between the two generations concerned (Statistics Canada, 1994). Participants spoke French as their mother tongue and had no knowledge of Romanian, the language employed in the non-familiar speech condition.

Participants were drawn from a pool of volunteers living in the same small community. They had no history of neurological disease, psychiatric disorder or general anaesthesia in the past year. They did not consume medication known to affect memory or other cognitive functions. They all reported normal hearing and had normal or corrected vision.

The older adults were subjected to an extensive battery of neuropsychological tests in order to exclude participants with early signs of dementia (see Table 1). These tests included the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975) used to screen for major cognitive defects, the Wechsler Memory Scale (Wechsler, 1945) to estimate memory functions, and a visual discrimination test (Enjalbert, Salinier, & Chéron, 1988). Construction and ideo-motor praxes were evaluated by means of the praxis subtest of the PENO neuropsychological battery (Joanette et al., 1995). Only one participant performed sub-par on most of these tasks and was consequently dropped. The young participants were not tested as extensively given that they are not at risk for dementia. Nevertheless, they completed the Logical Memory and the Digit Span subtests of the Wechsler Memory Scale, on which they performed within the normal range.

Table 1

Results on Neuropsychological Assessment

Subtest	Mean[a]	Normative Value
Young		
Wechsler Memory Scale:		
Logical memory	9.5 (1.3)	10.45 (3.7)
Digits total	12 (2.2)	10.57 (2.3)
Aged		
Wechsler Memory Scale:		
Information	5 (1)	5.5 (0.8)
Orientation	5 (0)	4.9 (0.4)
Mental control	5 (2)	4.4 (2.5)
Logical memory	5 (2)	6.7 (3.3)
Digits total	9 (2)	8.4 (2.1)
Visual reproduction	6 (4)	4.8 (3.1)
Associate learning	15 (5)	10.9 (4.9)
Memory quotient (MQ)	102 (11.4)	100 (15)
Mini-Mental State	27.7 (1.1)	cut-off = 24

[a]Standard deviations in parentheses.

Materials

Memory task

Eighty series of seven digits from 1 to 9 were used. Digits were randomly ordered and could appear only once in each list. They were presented on a Macintosh monitor, in the center of the screen, using a program written with PsychLab (Gum, 1991).

Noise and irrelevant speech sources

Three types of auditory stimuli were created: white noise (non-verbal), familiar verbal noise, and non-familiar verbal noise. The white noise consisted of electronically generated FM modulations. The familiar noise was an excerpt from Madame de Staël's novel *Corinne ou l'Italie* read in French, the participants' mother tongue. The non-familiar noise was the same text read in Romanian.

Romanian was chosen because, although a Romance language like French, it is unfamiliar to French speakers living in Quebec, unlike other more common Latin languages such as Italian and Spanish. Thus, the two verbal noises used were phonologically akin but differed at the lexico-semantical level in that one was comprehensible to participants. A professional translator produced the Romanian version of the original French text. A female reader fluent in both French and Romanian was used for the recordings in order to have a voice with similar acoustic qualities in both versions, thereby ensuring a better comparison of the verbal conditions. The reader was instructed to read both versions in a steady rhythm without long pauses, while maintaining steady prosody and volume. This last control measure was taken in order to avoid possible orienting responses elicited by sudden variations in prosody or tone of voice. Each version lasted approximately 8 minutes.

The auditory stimuli were played on a Sony tape recorder (TMC-5000) and presented binaurally through Sony headphones (MDR-006). Noise intensity was 75 dB on average, as measured by a noise-level meter. Readings were taken twice each by two different examiners over 30-s periods. A level of 75 dB is well within the range of normal hearing for both young and older adults (Corso, 1977).

Procedure

Short-term memory (STM) span measure

STM capacity for visually presented digits was measured using a classic span procedure. Digits were presented one at a time for 750 ms, with a 250-ms inter-stimulus interval, in the center of a computer monitor screen. Testing began with sequences of two digits randomly selected from 1 to 9. The length of the sequences was increased by one digit every four trials. A 2-s visual warning (Ready) in the center of the screen preceded each sequence. At the end of a sequence, a table containing the digits 1 to 9 was displayed on the screen. The position of the digits in the table was randomized in order to prevent participants from using spatial cues. Participants were required to reproduce the entire sequence in correct order by pointing to each item serially with a finger. The experimenter recorded the responses. Participants were instructed to point to a question mark appearing on the right of the screen whenever they could not remember a digit. Testing ended once participants failed to report correctly at least two of four same-length sequences. STM span was defined as the longest sequence correctly recalled on 50% of the trials.

Experimental testing

Two sessions of about 30 min were required to complete the experimental testing. The digit recall procedure was the same as the one used in the STM span measure, except that only seven-digit sequences were used. Participants wore headphones in each noise condition, including the silent condition. They were instructed to ignore distracting noises and focus their attention on memorizing digits. Noise began 10 s before presentation of the first digit in a particular condition and continued until participants finished recalling the last sequence in the condition. Ten sequences were presented in each condition. A 10-min break was given after every two conditions. In the no-AS condition, participants were instructed to proceed in silence throughout the task. In the AS condition, they were asked to repeat continuously the segment *bla* during presentation and recall of digits. The AS and no-AS conditions were alternated in order to avoid fatigue effects.

The experiment thus assessed recall under four auditory backgrounds: silence, non-verbal noise, familiar verbal noise, and non-familiar verbal noise, each with and without AS. The effect of order of presentation of the noise conditions was counterbalanced using a Latin Square design. In the first session, two of the four noise conditions were combined with AS. In the second session, the order of noise conditions was the same for each participant, but AS this time was combined with the other two noise conditions. The order of presentation of the AS and no-AS conditions was alternated across participants and noise conditions.

RESULTS

A 2 x 4 x 2 (Age x Noise x AS) analysis of variance (ANOVA) was used to test our predictions. The dependant variable was the total number of digits recalled in the correct position under each noise condition. In addition, effect size (Cohen, 1988, in Hintze, 1991) was calculated for main effects and for interactions, and power analyses were performed to ensure that the absence of interaction with age was not due to inadequate sample size.

Before proceeding to the analysis of the noise condition effects, the general STM capacity of older and young participants was compared through their scores on the STM span measure. Results indicated a slightly larger span for young participants (6.5 vs. 6.0 digits), but the difference was only marginally significant, $t(15) = 1.651$, $p = .0597$ (one-tailed).

Figure 2 shows the percentage of digits recalled by young and older participants in the four noise conditions without AS, and Figure 3 gives the percent correct recall with AS. The ANOVA revealed a significant main age effect, $F(1,30) = 22.207$, $MSE = 759.55$, $p < .001$, indicating greater recall accuracy among young participants. The size of this effect was 0.83. The main noise effect also reached significance, $F(3,90) = 12.701$, $MSE = 38.19$, $p < .001$, which implies that the type of noise has a differential effect on retention. The size of this effect was 0.41. Finally, there was a main AS effect, $F(1,30) = 169.671$, $MSE = 157.79$, $p < .001$, suggesting that AS diminishes recall. The size of this effect was 0.87.

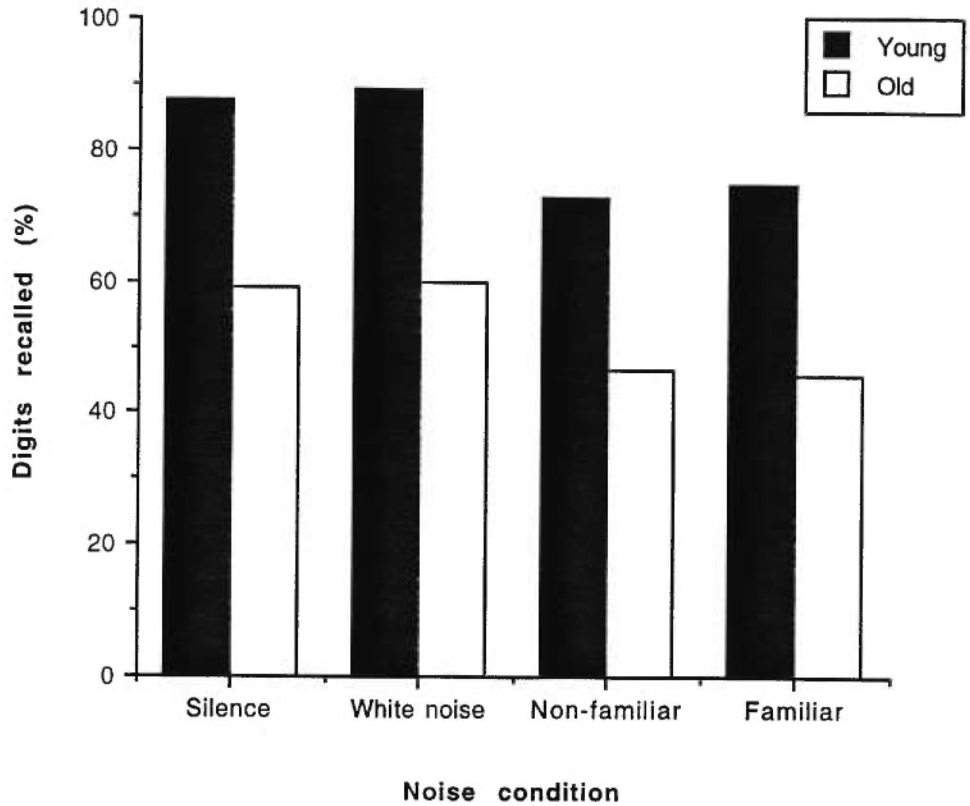

Figure 2. Percentage of digits recalled by young and older participants without articulatory suppression.

These main effects, however, were qualified by significant interactions. As expected, the Noise x AS interaction was significant, $\underline{F}(3,90) = 12.207$, $\underline{MSE} = 45.64$, $\underline{p} < .001$. An analysis of this interaction revealed a clear noise effect without AS, $\underline{F}(3,90) = 27.482$, $\underline{MSE} = 36.865$, $\underline{p} < .001$. As shown in Figure 2, the white-noise and silence conditions did not differ from one another and yielded a larger recall level than the two verbal conditions. Similarly, the familiar and non-familiar verbal noise conditions did not differ from one another. However, there was no noise effect with AS, $\underline{F} < 1$, $\underline{MSE} = 46.972$ (see Figure 3). The Age x AS interaction also was significant, $\underline{F}(3,90) = 5.284$, $\underline{MSE} = 157.79$, $\underline{p} < .05$. This may be due to the presence of a floor effect in older participants, which reduced the size of the AS effect: $\underline{F}(1,30) = 57.535$, $\underline{MSE} = 157.795$, $\underline{p} < .001$ for older participants compared with $\underline{F}(1,30) = 117.419$, $\underline{MSE} = 157.795$, $\underline{p} < .001$ for young participants.

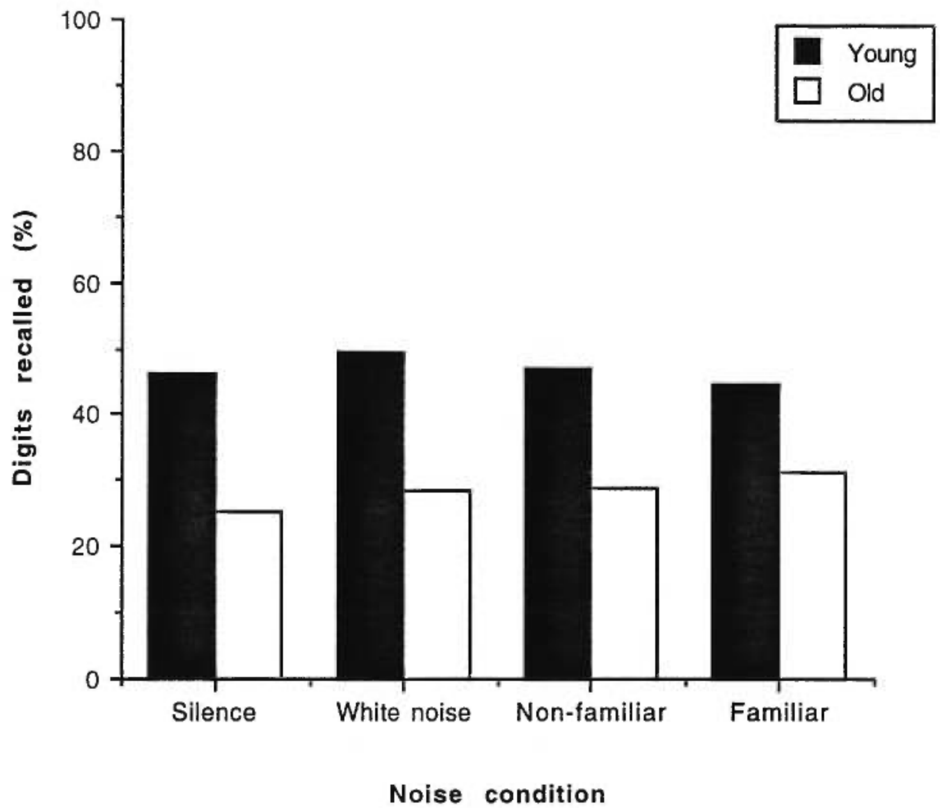

Figure 3. Percentage of digits recalled by young and older participants with articulatory suppression.

Of importance to our hypothesis is the fact that neither the Age x Noise interaction, $\underline{F} < 1$, $\underline{MSE} = 45.64$, nor the Age x Noise x AS interaction, $\underline{F} < 1$, $\underline{MSE} = 45.64$, was significant. Furthermore, both interactions yielded very small effect sizes

(0.107 and 0.09, respectively). The analysis of the Age x Noise interaction revealed that in order to reach a power level of .80, a sample size of 138 would be needed. For the Age x Noise x AS interaction, a sample size of 198 would be necessary.

This is a case, however, where power analyses must be interpreted with utmost circumspection. A closer look at Figure 2 reveals that the interaction that would be reached with this sample size would be in the opposite direction: If anything, the older participants would be less affected by the presence of noise. Consequently, results strongly support the absence of greater recall failure in older adults under conditions where inhibition mechanisms are called into play.

As the difference in years of formal education between young and older participants could influence memory, an analysis of covariance (ANCOVA) was performed with years of schooling as a covariable. Results were the same as in the ANOVA.

DISCUSSION

The results of this first experiment are in line with the literature in showing that verbal noises disturb immediate serial recall but that non-verbal noises do not (Colle & Welsh, 1976; Salamé & Baddeley, 1982). Furthermore, familiar and non-familiar speech produce an equivalent interference effect, confirming that the ISE does not depend on the semantic content of the verbal noise.

Results when AS was used show that preventing visually presented material from accessing the phonological store negates the ISE. This is compatible with the suggestion that the ISE stems from interference in the phonological store of working memory. This clear replication of the findings of earlier studies involving young adults indicates that the ISE is a strong and reliable phenomenon and that our evaluation procedure is sound.

The ISE was as important in the older participants as it was in the young. Unlike non-verbal noise, verbal background noise interferes with recall performance, but the effect disappears with AS. Thus, although older adults generally have a lower recall level than do young adults, they show the same ISE pattern. Figure 2 clearly shows that recall levels of older and young participants are strikingly parallel under the different noise conditions. Where our initial hypothesis is concerned, older participants are thus not more impaired in conditions that require them to inhibit irrelevant interfering auditory information.

These results run counter to the existing literature suggesting inhibition deficits in normal aging. One possible explanation for this discrepancy may lie in the presence here of a general group effect: Older participants performed at a significantly lower level than young participants in all conditions, including silence. This is coherent with our observation of a marginally significant span difference in the baseline measure between the two groups. In this regard, sequences of seven digits were generally more demanding on older than on young participants. As discussed by Meudell and Mayes (1982), this quantitative difference might conceal the presence of a genuine qualitative difference. This may be due to the presence of floor effects in older participants, which curb the effect of verbal noise. On the other hand, it is possible that inhibition is required only when the memory system is operating at high efficiency. Consequently, the inhibition deficit of older participants would fail to manifest itself if their inhibitory mechanisms are not solicited to the same extent as those of young participants.

One strategy to circumvent the sort of problems that quantitative differences create is to assess the effect of the variables of interest in conditions where the group effect is neutralized (Meudell & Mayes, 1982; Salthouse, 1985). The goal of Experiment 2 was thus to control for quantitative differences by adjusting digit-sequence length to the STM span of each participant. This would ensure that all participants were tested at the maximum limit of their individual STM capacity.

Experiment 2

METHODS

Participants

Thirty-two other participants (16 young and 16 old) taken from a pool of volunteers living independently in the local community were tested using the same task and materials of Experiment 1. The younger participants (8 males and 8 females) were from 18 to 30 years of age (M = 22.2) and had a mean of 13.5 years of education (SD = 1.6). The older participants (8 males and 8 females) ranged in age from 66 to 76 years (M = 70.9) and had a mean of 11.6 years of formal education (SD = 2.2). The difference in years of schooling was significant between these two groups, $t(15) = 2.29$, $p = .03$.

Participants did not undergo the same extensive neuropsychological testing as did those in Experiment 1, but their general verbal level was evaluated with the Mill Hill Vocabulary Test, a French-language version of the multiple-choice synonym subtest (Gérard, 1983) widely used in research on aging. A perfect score on this test is 44. Mean scores were 34.3 (SD = 4.48) and 36.5 (SD = 5.7) for young and older participants, respectively, well within the normal range. The difference, however, was not significant, $t(15) = -1.07$, $p = .3013$. The same exclusion criteria were applied as in Experiment 1.

Procedure

STM span was measured as in Experiment 1, except that participants were tested only with digit sequences length-adjusted to their individual STM span. In other words, the number of digits a participant had to recall in each condition corresponded to his or her own span. In addition, AS was not used given that the phonological locus of the effect was well established in Experiment 1. There were thus four experimental conditions (i.e., silence, non-verbal noise, non-familiar speech, familiar speech), the order of which was altered according to a Latin Square design.

RESULTS AND DISCUSSION

The STM span scores obtained by young and older participants in preliminary testing were first compared using a t-test. The mean spans were 7.5 (SD = 0.89) and

6.3 (SD = 1.45) digits for young and older participants, respectively, a difference that reached significance, $t(15) = 2.493$, $p = .0124$ (one-tailed).

The noise effect in each group was assessed through a 2 x 4 (Age x Noise) ANOVA, with percentage of correctly recalled digits as the dependent variable. Effect sizes were measured as in Experiment 1. Figure 4 shows the results obtained by both groups in the four noise conditions. As expected from our equalization procedure, there was no age effect, $F < 1$, $MSE = 693.77$; young and older participants showed the same overall performance level. The size of the main age effect was only 0.03. A sample size of 8,400 would be needed to reach a power level of 0.80. However, the main noise effect was significant, $F(3, 90) = 72.71$, $MSE = 506.62$, $p < .001$, indicating that noise generally impairs recall. The effect size for noise was 1.5.

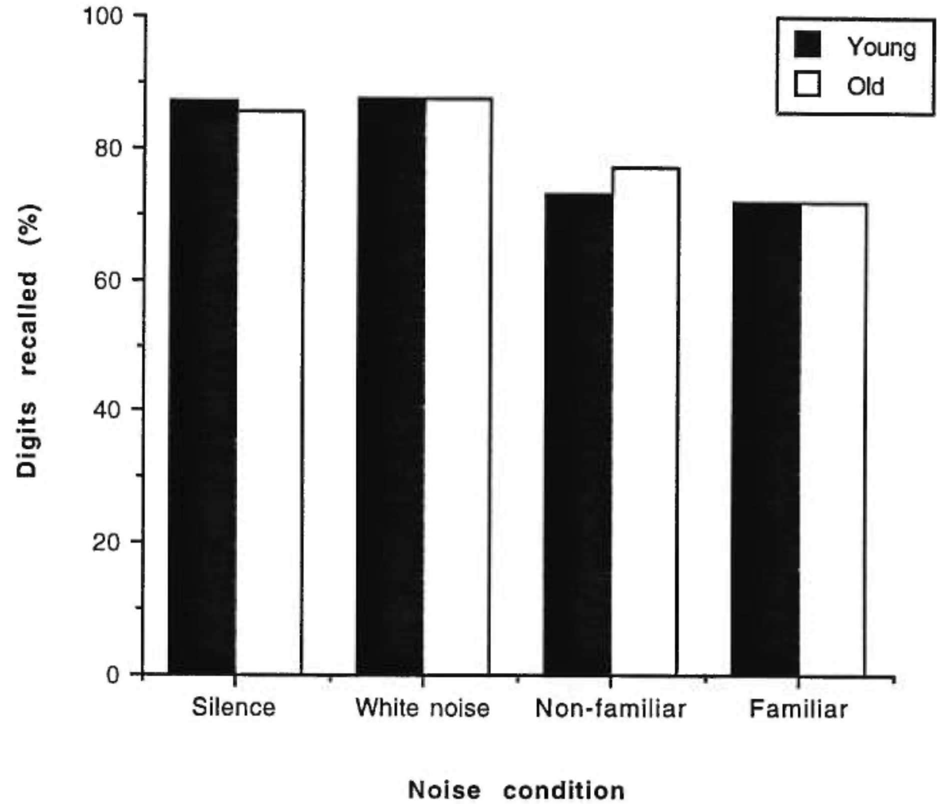

Figure 4. Percent correct recall in young and older participants when tested at their span level.

Figure 4 shows that recall clearly declined in the verbal-noise conditions, but not in the white-noise condition. This was confirmed by post-hoc comparisons indicating that, compared with silence, white noise did not decrease digit recall, but both verbal noises did ($p < .01$). Here again age did not interact with noise, $F < 1$, MSE = 506.62, revealing that older adults are not more impaired than young ones by the presence of verbal noise. Analysis of the Age x Noise interaction revealed an effect size of 0.04. In order to reach a power level of 0.80, a sample size of 1,892 would be needed.

The young participants in Experiment 2 demonstrated a slightly larger STM span than did the young participants in Experiment 1, although the difference between young and old was significant in both experiments. This discrepancy between the two groups of young adults is hard to account for. Though it may have something to do with experimental error, this explanation is improbable, as an ANCOVA with STM span as a covariable yielded the same results as the ANOVA, indicating that span size is not a factor influencing memory performance. Moreover, if span size did enhance performance, we would expect older participants to show lower recall in Experiment 2 compared with young participants. This is clearly not the case, however, as the effects observed are identical in both experiments.

In Experiment 2, the effect of irrelevant noise on the STM of older adults was assessed using a paradigm that controlled for quantitative effects. Despite this control, the results replicate the findings of Experiment 1. First, the paradigm yielded no main age effect but revealed a clear ISE in both groups. Second, older adults were not more disrupted than young adults by the presence of irrelevant background noise.

General Discussion

The goal of this study was to assess the effect of normal aging on the inhibition of irrelevant noise in a working-memory task. Results show that recall in both young and older adults is generally affected when they are subjected to irrelevant speech. More precisely, recall is impaired in the presence of familiar and non-familiar verbal noises but remains normal when distractors are non-verbal. This was found in two recall conditions, one where participants had to memorize standard sequences of seven digits (Experiment 1) and another where the length of the lists to recall was adjusted to individual STM span (Experiment 2). In both experiments, aging did not impair inhibitory abilities, as older adults had no more difficulty than young adults inhibiting verbal auditory distractors.

These results contradict those of other studies reporting inhibition deficits in aging (e.g., Connelly, Hasher, & Zacks, 1991; Tipper, 1991). This discrepancy, however, may be due to (1) methodological differences or (2) the existence of different types of inhibitory mechanisms. It is even possible that these two explanations are interrelated.

Where methodological differences are concerned, most studies that have reported inhibition deficits in normal old people used negative priming, not the ISE paradigm. The two procedures differ on a number of important counts. First, negative priming involves only the visual modality, whereas the ISE paradigm involves both the visual and the auditory. Second, the dependent variable in negative priming is response time, whereas in the ISE paradigm it is accuracy of response. Third, negative priming distinguishes interference from inhibition effects; in the ISE paradigm, the two phenomena are tightly knitted and cannot be experimentally dissociated.

Perhaps most important, in negative priming, participants must process both a target and a distractor during the priming half of the trial before providing an appropriate answer in the probe half (Connelly & Hasher, 1993). In the ISE paradigm, instead, participants are instructed to ignore all irrelevant material. Even if the irrelevant information does access the phonological store, participants do not have to process it to the same extent as they do in negative priming. It is thus possible that older individuals show inhibitory deficits only in situations where the distracting information is processed at a deeper level.

Yet another difference between the two procedures that may have a bearing on outcome relates to the locus of the inhibition that each induces. It is very possible that the two tasks assess completely different aspects of inhibition. The inhibition effect of negative priming has been interpreted as the result of the residual activation of the *representation* of the distractor (Tipper, 1985). Therefore, it may reflect inhibition at a lexical level rather than within the phonological store of working memory, as is the case with the ISE paradigm.

Our results are compatible with the existence of different specialized parallel inhibitory subsystems, only some of which are affected by normal aging. In a recent study, Connelly and Hasher (1993) found that, whereas older people do not inhibit the identity of letter distractors, they show normal inhibition of their spatial location. This led them to conclude that different inhibitory mechanisms may be differentially sensitive to normal aging (see also Stine & Wingfield, 1994). The inhibition of spatial location may be spared though the inhibition of identity is impaired. These authors proposed also that inhibitory mechanisms that deteriorate with age are ones that act on irrelevant "semantic-meaning-bearing" information. Our results may be interpreted along the same lines. Indeed, as was discussed earlier, there is ample evidence to suggest that the inhibitory processes required when performing the ISE task do not operate at a lexico-semantic level, but rather at a phonological one. Consequently, our results remain compatible with the hypothesis that lexico-semantic inhibition is impaired in normal aging. Furthermore, the results reported here suggest that phonological inhibition is preserved in older people. Inhibition of spatial location thus may not be the only inhibition subsystem resistant to the effect of age.

The dissociation of apparently different forms of inhibition in normal aging is likely to have important theoretical consequences both for conceptual models of inhibition and for our understanding of age-related impairment. With respect to current theories, these results suggest that inhibition is not a monolithic entity but can be separated into distinct subsystems. At present, it seems that these systems may be specialized according to the particular *nature* of the processing that comes into play, for example, spatial, phonological or lexico-semantic. With respect to how normal aging is characterized, our results, along with those of others, challenge the notion of a general age-related deficit of inhibition, given that important aspects of inhibition are spared in aging. However, it remains to be explained why certain systems are impaired and others not. One possibility is that impairment within a particular domain of inhibition, for example, spatial inhibition, relates to an underlying deficit of the whole processing system. This, however, is probably not the case. It is a well documented fact that older people show difficulties in visuo-spatial tasks (see Salthouse, 1992, for review) and yet, they exhibit normal spatial inhibition.

Theories of inhibition are thus likely to benefit from studies aimed at establishing the limits of the inhibition deficits manifested by older people and accommodating these within a coherent theoretical framework. This would strengthen our grasp of the inhibition phenomenon which, useful and captivating as it may be, stands to benefit from being more formally defined. A better definition of the conditions under which older adults do or do not show inhibition is likely to broaden our understanding of the cognitive aspects of normal aging.

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Footnote

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Article n° 2

Effect of normal aging on the manipulation of information in working memory

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MEMORY AND COGNITION (Sous Presse)

Abstract

The goal of this study is to examine the central executive of working memory in normal aging, specifically focusing on its capacities to manipulate or modify the format of the to-be-recalled material. The central executive was measured with the alphabetical span procedure, during which subjects were asked to recall a random series of words in their alphabetical order. The storage demand was equalized across subjects by adjusting the list lengths according to individual span. Experiments 1, 2 and 3 showed that elderly subjects were not impaired in manipulating information relative to young controls even when the difficulty of the task was increased. In Experiment 4, validity was tested by asking young subjects to perform the task under the conditions of full or divided attention. Alphabetical recall was more impaired than direct recall during the divided attention condition, suggesting a larger involvement of the central executive component in the former. These results are discussed in relation to the hypothesis of a central executive impairment associated with normal aging.

Introduction

Working memory (WM) is a short-term memory system involved in tasks that require concurrent retention and processing (Baddeley, 1986; Baddeley & Hitch, 1974; 1994; Salthouse, 1994). In Baddeley's theoretical framework, WM is a tripartite system composed of two specialized slave systems, the phonological loop and the visuo-spatial sketch-pad, and a central executive. The phonological loop contributes to the retention of verbal information and is subdivided into a passive phonological store and a rehearsal procedure. The visuo-spatial sketch-pad holds images and spatial information. The central executive is an attentional component involved in the control and distribution of limited resources (Baddeley and Hitch, 1972; Baddeley, 1986; 1992). This study focuses on the manipulation capacities of the central executive in normal aging. Manipulation is defined as the process of actively and consciously modifying the format of the information to be recalled. Within a WM framework, manipulation would require involvement of the central executive component.

Recent theoretical and empirical attempts have been made to examine the functioning of the central executive component and to specify the nature of its involvement in cognitive activities. One example is the "model for action control" elaborated by Norman and Shallice (1984), which was proposed as a potentially fruitful theoretical framework for the central executive. This model suggests that well-known actions are performed through the activation of automatic schemas. When activated schemas are incompatible (e.g. opening a door while holding a bag), semi-automatic plans of action (or contention scheduling in the Norman and Shallice terminology) occur to resolve the conflict. Hence, the bag would be rapidly transferred to the non-dominant hand allowing use of the dominant hand to open the door. There are situations that cannot be resolved by simple contention scheduling, and in these cases the system can rely on a second form of control: the supervisory attentional system (SAS). This form of control is non-automatic; it is slow and conscious. The SAS acts by modulating the pattern of activation of particular schemas so that the most appropriate actions take place. For example, the SAS would be involved in a situation when a subject has to open a door while holding a bag in one hand and a cup of coffee in the other hand. In this case the subject might stop, look around for a nearby place to rest the coffee, put down the cup of coffee, open the door, and subsequently pick up the cup of coffee. In the Baddeley and Hitch view (Baddeley, 1986; 1992; Baddeley & Hitch, 1994), the central executive of WM corresponds to the SAS. According to this framework the central executive would be involved in a number of different activities: realization of new actions, planning and decision making, time sharing, inhibition of automatic behavior, as well as the updating and manipulation of information in WM.

A number of studies have observed that elderly people are impaired in tasks that require the manipulation of the information retained in WM (Craik, 1986; Dobbs & Rule, 1989; Foos, 1989; Tun, Wingfield & Stine, 1991; Wright, 1981). One interesting example of a manipulation task is provided by Craik (1986). Gick and Craik (reported in Craik, 1986) assessed manipulation abilities in normal aging using an alphabetical span procedure. Subjects were presented a random series of words which they were required to rearrange mentally and report in alphabetical order (Craik, 1986). Serial ordered recall is usually spontaneously adopted by subjects during the immediate recall of short lists. One reason might be that the format of recall is then perfectly congruent with the format of presentation. Furthermore, the phonological loop retains an ordered representation of the material. In contrast, alphabetical recall requires that subjects organize and control their retrieval. This corresponds closely to one of the roles that the SAS system is hypothesized to play in memory. When asked to modify the format of the input, the subject has to be break down the ordered representation, extract alphabetical order from long-term memory, and scan that order while items are held in the phonological loop. The subject has to verify the output while controlling these different operations. Completion of this task is impossible using automatic processes, and very unlikely using simple contention scheduling. Rather, the task requires that automatic schemas (for example, reading the content of the ordered representation in the phonological loop) be inhibited and that information from long-term memory be activated. The alternation between the reading of each information type, the items and the alphabet, would then be done by modulation of each process. The task most likely requires usage of the SAS control system, or central executive, the role of which is to provide control over cognitive operations. The performance of elderly and young normals on the alphabetical recall of words and on serial digit recall was compared by Gick and Craik. Elderlies were found to be impaired on the alphabetical task, yet were unimpaired relative to young normals on the digit span task. The authors suggested that the alphabetical recall impairment was not due to a decrease in passive storage, since aged and young subjects did not differ when reporting sequences of digits. This led them to conclude that aged subjects were impaired in WM tasks involving active manipulation of the material.

Although the original alphabetical span procedure is quite appealing, it suffers from a potentially important methodological weakness. Specifically, the use of digit span might not have been an appropriate control for passive storage capacities. The implicit assumption in the protocol used by Gick and Craik is that only one difference exists between alphabetical and digit recall; the first task requires manipulation, while the second does not. It must be noted, however, that the two conditions also differ in their material format; words versus digits. This difference in material format may underlie the apparent interaction between age and recall type. Studies that have compared digit versus word spans have at times observed intact digit spans but impaired word spans in normal aging (Light & Anderson, 1985, Exp.1; Wingfiel, Stine, Lahar & Aberdeen, 1988). In these studies, a difference of about one unit was found between the word spans of young subjects and those of aged subjects. This corresponds to the difference in the alphabetical recall of words reported by Craik between the two age groups. Consequently, the age difference observed by Gick and Craik in the alphabetical condition may simply reflect a word span impairment rather than an impairment in manipulating information. This word span reduction is also indicative of an impaired storage capacity in aged subjects, a suggestion that is congruent with other studies (Dobbs & Rule, 1989; Foos, 1989). A passive storage deficit in elderly people might thus be responsible for their observed difficulties in manipulating information, as it makes them particularly sensitive to tasks requiring both the retention and the manipulation of information.

Loftus (1978) has pointed out the complexities of interpreting interaction effects in memory research because the shape of the function that relates response probability to a particular theoretical component is generally unspecified. Salthouse (1985) has raised the same concerns in aging research mentioning that the frequently observed baseline differences between young and elderly subjects is a serious problem when examining interaction effects. The finding of an interaction between the variable of interest and age is obscured if the two groups differ according to their baseline performance as this variable of interest may have differential effects when it occurs at different points of the performance range. For example, manipulation operations are certainly more difficult to perform on weak memory traces than on strong ones. The direct implication is that a performance deficit may be manifested not because manipulation is impaired but rather because the operation acts on a weaker trace. Other problems may arise when the two groups have different baselines. For example, a ceiling effect in young subjects, but not in older ones, might be responsible for the detection of an interaction. One solution proposed to resolve the problem of unequal baselines is to manipulate the conditions of testing to ensure comparable levels of performance in both groups (Belleville, Malenfant, Peretz & Chatelois, 1992; Meudell & Mayes, 1982; Salthouse, 1985; Salthouse, Fristoe, Lineweaver & Coon, 1995; Somberg & Salthouse, 1982).

The alphabetical span procedure represents an attractive assessment tool of manipulation abilities; we will thus re-employ this procedure to assess manipulation abilities in aged individuals. However, the present study controlled for an impairment in the storage capacities of older subjects before introducing a manipulation requirement into the task. This was done by first assessing each subject's word span and by adjusting the length of the experimental sequences according to this span. Subjects were then tested with word series in the condition of direct (or serial) recall and in the condition of alphabetical recall. Due to the adjustment of the length of the sequences relative to each subject's span, the performance of aged and young subjects should not differ in the direct recall condition. However, if aged subjects experience a genuine manipulation deficit they should be impaired in the alphabetical condition. In Experiment 1, subjects were tested with sequence lengths that are one word smaller than their individual span capacity. In Experiments 2 and 3, the number of items to manipulate in the task was increased by one in order to make the task more demanding.

Experiment 4 addressed the construct validity of the different procedures used to assess the central executive of WM. Construct validity refers to a task's ability to be a true measure of the component that it is proposed to examine. Independent evidence that particular tasks or dependent variables are true measures of central executive function represent crucial validation, especially in experiments failing to report age differences. Even if there are theoretical reasons to believe that alphabetical recall involves the SAS system, it is still possible that it can be resolved with semi-automatized forms of controls. In order to address this problem, we took advantage of the fact that time sharing paradigms call on the central executive. A third experiment assessed whether the alphabetical span is sensitive to divided attention. Young healthy subjects were asked to perform the direct and alphabetical recall in either a divided attention condition or a full attention condition. According to Baddeley (1996) the central executive is involved in the division of attention or time sharing. Performing a task that requires extensive central executive capacities (alphabetical recall) should be particularly problematic when the central executive is simultaneously involved in dual-task coordination. Divided attention is likely to alter performance on any concurrent task, provided it is non-automatic. However, if alphabetical recall requires more central executive input than direct recall, it should also be more susceptible to divided attention.

Experiment 1

In this experiment, young and elderly normal subjects were required to report a sequence of words in the presented order or in alphabetical order. Subjects were tested with individually adjusted sequences the length of which corresponded to their word span minus one item. The immediate serial recall procedure used in the direct condition was the same as that used in a typical span test. Since the sequence length was adjusted according to individual word spans, the performance of young versus elderly subjects should not differ on the direct recall condition. However, if the manipulation capacities of the central executive are dysfunctional in aged subjects, they should be impaired in the alphabetized condition relative to young subjects.

METHOD

Subjects

Thirty-two normal francophone subjects, 16 young and 16 elderly, participated in the experiment. All subjects were taken from a pool of volunteers living in the community. They had no history of neurological disease, psychiatric disorder, or recent (within a year) general anesthesia, and did not take any medications known to affect cognitive functions. A medical questionnaire was used to assess the inclusion criteria prior to the subjects acceptance into the protocol. The young subjects (6 males and 10 females) were on average 22.38 years of age (SD = 2.63, range 19-28), and had a mean of 13.31 years of education (SD = 1.54). The older subjects (2 males and 14 females) had a mean age of 71.75 years (SD = 4.67, range 68-78) and a mean educational level of 12.75 years (SD = 3.51). The difference in formal education between aged and young subjects was not significant, 0.56 ± 1.97 (where 1.97 is the 95% confidence interval). General verbal performance was assessed using the Mill Hill Vocabulary Test (Gérard, 1983). This is a widely used francophone test in which subjects have to identify the synonym of a target word among six choices. On this test, young subjects had a mean score of 32.15/44 (SD = 4.81; the result of 1 young subject was not available on this test) and older subjects had a mean score of 35.56/44 (SD = 5.48). The difference in vocabulary score was not significant, 3.41 ± 3.76.

Materials

Two hundred and eleven monosyllabic words were chosen according to the following criteria: 1) the words had to be frequent (Baudot, 1992) and imaginable substantives; and 2) the words were unambiguous with respect to the print-to-sound correspondence of their first letter. For example, a word like *phare* in French (which is pronounced [fAR]) would have been excluded. Furthermore, words having homophones of a higher frequency were not used.

These words were used to construct sequences of words the length of which ranged from two to eight items (to be used with subjects of a span size from 3 to 9). There were 20 different sequences for each length, 10 to be used in the direct condition and 10 to be used in the alphabetical condition. Words included in a sequence differed according to their first letter and had no phonological or semantic similarity. In addition, the manipulation requirement was controlled by measuring three factors: 1) the distance between the first letter of the words in a sequence. According to a pilot study from our laboratory (Belleville & Sauvage, 1996), it is easier to judge the alphabetical order of letters that are farther apart; 2) their position in the alphabet since letters at the beginning of the alphabet should be easier to arrange in alphabetical order, and 3) the total number of manipulations to perform into each sequence (e.g. there is one manipulation in the series *bloc, pneu* and *crabe* but two manipulations in the series *rose, pomme* and *lune*). By using these criteria, the manipulation requirement was made equivalent for the different sequence lengths. Mean word frequency was equivalent across sequence length as well as for the direct and alphabetical condition at a given list length. None of the words were repeated across different sequences for a given length. Sequences of different lengths (thus submitted to subjects of different span sizes) originated from the same pool of words but were not identical with respect to order and items for the reasons outlined below. For example, subject A with a span size of 7, was tested with 20 sequences of 6 items (10 in alphabetical and 10 in direct). The 20 sequences were different and made up of non-repeated words. Subject B, with a span of 6, was also tested with 20 sequences. These were necessarily different from those used for subject A, as they contained one less item. However, sequences were controlled so that frequency and manipulation requirements were equivalent for both subjects. We did not construct the different sequence-lengths by simply removing (or adding) one item from the longer (or smaller lists) because it was impossible to do so without causing serious imbalance across sequences in the manipulation difficulty.

Procedure

Pre-experimental phase

As a first step, a classical word span procedure was used to assess the short-term memory capacity of each subject. The words chosen for the span procedure fit the same criteria as those on the experimental list in terms of length, frequency, and imageability yet did not overlap with the experimental list. The items were chosen without replacement. Sequences of words were read to the subjects at the rate of one item per second, starting with short sequences of two words. The length of the sequences was increased by one word every two trials. However, if an error occurred on one of these two trials, the subjects were given two additional trials. Subjects were instructed to orally report items in serial order. Testing was interrupted when subjects failed to report correctly two of the four sequences at a particular length. The word span was defined as the longest sequence correctly recalled on 50% of the trials.

Experimental phase

Following the span measurement, subjects were assessed in two conditions, direct and alphabetical recall. Words were read to the subjects at the rate of one item per second and subjects recalled the words orally. In the direct condition, subjects performed an immediate serial recall of the words. In the alphabetical condition, they were asked to rearrange and recall the words in their alphabetical order. For example, the words *route-nappe-poivre* should be recalled *nappe, poivre, route* in this condition. Ten sequences of words were recalled in each condition. The number of words to be recalled in a sequence corresponded to the subjects' span, as determined in the pre-experimental phase, minus one item. For example, a subject with a word span of five was tested with sequences of four words. The order of presentation of the direct and alphabetical conditions followed an ABBA design, starting with the direct condition. This allowed to control for possible effects of fatigue or practice. The whole procedure was completed within a single testing session.

RESULTS AND DISCUSSION

A preliminary analysis was performed that compared the span size of young and aged subjects as assessed in the pre-experimental phase. The average span was smaller in aged subjects (M = 4.38, SD = 0.72) than in young subjects (M = 4.88, SD = 0.81), and this difference was significant, 0.5 ± 0.547. A second preliminary analysis was done to assess the effect of the order of presentation due to the ABBA design. A 2 (Age: young, old) x 2 (Order: first, second) x 2 (Recall: direct, alphabetical) ANOVA was thus conducted. The analysis showed that neither the main effect of

Order, nor any of the interactions with this factor reached significance, $F<1$, in all cases. This indicates that the order of presentation of the conditions had no influence on performance, and that no fatigue or practice effects were affecting the results. For this reason, the data from the two orders of presentation was pooled in the subsequent analyzes.

Figure 1 shows the number of sequences correctly recalled by elderly and young subjects in both conditions. To be considered as correct, the whole sequence of items had to be correctly recalled. Alphabetical recall yielded a diminished absolute level of performance in comparison to direct recall (see Figure 1). However, the decrement due to alphabetical recall is not larger in older subjects. This is confirmed by a 2 (Age: young, old) x 2 (Recall: direct, alphabetical) ANOVA. The analysis revealed a significant main effect of Recall, $F(1, 30) = 45.76$, $MSE = 1.31$, $p<.001$, reflecting the reduced performance level in the alphabetical condition. A power analysis indicated that the effect size of the main effect of Recall (Hintze, 1991, according to Cohen, 1988) was 0.846. There was no main effect of Age, $F<1$, $MSE = 4.53$, indicating that elderly and young subjects exhibited the same performance level. The effect size for the main effect of Age was 0.145, and a group of 388 subjects would be needed to reach a power level of .80. Contrary to the prediction, the Age by Recall interaction was not significant, $F<1$. A power analysis of the interaction showed an effect size of only 0.03 and indicated that a sample size of 630 subjects would be required to reach a power level of .80.

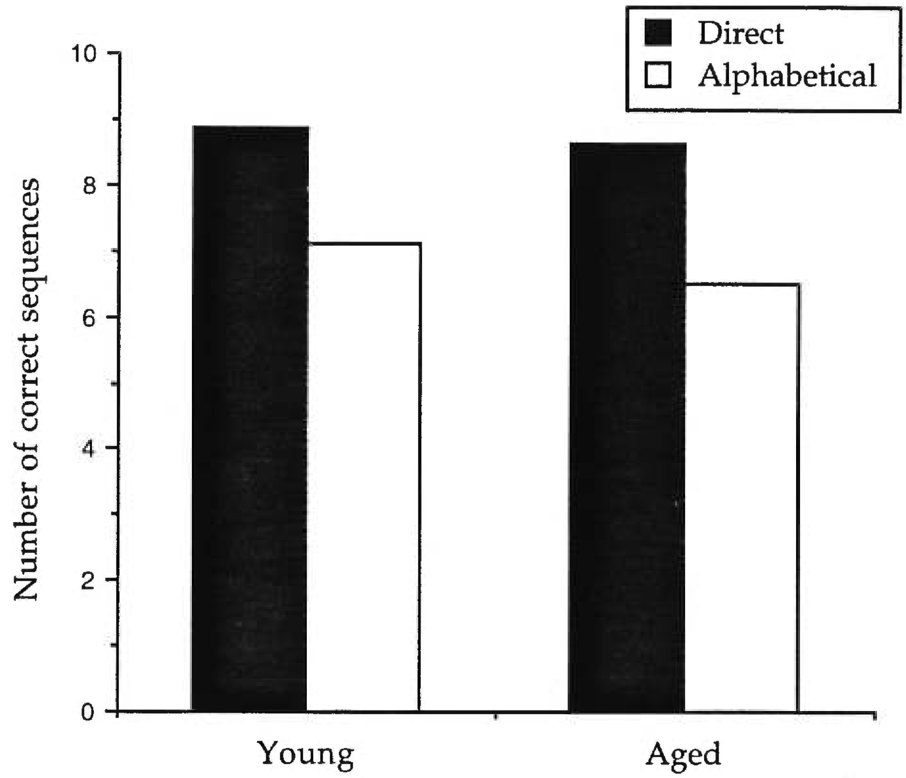

Figure 1. Number of sequences correctly recalled by young and elderly subjects in condition of direct (shaded columns) and alphabetical recall (white columns) of Experiment 1. Subjects were tested using sequences with lengths that were one item smaller than their span.

Another set of analyses of variance was performed using the proportion of correctly recalled *items* (see Table 1). Since the number of items represents a finer measure of recall, it might be more sensitive to an interaction between Age and Condition. An item was considered as correct when it was recalled in the position appropriate to the recall condition (serial or alphabetical). The total number of words recalled was then transformed to a percent correct value. The same ANOVA as above was performed and showed similar insignificant results (no interaction, $F<1$).

Table 1
Proportion of Correct Items for Young and Aged Subjects Tested at Span Minus One

	CONDITION	
	Direct recall	Alphabetical recall
Young subjects	96.44 (4.07)	84.60 (12.32)
Aged subjects	93.9 (8.63)	81.31 (11.80)

Note. Standard deviation in parenthesis

In summary, alphabetical recall yields a decreased performance level in comparison to direct recall, which suggests that there is a cost to the manipulation requirement of the task. However, elderly and young subjects, equalized in the direct condition, do not perform differently in the alphabetical condition. This suggests that manipulation is not particularly difficult for normal elderly people as long as basic storage is controlled for. The absence of an age effect in alphabetical recall may, however, relate to a relative lack of task sensitivity. It must be noted that all subjects performed quite well on both the direct and alphabetical conditions; this might be explained by the observation that the subjects were tested below their span limits. In fact, a ceiling effect was observed in most subjects in the direct condition as well as in some of the subjects in the alphabetical condition. Another possibility is that the task was not sufficiently demanding, and that the proposed deficit in elderly normals would be manifested by a more rigorous condition that tests the limits of the SAS. For this reason, a second experiment was devised in which the task was made more difficult by increasing the number of items in each sequence by one.

Experiment 2

In this experiment, the procedure was slightly modified in order to eliminate performance at the ceiling level and increase the task demand. This was done by increasing the length of the sequences by one item. Subjects were thus tested at the very limit of their short-term memory capacity with sequence lengths corresponding to their span.

METHOD

Subjects

Thirty-two different subjects (16 young normals and 16 elderly normals), participated in this experiment. Subjects were selected according to the same exclusion and inclusion criteria as in Experiment 1. The young subjects (7 males and 9 females) were on average 22.31 years of age (SD = 2.73, range 19-26), and had completed on average 14.25 years of education (SD = 1.84). The older subjects (2 males and 14 females) had a mean age of 73.69 years (SD = 3.55, range 66-79) and a mean educational level of 11.69 years (SD = 3.01). The difference in formal education between aged and young subjects was significant, 2.56 ± 1.82, with the young normals having achieved slightly higher educational levels. However, the general verbal performance, as measured with the Mill Hill Vocabulary test was significantly higher in aged subjects (M = 38.21, SD = 3.38) than in young subjects (M = 34.62, SD = 4.56, note that 2 young subjects did not complete the task), 3.59 ± 2.92.

Materials

The same materials as in Experiment 1 were used.

Procedure

The same procedure as in Experiment 1 was used, except that the number of words to be recalled corresponded to each subject's span size as determined in the pre-experimental phase.

RESULTS AND DISCUSSION

Two preliminary analyses were performed. First, the span sizes of young and elderly subjects were compared. Elderly subjects showed a smaller span than young subjects (4.7 words in young and 4.4 in elderly) and this difference was marginally significant, 0.30 ± 0.354. The effect of the presentation order of the conditions was again assessed with a 2 (Age: young, elderly) x 2 (Order: first, second) x 2 (Recall:

direct, alphabetical) ANOVA. There was no main effect of Order of presentation, $F<1$, and none of the interactions with Order reached significance; Age by Order and Recall by Order, $F<1$; Age by Order by Recall, $F(1, 30) = 1.67$, $MSE = .92$, $p=.21$. The datum from the two orders were thus pooled in the following analyses.

Figure 2 shows the number of sequences recalled correctly in both the direct and alphabetical conditions. As in Experiment 1, performance in the alphabetical condition is severely depressed compared to that in the direct order condition. However, this reduction is again equivalent for both groups. This was confirmed by an ANOVA which revealed a significant main effect of Recall, $F(1, 30) = 42.46$, $MSE = 2.80$, $p<.001$, associated with an effect size of 1.15, but no interaction between Age and Recall, $F<1$. A power analysis of the interaction yielded an effect size of 0.169. and indicated that the sample size needed here to reach a power level of .80 would be 288 subjects. Note that according to Figure 2 the interaction would be in the opposite direction than that expected, that is the Age difference would be larger in the direct than alphabetical condition. Although aged subjects do appear to have a lower global level of performance, the main effect of Age was not significant, $F(1, 30) = 2.26$, $MSE = 8.35$, $p=.14$. The effect size of the main effect of Age was 0.2657, and 114 subjects would be required to reach a power level of .80.

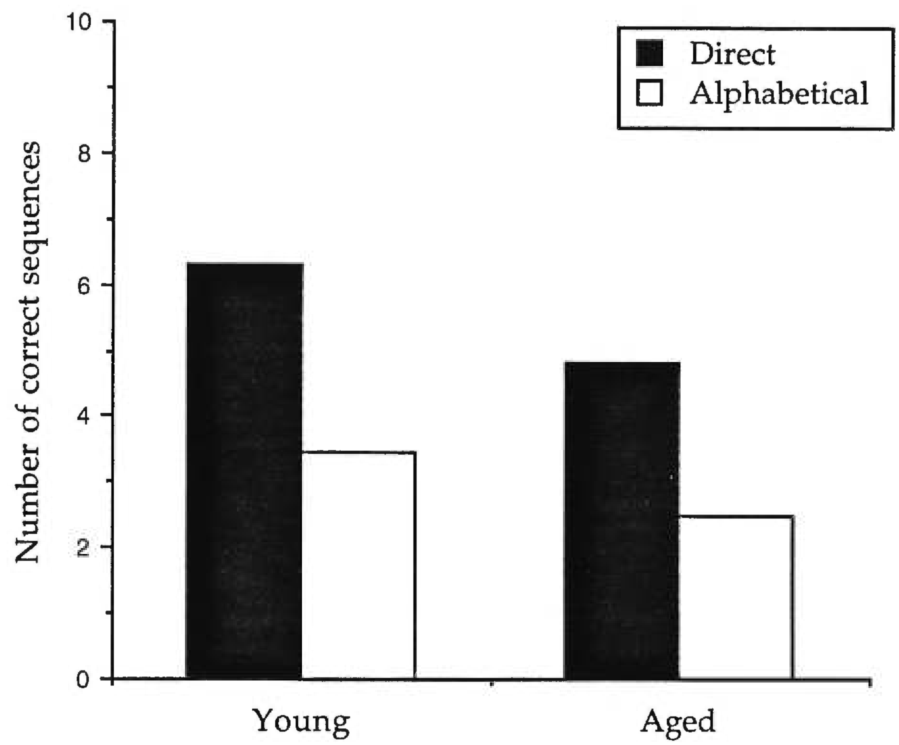

Figure 2. Number of sequences correctly recalled by young and older subjects in condition of direct (shaded columns) and alphabetical recall (white columns) of Experiment 2. Subjects were tested with sequences corresponding to their span.

As in Experiment 1, the analysis was conducted using the percentage of correctly recalled items as the dependent variable (see Table 2a). The results of the analysis were similar to those obtained when correctly recalled sequences was used as the dependent variable: the interaction was not significant, $F<1$, yet the main effect of Age was significant, $F(1, 30) = 5.95$, $MSE = 352.03$, $p< .05$.

Table 2

Proportion of Correct Items for Young and Aged Subjects Tested at Span in a) Experiment 2 and b) Experiment 3

	CONDITION	
	Direct recall	Alphabetical recall
a)		
Young subjects	85.38 (9.15)	64.19 (15.02)
Aged subjects	73.55 (18.42)	53.13 (15.76)
b)		
Young subjects	93.56 (6.98)	75.2 (8.85)
Aged subjects	90.56 (8.66)	73.5 (17.42)

Note. Standard deviation in parenthesis

In conclusion, elderly subjects do not appear to show any differential effects of alphabetical recall on WM when compared to young subjects. The procedure used here intended to equalize recall in the direct condition by testing subjects at their short-term memory span. Unfortunately, we have only partially succeeded in doing so. While young and aged subjects recall an equivalent number of sequences, this is not the case when measuring the number of correct items. Young subjects do recall more items than older ones in the direct condition. It is worth pointing that there is clearly no interaction between Age and Condition in spite of this age effect on the number of items: the Age difference is not larger in the alphabetical condition than in the direct condition. However, the presence of a Group effect is a problem because it is still possible that an interaction would come out in a transformed version of the data (Loftus, 1978). In principle, this Group effect should not have been found because subjects were tested with sequence length that corresponds to their span as measured in the pre-experimental phase. One possible explanation is that aged subjects are simply more sensitive to fatigue. Whereas possible, this explanation is disconfirmed by the fact that no Group by Order effect was found in the preliminary analyses on the experimental trials. However, fatigue effects could have occurred between the pre-experimental and experimental trials. As a result, it is possible that the span measurement was not accurate in aged subjects. We have evidence to suggest that this might be the case in aged subjects and that they were outperforming their baselines during the span measurement procedure of the pre-experimental phase. In the pre-experimental phase the span measurement is done with only two trials at each length. Subjects move rapidly through the incremental list lengths as only two trials are used to estimate the span. If the number of trials are not sufficient to take into account a potential fatigue effect in the aged, these subjects may fail to maintain the same level of performance in the experimental phase where 10 trials are given in each condition. Examination of the data suggests that this is the case. First, the span size measured in the pre-experimental phase is quite large in our aged subjects and does not differ from that of younger ones. Second, Figure 2 shows that aged subjects recall less than 50% of the sequences in the direct condition (48.3% precisely). Yet, the sequences presented should yield higher performance level as it is supposed to correspond to their span which is defined as the length for which subjects reach a minimum of 50% correct performance. On the few trials available in the pre-experimental phase for the same lengths, the performance of aged subjects was much higher, reaching about 70%. There was thus a decrease in performance from the pre-experimental to the experimental trials. Of note, a look at individual data shows that it is those subjects tested with the fewest trials that show the largest decrease from the pre-experimental to experimental phase. The measure used here thus seems to have over-estimate the span size of some of our aged subjects because not enough trials were provided at each length. This, interacting with fatigue effects, contributed to alter the span estimate of aged subjects. A third experiment was undertaken to take this into account with regard to span measure in an attempt to eliminate the Group effect.

Experiment 3

In Experiment 3 the span measurement procedure in the pre-experimental phase was slightly modified to provide a more accurate estimate of span capacity, as we suspected that errors in the span measurement of our elderly subjects was the source of our failure to equalize performances in Experiment 2. The procedure was thus modified to allow a more rigorous criterion for span capacity. This should ensure equalization of recall across groups in the direct condition and allow us to measure interactions without the possible confounding effect of differences in baseline performance.

METHOD

Subjects

Twenty new subjects (10 young and 10 elderly) participated in this experiment. Subjects were selected according to the same exclusion and inclusion criteria as in the previous Experiments. The young subjects (10 females) were on average 21.70 years of age (SD = 0.95, range 20-23), and had completed on average 16.40 years of education (SD = 1.07). The older subjects (1 male and 9 females) had a mean age of 73 years (SD = 4.55, range 68-79) and a mean educational level of 15.50 years (SD = 1.51). The difference in formal education between aged and young subjects was not significant, 0.90 ± 1.07. However, the general verbal performance, as measured with the Mill Hill Vocabulary test, was significantly higher in aged subjects (M = 29.40, SD = 2.88) than in young subjects (M = 26, SD = 3.92), 3.40 ± 0.82.

Materials

The same materials as in Experiment 1 were used.

Procedure

The same procedure as in Experiment 2 was used, except for the span measurement of the pre-experimental phase which differed as explained below. Span was established using a staircase procedure. One trial was presented for each sequence length starting with sequences of two items. A correct recall was followed by the presentation of sequences one item longer. When subjects failed on a trial, three more trials of the same sequence length were presented. If subjects succeeded on two trials, six other trials were provided for a total of ten trials. If the subjects did not recall two of the trials, a total of ten trials were presented at the smaller sequence length. A 50% correct performance on a series of ten trials was required for the sequence length to be considered as the subject's span. A 20-minute pause was provided to the subjects between the pre-experimental phase and the experimental phase.

RESULTS AND DISCUSSION

As a preliminary analysis, the span sizes of young and elderly subjects were compared. Elderly subjects showed a smaller span than young subjects (4.9 words in young and 4.2 in elderly and, 0.7 ± 0.31. Figure 3 shows the number of sequences recalled correctly in both the direct and alphabetical conditions. The ANOVA revealed a significant main effect of Recall, $F(1, 18) = 49.23$, $MSE = 75.63$, $p<.001$ but neither an Age effect ($F<1$) nor an interaction between Age and Recall, $F(1, 18) = 2.75$, $MSE = 4.23$, $p=.11$. A power analysis of the interaction showed an effect size of only 0.1943 and indicated that a sample of 192 subjects would be required to reach a power level of .80. The same results were obtained when using the percentage of correctly recalled items as the dependent variable (see Table 2b): neither the main effect of Age, nor the interaction was significant, $F<1$ in both cases, yet the main effect of recall was, $F(1,18) = 38.05$, $MSE = 26.1$, $p< .001$. The power analysis was done for the interaction and showed a somewhat larger effect size (0.3909). It also indicated that the use of 50 subjects would yield a power of .80. However, it is worth pointing out here that the interaction would be in the direction opposite to what is predicted by an age-related manipulation decline (See Table 2b).

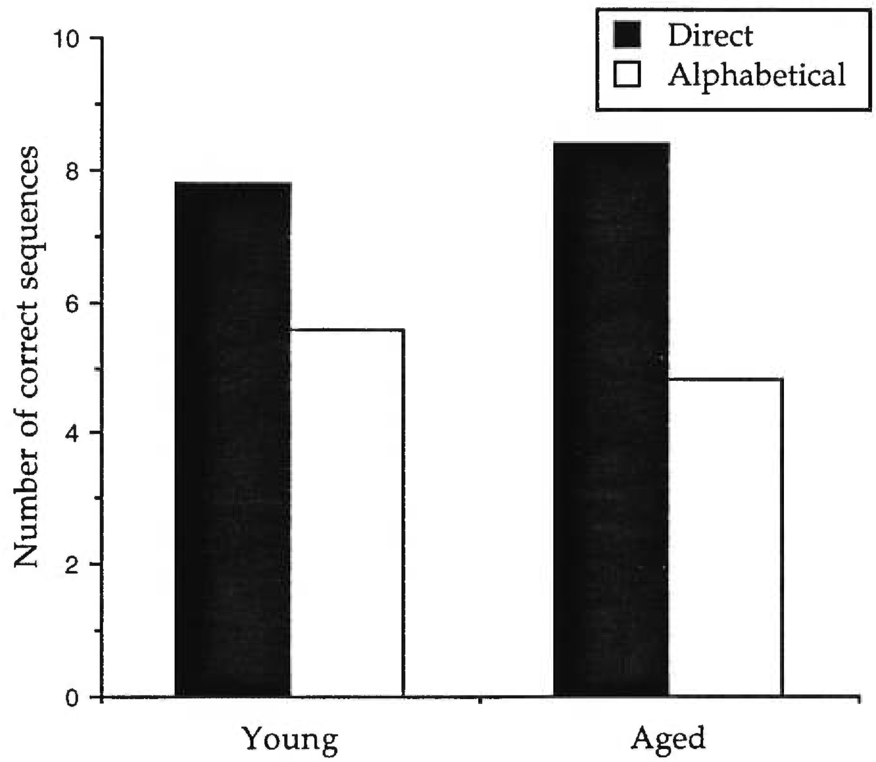

Figure 3. Number of sequences correctly recalled by young and older subjects in condition of direct (shaded columns) and alphabetical recall (white columns) of Experiment 3. Subjects were tested with sequences corresponding to their span.

In summary, a modification of our span measurement technique was sufficient to permit an equalization of the performance of aged and young subjects in the direct recall condition. Yet again, no interaction between Group and Recall was observed further confirming that elderly subjects are not more impaired by the alphabetical recall condition when compared to young subjects.

Experiment 4

The goal of Experiment 4 was to evaluate the validity of our manipulation procedure. For that purpose, the same paradigm was applied to young subjects in the condition of either full or divided attention. In the divided attention condition, subjects performed either the direct or alphabetical recall condition as well as a concurrent visuo-spatial tracking task. This concurrent task was chosen because it does not compete with words for space in the verbal short-term store or for phonological processing. Any performance decline in the divided attention condition can thus be explained by the central executive involvement in coordinating the two tasks. If alphabetical recall requires the central executive, it should thus be more affected than direct recall by the divided attention condition.

METHOD

Subjects

In all, 32 French-speaking students volunteered to participate in the experiment. The same inclusion criteria as those of Experiments 1 and 2 were used here. The subjects were randomly assigned to the two different conditions of attention, full or divided. The first group (full attention) was composed of 7 men and 9 women between the ages of 19 and 30 (M = 21.63, SD = 3.52). Their average level of education was 14.84 years (SD = 2.71) and their average score on the Mill Hill Vocabulary Test was 34.50 (SD = 2.85). The second group (divided attention) included 6 men and 10 women between the ages of 18 and 29 (M = 22.06, SD = 3.13). This group had a mean of 14.87 years of education (SD = 2.10) and an average score on the Mill Hill Vocabulary Test of 36.75 (SD = 2.95). No significant differences in age, 0.43 ± 2.42, formal education, 0.03 ± 1,76, or Mill Hill Test scores, 2.25 ± 2.11, were found.

Materials and Apparatus

This experiment utilized the identical word span and memory tasks task as described in Experiments 1 and 2. In addition, a visuospatial tracking task was required for the divided attention condition. This latter task was presented on the screen of a Macintosh Classic computer and consisted of maintaining, via the computer mouse, a rectangular cursor (0.2 by 0.5 cm) within a diagonally moving rectangle (0.7 by 0.9 cm).

Procedure

Pre-experimental phase

The subjects were tested individually. The word span was measured for all participants using the same procedure as in Experiments 1 and 2. Then, the tracking threshold on the visuospatial task was established. This started with a familiarization phase during which subjects were introduced to computer mouse manipulation and the tracking task. During this phase, subjects tracked the moving target once at slow paces (0.2 pixel/s and 0.4 pixel/s) along a horizontal, vertical and oblique axis. Then, the tracking threshold was obtained for each subject. During 10-second trials, subjects were required to track the oblique moving target. The speed of the target changed on every trial. The initial speed was set at 0.5 pixel/s and was increased by 0.2 pixel/s increments after each trial. Increments were continued until subjects failed to maintain the cursor in the target during 65% of the trial, as recorded by the computerized program. Speed was then decreased by 0.2 pixel/s on every trial until the subject reached 90% correct tracking performance. The presentation of such ascending and descending series of speeds was repeated until a 70% correct performance level (between 65% and 75%) was obtained for a given speed on two successive trials. Therefore, a specific target speed was obtained for each subject corresponding to the fastest speed at which they maintained performance approximately 70% of the time. This represented the speed to be used in the experimental phase. All participants completed the tracking threshold measure in order to ensure that the two groups did not differ in regards to fatigue.

Experimental phase

Following the tracking threshold measure, the subjects underwent the memory task according to the same procedure as in Experiment 1 and 2. In addition, subjects in the divided attention condition were asked to perform the visuospatial tracking task concurrently with the presentation and recall of the word sequences. The target in the tracking task moved obliquely at threshold speed.

Subjects were instructed to maintain tracking accuracy to the same level as measured in the pre-experimental phase. They were thus required to put emphasis on the visuo-spatial task. These instructions were given in order to reduce trade-off effects with the memory task. An average performance of about 70% correct tracking was thus expected on the visuospatial tracking task whether concurrently performed with either the direct or the alphabetical condition. A tracking accuracy measure was taken after every five sequences, in agreement with the ABBA order of presentation.

RESULTS

The average word span for each group was compared. Subjects in the full attention condition had a mean span of 5.06 words ($\underline{SD}$ = 0.77) and subjects in the divided attention condition had a mean span of 4.94 words ($\underline{SD}$ = 0.68). The difference in span between the two groups was not significant 0.12 ± 0.53. The effect of presentation order was then assessed with a 2 (Attention: full, divided) X 2 (Order: first, second) X 2 (Recall: direct, alphabetical) ANOVA. No main effect of Order was found, $\underline{F}(1,30) = 1.55$, $\underline{p} = .2233$, and this factor did not interact with Attention, $\underline{F}(1,30) = 1.55$, $\underline{p} = .22$. However, the Order by Recall interaction was significant, $\underline{F}(1,30) = 5.24$, $\underline{p} < .05$. Simple effects analysis showed an Order effect in the direct condition, $\underline{F}(1,30) = 11.68$, $\underline{p} < .01$, $\underline{MSE} = 0.39$. Performance on the last five trials was superior to performance on the first five trials, a result that is congruent with a practice effect. However, there was no order effect in the alphabetical condition, $\underline{F} < 1$. The absence of a three-way interaction is of note, $\underline{F}$ <

1. Consequently, results obtained from the different orders were pooled in the following analyses.

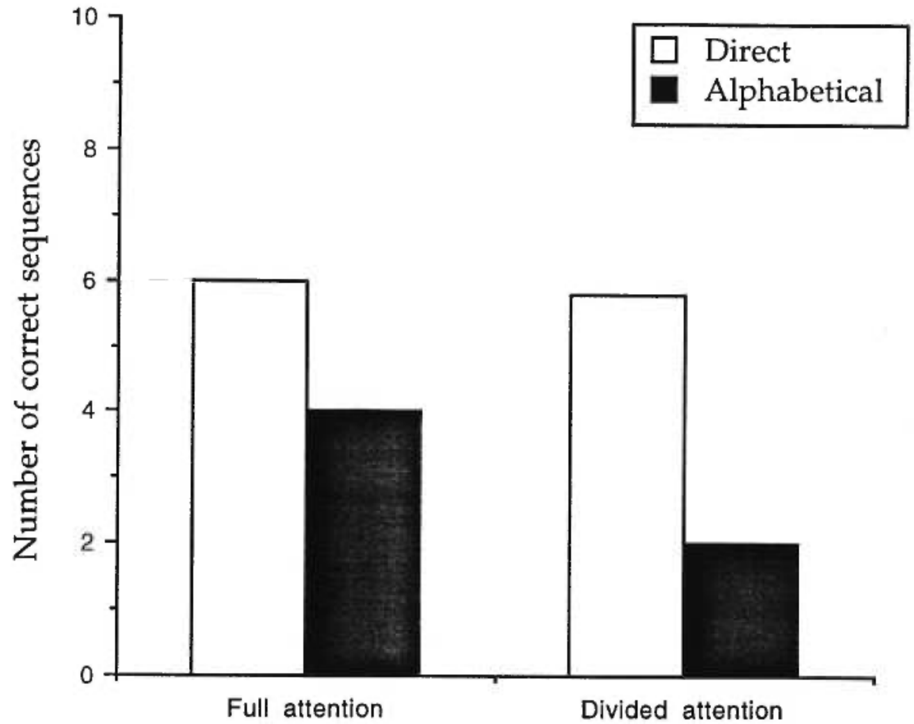

Figure 4. Performance of young subjects in the direct (white columns) and alphabetical (shaded columns) recall condition when tested in the condition of full or divided attention.

Figure 4 presents the direct and alphabetical recall of the sequences for each attention group. Examination of this figure indicates that the performance decline in the alphabetical condition is larger for subjects in the concurrent divided attention condition than for those in the full attention condition. The ANOVA performed on the number of correct sequences yielded a significant main effect of

Recall, F(1,30) = 60.92, MSE = 2.12, $p < .0001$; effect size, 1.38. This confirms that fewer sequences were recalled in alphabetical order than in direct order. The main effect of Attention was marginally significant, F(1,30) = 3.40, MSE = 7.73, $p = .0752$, with an effect size of 0.33. However, main effects were qualified by a significant interaction between Recall and Attention, F(1,30) = 5.36, MSE = 2.12, $p < .05$ with an effect size of 0.41. An analysis of the simple effects showed that no Attention effect was present in the direct condition, (F < 1, but that this effect was present in the alphabetical condition, F(1,30) = 8.10, MSE = 4.46, $p < .005$. Furthermore, the reduction due to alphabetical recall was larger in the divided attention condition, F(1,30) = 51.22, MSE = 2.12, $p < .0001$, than in the full attention condition, F(1,30) = 15.07, MSE = 2.12, $p < .001$. Subsidiary analyses using the percentage of items recalled (see Table 3) confirmed the analysis performed on the number of correct sequences as described above: the interaction was statistically significant, F(1,30) = 4.27, MSE = 100.80, $p < .05$.

Table 3

Proportion of Correct Items in Condition of Focused and Divided Attention

	CONDITION	
	Direct recall	Alphabetical recall
Focused attention	85.37 (9.15)	69.49 (13.82)
Divided attention	79.8 (13.34)	53.55 (14.77)

Note. Standard deviation in parenthesis

We also assessed performance on the tracking task to verify if the interaction effect relates to the presence of a tradeoff. When recalling the words in direct order, subjects showed an average tracking performance of 70.01% (SD = 8.33, range 54-82), while when recalling words in alphabetical order, tracking performance was at 68.07% (SD = 8.67, range 54.4-84.4) . Tacking performance in both conditions was fairly close to the tracking threshold (70% in principle) and the difference across condition was not significant, 1.94 ± 2.18, two-tailed. There was thus no evidence of a trade-off between the two tasks.

General Discussion

The results of our four experiments are quite straightforward. First, the alphabetical span procedure, which requires the manipulation of information within WM, is more difficult than a passive task in which direct recall is required. Furthermore, alphabetical span is more affected by divided attention. This is congruent with the substantial role of the central executive in the performance of the manipulation task. Surprisingly, elderly normal subjects' performance on the manipulation tasks is identical to that of young controls. These manipulation abilities of elderly people are retained when the difficulty of the manipulation task is increased.

Prior to discussing the theoretical relevance of this data, we shall first assess if any of the methodological aspects of our task can explain the pattern of results observed here. The questions of power, sensitivity of the dependent variable, and relevance of the measure will be addressed. We will also discuss how the equalization procedure might account for the difference between our data and those previously reported in the literature.

First, it is possible that our failure to observe a difference between the two age groups relates to insufficient power. This is particularly important in analyses where the null hypothesis is confirmed. For this reason, we performed power analyses on our data, which showed a very small effect size for the interaction between Recall and Age. Furthermore, the number of subjects required to obtain a power of 0.80 was above 250 in both Experiments 1 and 2. When such a large number of subjects is required for a significant difference to be obtained, the effects are usually judged as negligible (Cohen, 1988). When a smaller number of subjects is required (as in Experiment 3), the interaction found is in the direction opposite to what is expected in the case of a manipulation defect. It is important to note that the significant effect of Recall (direct compared to alphabetical recall) yielded large effect sizes (Cohen, 1988), indicating that the manipulation procedure was sound and afforded little variability. This result was replicated with different samples in three experiments. Although the problem of lack of power is an important issue in aging research we do not believe that it is sufficient to explain these results.

An alternative explanation is that the absence of an age effect might relate to a lack of sensitivity in the measure. More precisely, it is possible that the manipulation requirement of the alphabetical condition was insufficient to identify a difference between the two groups. This criticism cannot be completely rejected, yet there are three reasons that lead us to believe that our procedure was sensitive to a central executive deficit. First, the alphabetical recall condition is clearly more demanding than the direct recall condition because it systematically yields a lower performance level. Furthermore, this effect is large and robust. Second, we have shown in Experiment 4 that a small resource reduction in young subjects is sufficient to decrease their performance substantially on the alphabetical recall condition relative to direct recall. Finally, Experiment 2 and 3 added to the task demand by potentially increasing the number of manipulations to be performed in WM. It is of note that the performance decline in the alphabetical condition relative to the direct condition is larger in the second and third than in the first experiment. This suggests that the task was indeed more difficult for the subjects and thus taxed the limits of the system. Nonetheless, aged subjects remain unimpaired in the alphabetical recall condition relative to young subjects. We are thus quite confident that a lack of sensitivity is insufficient to explain the absence of an interaction between age and recall.

Another possible objection regarding our results is that the task used here is not a true measure of central executive functioning. However, both theoretical and empirical arguments suggest that the alphabetical task is a genuine measure of the central executive component of WM. Manipulation tasks require that subjects organize and control their retrieval strategies, and this fits one of the functions occupied by the central executive. Non-automatized, complex, or new tasks would involve conscious control from the central executive (or the SAS; Norman & Shallice, 1986). This control would take place by modulating existing schemas.

This theoretical argument was confirmed in Experiment 4 which showed that alphabetical recall is more sensitive to the concurrent completion of a tracking task than direct recall. The utilization of a concurrent visuo-spatial task precludes competition for space in a phonological loop. Rather, the coordination of the two tasks probably requires the control of the central executive system. The fact that divided attention dramatically diminishes alphabetical recall, especially when compared to its effects on direct recall, supports the notion that the task requires commitment from the central executive.

The observation of normal manipulation capacities in aging is in disagreement with a number of previous studies. Other experiments have reported adult age differences on tasks which have also involved a manipulation of the information retained in WM (Craik, 1986; Dobbs & Rule, 1989; Foos, 1989; Tun et al, 1991; Wright, 1981). This was thought to reflect the impairment experienced by aged individuals in novel and demanding situations, or in conditions requiring active processes, and was explained by a central executive defect. One of these previous experiments used the alphabetical span procedure presented here but with digits as the control condition (Craik, 1986). Although statistical details are not provided by the author, the results indicate that elderly people are impaired on an alphabetical recall condition but not on a typical digit span task (Craik, 1986).

One major difference between our paradigm and those used in the past is that we have equalized storage requirements across groups, and this control procedure might be sufficient to account for the different outcomes. Indeed, studies that have assessed either processing capacities or storage capacities have found impairments in elderly subjects (Dobbs & Rules, 1989; Foos, 1989; Light & Anderson, 1985; Wingfiel et al, 1988). In the present study, a small but systematic difference was observed between the two groups' word spans. The performance of elderly normal subjects and young normal subjects are thus not completely akin; aged subjects appear to have a smaller storage capacity. Thus, if we had tested both groups with sequences of equal lengths, the task would have been slightly easier for young subjects than for elderly subjects. Furthermore, a reduction in storage capacity makes older subjects more vulnerable to a task that requires a manipulation of the information in addition to storage. The lack of control for storage differences in past studies may have induced a spurious manipulation decrement. Aged subjects were compared to young subjects in conditions that were more difficult to them for reasons other than the manipulation requirement. Our control procedure ensured that a storage impairment did not contribute to the manipulation deficit of elderly individuals.

One might object that the equalization procedure modified the nature of the task. It may be argued that testing subjects with sequences differing in size qualitatively modified the task across the two groups of subjects. However, the equalization procedure was not arbitrarily chosen: we have ensured that subjects were tested at the limit of their short-term memory capacity by using a classical estimate of this capacity (i.e. the span task). The number of items to recall thus corresponded to a genuine psychological limit for each individual subject. Consequently, we believe that equalizing subjects ensured that the task was qualitatively equivalent across subjects. When controlling for passive storage, as was done in the present case, the manipulation deficit of aged individuals vanishes.

A similar pattern has occurred in time sharing tasks. Impaired levels of performance have been observed in elderly subjects on divided attention paradigms (Inglis & Caird, 1963; McDowd & Craik, 1988; Salthouse, Rogan & Prill, 1984; Tun et al, 1991; Wright, 1981). However, many studies have also failed to observe age differences in divided attention (for example, Baddeley, Logie, Bressi, Della Sala, & Spinnler, 1986; Belleville et al, 1992; Gick et al, 1988; Morris et al, 1988; Somberg & Salthouse, 1982; Wickens, Braune & Stokes, 1987). The discrepancy observed here might relate to the failure of previously used paradigms in controlling for the processing requirement of the individual tasks. The time sharing deficit observed on occasion in elderly subjects may thus have arisen from a difficulty in performing the individual tasks, and this difficulty would be exacerbated in a condition where they had to perform both tasks simultaneously (Hartley, 1992; Belleville et al, 1992; Salthouse et al, 1995). Elderly individuals are thus probably not more impaired than young people on time sharing paradigms as long as the degree of difficulty of the individual tasks is made comparable for the two groups.

The absence of a manipulation deficit when controlling for passive storage capacities is of theoretical relevance for the hypotheses regarding the source of the age-related decline in cognition. Salthouse (1988; 1991) has questioned the level at which age-related impairments are found and proposed that normal aging only affects elementary processes. In his view, a restricted number of general elementary processes (or resources) underlie the functioning of the specialized cognitive components. An impairment of one of these elementary processes in normal aging would thus affect a large number of cognitive activities to varying degrees. In normal aging, complex cognitive tasks would be difficult to perform only because they rely on impaired elementary processes. These elementary processes remain to be identified but possible candidates have been proposed by Salthouse (1988; 1991). These include working memory, speed and attention. Both the storage and manipulation aspects of working memory were foreseen as impaired elementary processes (Salthouse, 1991). However the present experiment indicates that the manipulation aspect of working memory is not a primary source of the age-related impairment. In contrast, the present results are compatible with storage capacities as a primary source of the age-related impairment. Indeed, it can be argued that the equalization procedure had the effect of compensating for a deficiency at the level of one of the elementary processes. Given that the equalization of storage capacities was performed, our results would suggest that storage space might be one of the elementary resources impaired in aging. Other investigators have proposed that reduced storage is a primary source of impairment in normal aged people. For example, Parkinson and collaborators (Inman & Parkinson, 1983; Parkinson, Inman & Dannenbaum, 1985) have observed that matching subjects on the basis of storage space eliminates many of the age-related memory impairments.

Yet, this storage impairment is probably not related to a phonological deficit or to an absence of rehearsal procedures. There have been numerous descriptions of patients who after localized brain-damage present with a verbal working memory deficit related to an impairment of the phonological storage (for example, Vallar & Baddeley 1984) or of the articulatory rehearsal (for example, Belleville, Peretz & Arguin, 1992; Waters, Rochon & Caplan, 1992). These patients are characterized by a severe span reduction resulting in a capacity of 2-3 items and are also not sensitive to the phonological similarity and/or articulatory length of the items. The pattern of impairment of normal aged individuals is different because their span reduction is much smaller and because we have shown them to be as sensitive as normal young subjects to the phonological similarity and length of items in immediate serial recall (Belleville, Peretz & Malenfant, 1996). Nonetheless, it remains possible that articulatory speed or storage space is reduced in normal aging.

It is important to point out that age differences have been reported in central executive tasks other than manipulation and time sharing paradigms. For example, aged individuals are impaired when increasing the syntactic complexity of the to-be-verified sentences on the sentence span procedure (Gick et al, 1988; Morris et al, 1988; Wright, 1981). Although this has been interpreted as arising from a deficit in the active process of working memory, it may also relate to a specific impairment in syntactic processing. Van der Linden and collaborators (Van der Linden, Brédart & Beerten, 1994) have reported age differences in a task that requires subjects to monitor and update information in WM. Baddeley (1986) has found age differences in a random generation task where subjects are required to produce series of elements that mimic a randomization. This task would require individuals to monitor the ongoing productions and to avoid the repetition of patterns, as well as the production of automatic series or acronyms (such as USA).

These paradigms, however, have not controlled for group differences in storage or speed and the results may be partially accounted for by a deficiency at this level. Alternatively, these tasks might tap into some component process of the central executive that, while different from component processes investigated here, is affected by normal aging.

In the same line, there has been numerous recent works showing that aged people are impaired in tasks that are sensitive to frontal lobe damage. For example, aged individuals show deficits in the self-ordered pointing task (Daigneault & Braun, 1993; Shimamura & Jurica, 1994), and in more classical tests of frontal executive functions such as the Stroop or the Wisconsin card sorting task (WCST) (for reviews see Albert & Kaplan, 1980; Moscovitch & Winocur, 1992; Shimamura, 1990; West, 1996). They also exhibit impairment in retaining contextual information in long-term episodic memory (McIntyre & Craik, 1987; Schacter et al, 1984; Stanhope, 1988). Some authors have argued that this pattern of impairment relates to a frontal lobe dysfunction. This "frontal lobe hypothesis" is congruent with the suggestion that normal aging is accompanied by a deficit in the executive component of working memory. However, care must be taken in interpreting previous data on frontal lobe tasks. For example, Houx, Jolles & Vreeling (1993) have observed that when considering mild biological or environmental factors, the age effect was much reduced on the Stroop interference test. Paolo and collaborators (1995) have shown that the WCST in normal elderlies does not strongly share construct validity with other frontal and memory tasks. They suggests that this task provides more information about the elderlies' problem solving strategies than their attentional functions.

Finally, it is worth mentioning that classical tests of "frontal lobe functions" are not exempt of the methodological limitations reported here for working memory tasks. It is possible that a portion of this "frontal lobe deficit" would vanish if appropriate controls of some, as yet unknown, general factor was performed for these task. Nevertheless, it has been shown that even when controlling for Group effects, some "frontal-lobe functions" remain impaired in normal aging. Parkin and Walter (1992) have shown that an impairment in contextual memory was still present when comparing a subgroup of young and aged subjects matched with respect to their memory for facts. However, this finding was reported in a task that measured the contribution of frontal lobe functioning to long-term memory and not to working memory. This might again highlight the importance of subdividing the general class of "executive functions" into finer categories. Executive functions have been measured with a wide range of heterogeneous tasks that do not have the same cognitive requirements and likely reflect a variety of processes. For instance, some of these tasks might assess inhibition (for example, the Stroop test) while others appear to rely largely on planning (for example, the WCST). If there are different executive functions, it is likely that not all are impaired in aged individuals as is shown here.

In summary, we have failed to observe age differences in a task that requires the active manipulation of information within working memory. This was found in three different experiments and thus appears to be a robust observation. Furthermore, this was observed even if the manipulation demand of the task was increased. The absence of an age decrement could relate to the fact that this study controlled for a potential age-related impairment in basic storage capacity. A diminution in storage capacity might thus represent a source for the cognitive decline observed in normal aging. The present results cast some doubts on the hypothesis of a general central executive deficit in normal aging. Like time sharing, manipulation is probably not impaired in normal elderly subjects. The central executive of normal aged people is thus at most only partially impaired. However, it is the goal of future research to determine which central executive functions are impaired versus those that are not, and to integrate these empirical findings within a coherent description of the central executive.

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Article n° 3

Inhibition and manipulation capacities of working memory: Dissociations in patients with dementia of Alzheimer type

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Abstract

Inhibition and manipulation capacities of working memory were measured in patients with dementia of the Alzheimer type (DAT), normal aged individuals and young subjects. Experiment 1 compared serial word recall to recall of words in the order of the alphabet. Alphabetical recall would require active manipulation of the content of working memory. Patients were severely impaired in the alphabetical recall task but normal aged subjecs were comparable to young ones. Experiment 2 measured phonological inhibition by measuring short-term digit recall in the presence of different irrelevant noise. In this task, both normal aged and DAT patients performed similarily to the group of young subjects indicating that irrelevant auditory noise can be inhibited with comparable efficacy. Heterogeneity was assessed in the group of DAT patients. It was found that both tasks yield heterogeneous performance levels. Finally, absence of any systematic relationship between the two tasks suggest that they measure different aspects of the central executive of working memory.

Working memory (WM) is a short-term retention system involved in on-line processing and retention of information. This memory system plays a major role in numerous cognitive tasks including language comprehension, mental calculation, reasoning and control of action. No need to say thus that any impairment of this component is likely to severely hinder activities of the daily life. According to Baddeley's model (1986), WM has multiple components. The phonological loop and the visuo-spatial sketch-pad are modular slave systems involved in the maintainance of verbal and spatial material, respectively. The central executive is the attentional component of WM. It is involved in the control of the slave systems, in strategy choice and in planification. Recent studies suggest that the central executive is impaired in dementia of the Alzheimer type (DAT) and that this impairment might help dissociating DAT from normal aging. The present study adresses two major questions pertaining to central executive impairment in DAT. The first relates to the extent of central executive impairment in DAT. There has been recent suggestions to fractionate the central executive of WM and it is important, both theoretically and clinically, to know whether DAT impairs all central executive functions. In the present study, we investigate two central executive funtions, manipulation and inhibition capacities. The second question asked by the present study is whether a single central executive profile characterizes all DAT patients considering the growing demonstration of heterogeneity in this disease.

Fractionation of the central executive

The central executive is a key component of Baddeley's WM model. Baddeley has frequently mentionned (e.g.: Baddeley, 1986; Baddeley, 1992; Baddeley, 1996) that the supervisory attentional system (SAS) proposed in the Norman and Shallice's model of action control (1986) is an appropriate modelisation of the central executive. In this model, familiar actions are performed through the activation of appropriate schemas. This schema selection occurs automatically and does not require attention. However, there are situations where activation of the usual schemas are inappropriate or insufficient. This would occur in tasks that rely on decision making, that are new or demanding, or that cannot rely on automatic processes. The SAS would be involved in these cases to modulate the amount of activation or inhibition of schemas. Unusual yet more relevant schemas would receive additional activation whereas schemas inappropriate to the situation would receive inhibition from the SAS.

The central executive is a crucial and complex system which is not very likely to function as a single unit. Different authors, among which Badddeley and Shallice, have suggested that the central executive (or SAS) is fractionable (e.g: Stuss et al, 1995; Baddeley, 1996; West, 1996). As a consequence, different functions or subcomponents have been recently proposed at a theoretical level. However, very little empirical work has been done to assess if dissociations between the different putative functions of the central executive occur in brain-damaged patients. Yet the pattern of central executive deficit of neurologically impaired patients might provide evidence to support its fractionation. In this context, studies of DAT patients, in whom a central executive impairment is highly probable, can contribute to the understanding of this component of WM. This study focuses on two possibly different functions of the central executive: manipulation and inhibition.

Manipulation refers to the action of consciously and actively modifying the format of the information retained in WM (Belleville et al, in press). This process is likely to be heavily involved in mental activities such as calculation or reasonning because these require an active processing of the content of WM. Other cognitive abilities, such as sentence comprehension where the verbatim information is essential, probably relies on other than manipulation capacities. Inhibition is involved in the modulation of schema. It also used to prevent irrelevant information from entering and crowding WM (Hasher & Zack, 1988). The present study is interested in subjects' ability to inhibit irrelevant phonological information (such as speech) present in the environment when performing a short-term memory task. Our previous works provided evidence that neither manipulation nor phonological inhibition capacities are affected by normal aging (Rouleau & Belleville, 1996; Belleville, Rouleau & Caza, in press). Thus, one important question is whether it is impaired in DAT. In addition, there is the possibility of finding a dissociation between the two components leading to a neuropsychological dissociation and supporting the fractionation of the central executive.

Impaired central executive in dementia of the Alzheimer type

Alzheimer's disease is the first cause of dementia. As no biological marker of Alzheimer's disease exist yet, a diagnosis of DAT has to rely on an extensive neurological and neuropsychological assessment. Clinical neuropsychologists have to find evidence for the presence of a cognitive impairment which goes beyond that observed in the normal course of aging. There is empirical data suggesting that the central executive, or SAS, of WM is impaired in DAT. The decrease in span capacities of DAT patients has been reported frequently for words (Morris, 1984; Spinnler, Della Sala, Bandera & Baddeley, 1988; Hulme, Lee & Brown, 1993; Belleville, Peretz & Malenfant,1996), letters (Morris, 1984; Dannenbaum et al., 1988; Belleville et al., sous presse) and digits (Kaszniak et al., 1979; Corkin, 1982; Kopelman, 1985; Morris, 1987; Orsini et al., 1988; Belleville et al., 1996; but see Martin, Brouwers, Cox & Fedio, 1985; Corkin, 1982 and Orsini et al., 1988 for unimpaired digit span in early DAT patients). This span decrease has been attributed to a dysfunction of the central executive component (Morris & Kopelman, 1986; Morris & Baddeley, 1986; Belleville, Crépeau, Caza & Rouleau, 1995).

First, DAT patients are impaired in an adapted version of the Brown-Peterson procedure (Morris, 1986; Belleville, Peretz & Malenfant, 1996). In Morris' study, three letters presented to the subjects were asked to be reported following delays of various lengths (0-20 sec). Interference tasks of increasing difficulties were introduced during the delay (e.g.: finger tapping, articulation, digit addition or digit reversal). Morris (1986) found an impaired retention in DAT patients which interacted with interference task difficulty. Larger impairment was observed with more difficult interfering tasks. The interpretation is that the central executive plays a role in the task which involves some form of divided attention: during the delay, subjects have to monitor the interference tasks while holding the letters in WM. The impairment would reflect DAT's impaired central executive. This result was confirmed by the study of Belleville et al (1996) which also showed that DAT but not normal aged people were impaired when interfering tasks were preformed during the delay. However, the Brown-Peterson task is not a pure measure of the central executive since it also assesses the strength of the trace in the phonological store (for a discussion of this issue, see

Kopelman, 1994; Belleville et al, 1996). In the calculation interference task, which was considered as the most demanding condition, subjects are prevented from rehearsing the letters. As a portion of DAT patients exhibit phonological deficits (Belleville et al, 1996), their impairment on the Brown-Peterson task may arise from a phonological deficit. In other words, the lower recall observed in DAT patients in the demanding condition of the Brown-Peterson procedure may simply reflect a more rapid decay or a weaker trace in the phonological storage system.

Baddeley and collaborators (Baddeley et al, 1986) have used a divided attention task which circumvents this difficulty. In their task, subjects were required to track a visual target with a stylus while at the same time performing a concurrent task of increasing complexity (articulation, tone detection or recall of sequences of digits). The speed of the moving target as well as the digit sequence length were adjusted to each individual's capacities. The performance of DAT patients was much affected by the dual task condition particularily when the task was made more complex with digit recall. Furthermore, the investigators showed in a longitudinal study that the dual task impairment increased with evolution of the disease (Baddeley et al, 1991). This impairment is explained by the central executive deficit of DAT patients, central executive being likely involved in dual-task coordination.

These three studies provide fairly convincing evidence for a central executive impairment in DAT. Furthermore, this impairment might provide a qualitative marker of the disease as recent studies suggest that normal aged people are unimpaired on targeted central executive tasks (Baddeley et al, 1986; Salthouse et al, 1995; Belleville et al, sous presse; Rouleau & Belleville, 1996). However, the extent of the central executive impairment of DAT patients has to be tested with other tasks. Furthermore, most past studies have relied on group data. Yet there are indications to suggest that WM is not similarily impaired in all DAT patients.

Heterogeneity in dementia of the Alzheimer type

Confirming an observation that clinicians had made a long time ago, one major research progress of the last few years has been to demonstrate heterogeneity of DAT at both the neurobiological and cognitive level (Martin et al, 1986; Neary et al, 1986; Martin, 1990; Habib, Joanette & Puel, 1991; Joanette, Ska, Béland & Poissant, 1992; Ritchie & Touchon, 1992). This has major consequences because it suggests that relying only on averaged group data risks to mask performance of each individual. The present cognitive description of DAT might thus be inadequate for many of the patients. A similar difficulty arises with our present understanding of the WM deficit in DAT and it is important to know whether a common central executive impairment defines individual DAT patients.

Some researchers have looked at the different patient profiles on WM tasks and the results are compatible with heterogenity within WM. Grossi and collaborators (1993) reported normal visuo-spatial span in some patients and impaired performance in others. Becker (1988) and Baddeley, Della Sala and Spinnler (1991) reported cases of DAT patients with pronounced central executive impairment. Baddeley, Della Sala and Spinnler (1991) reported that two DAT patients exhibited verbal or spatial span deficiency compatible with dysfunctional slave systems whereas at least one pure case of dysexecutive deficit was found. We have examined in details the different components of WM in DAT patients (Belleville et al, 1996). We observed that most patients (80%) were impaired on the adapted Brown-Peterson procedure whereas a substantial portion was also impaired in tasks measuring the phonological loop (40%). A smaller portion of patient (20%) was normal on both tasks. There is thus fair evidence for a central executive deficit in DAT patients but there also seems to be presence of heterogeneous WM profiles. This heterogeneity could also be found among subcomponents of the central executive. A final goal of this study was to assess the presence of heterogeneity within the possible deficits affecting manipulation and inhibition capacities of central executive.

The present study

Central executive was assessed in two different experiments. Experiment 1 measures manipulation capacities in a task that requires subjects to report a list of words in alphabetical order and in the order of presentation. In the procedure, care was taken to control for a phonological storage deficiency. This was done in a manner similar to Baddeley and collaborators (1986) by adjusting the phonological storage demand of the tasks to each individual subject. List length was thus adjusted according to individual subjects span so that any phonological storage deficiency in our patient does not contribute to their impairment on the manipulation task. Experiment 2 assesses phonological inhibition in a task that measures irrelevant speech effect. Verbal (Romanian and French) and non-verbal (white noise) stimuli are presented while the subject memorizes lists of digits. Again, the length of the lists to recall is individually adjusted so that only inhibition is measured. In both experiments, an analysis of the distribution of individual performances follows the group analysis to identify patients with divergent patterns of performances. In the two experiments three groups of subjects were tested, young individuals, healthy elderly individuals and persons suffering from dementia of the Alzheimer type. The use of a group of young subjects allows to compare the effect that normal aging has on on our tasks to that of DAT. It should allow to confirm the qualitative distinction between normal aging and DAT.

We wished to assess the relationship between individual performance on the two tasks. Indeed, if the central executive is a monolithic component, there should be a strong relationship between the performance on each task in individual DAT patient. If there is a fractionation of the central executive, the two tasks might dissociate at the group level. Thus DAT patients might be impaired on one but not on the other task. Furthermore, performance should also dissociate at the individual level: impairment on one task should not be related to impairment on the other task in individual subjects. Some of our patients have been tested on both tasks which provides the opportunity to compare the two central executive functions in individual patients. This will be done in a final part of the result section.

Experiment 1: Manipulation capacities

METHOD

Participants

Sixty one participants, 23 DAT patients, 23 elderlies and 15 youngsters took part in the experiment. The young adults (7 males and 8 females) ranged in age from 18 to 30 years (M = 24.6, SD= 3.98) and had a mean of 13.5 years of education (SD = 2.03). Elderlies (19 females and 4 males) ranged in age from 62 to 83 years (M = 71.35, SD =

5.59) and had a mean of 11 years of schooling (SD = 3.67). The patients (17 females and 6 males) had a mean age of 72.8 years (SD = 5.88) (range 64-87) and an average of 10.34 years of education (SD = 3.52). Each patient was individually matched with his normal aged control with regard to age and education. There was no difference in formal education between age-matched controls and DAT patients, t_{44}= -.6148; p=.5417, two-tailed. However the difference in education was significant between normal aged and young subjects, t_{36}= -2.4038; $p<0.05$, two-tailed. This difference correponds to the increase in the average educational level in Quebec between the two generations concerned (Statistics Canada, 1994). Subjects all reported normal hearing and had normal or corrected vision.

Patients were selected from a pool of volunteers seeking for medical, neurological and neuropsychological investigations in three hospitals (Centre de recherche du Centre hospitalier Côte-des-Neiges -Canada- , Hôpital Universitaire de Liège and Hôpital St-Luc -Belgium-). The patients were refered by neurologists or medical practioners as suffering from DAT. The patients were then tested with an extensive neuropsychological battery with the goal of documenting all components of cognition. Most of them also undertook complete clinical examination (e.g.: PET, functional MRI, blood analysis). Their diagnosis was then confirmed as probable (n=20) or possible (n=3) DAT, according to the NINCDS-ADRDA criteria (McKhann, 1984). The severity of their disease ranged from mild to moderate on the basis of the neurospychological investigation. Their average score on the Mini-Mental test was 22.57/30 (range= 18-29).

Young and normal aged participants were drawn from a pool of volunteers living in the same community as DAT patients. They had no history of neurological disease, psychiatric disorder, or general anesthesia in the past year. They did not use medication known to affect memory or other cognitive functions. Aged subjects were submitted to a battery of tests to exclude participants with early signs of dementia. These tests included the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975) used to screen for major cognitive defects, the Mattis Dementia Rating Scale (Mattis, 1976) which provides an estimate of attention, initiation, construction, concepts, and memory (four patients were not tested on this battery). Subtests from the Weschler Memory Scale (Wechsler, 1945) were used to estimate memory functions (logical memory and visual reproduction) and the Stroop task (Golden, 1976) was used to measure frontal-lobe functions. All control subjects performed normally on this test battery. As young participants are not at risk for dementia, they only completed the Mill Hill Vocabulary test (adapted in French, Gérard, 1983) on which they performed within normal range.

Materials

Two hundred and eleven monosyllabic words were selected. These words were frequent (Baudot, 1992) and imaginable substantives. They were not ambiguous with respect to the print-to-sound correspondence of their first letter. For example, a word like *scie* in French (which is pronounced /si/) would have been excluded because its first sound can also be written with an initial c. Finally, words having homophones of a higher frequency were not used when this homophone started with different letters (for example, the word *fard* is homophone of a more frequent word, *phare* and was thus rejected).

Sequences of words the length of which ranged from two to eight items (to be used with subjects of a span size from 3 to 9) were constructed with these words. There were 20 different sequences for each length, 10 to be used in the direct condition and 10 to be used in the alphabetical condition. Words included in a sequence differed according to their first letter and had no phonological or semantic similarity. Mean word frequency was equivalent across sequence length as well as for the direct and alphabetical condition at a given list length. None of the words were repeated across different sequences for a given length.

The manipulation difficulty was controlled for the sequences to be used in the alphabetical condition.This was done first by measuring the distance between the first letter of the words in a sequence. Indeed, according to a pilot study from our laboratory (Sauvage and Belleville), it is easier to judge the alphabetical order of letters that are farther apart in the alphabet. The position in the alphabet of the first letter of words was also controlled since letters at the beginning of the alphabet should be easier to arrange in alphabetical order. Finally, the total number of manipulations to perform into each sequence was controlled (e.g. there is one manipulation in the series *bloc, pneu* and *crabe* but two manipulations in the series *rose, pomme* and *lune*). By using these criteria, the manipulation requirement was made equivalent for the different sequence lengths.

Procedure

Pre-experimental phase. As a first step, the short-term memory capacity of each subject was assessed with a classical word span procedure. The words chosen for the span procedure fit the same criteria as those on the experimental list in terms of length, frequency, and imageability but differed from those used in the experimental phase. The items were chosen without replacement. Sequences of words were read at the rate of one item per second, starting with sequences of two words. The length of the sequences was increased by one word every two trials. However, if an error occurred on one of these two trials, the subjects were given two additional trials. Subjects were instructed to orally report items in serial order. Testing was interrupted when subjects failed to report correctly two of the four sequences at a particular length. The word span was defined as the longest sequence correctly recalled on 50% of the trials. This span was later used to determine the list length at which subjects were tested in the experimental phase.

Experimental phase. In this phase, subjects were assessed in the direct and alphabetical condition of recall. Words were read to the subjects at the rate of one item per second and subjects recalled the words orally. In the direct condition, subjects performed an immediate serial recall of the words. In the alphabetical condition, they were asked to rearrange and recall the words in their alphabetical order. For example, the words *route-nappe-poivre* should be recalled *nappe, poivre, route* in this condition. Ten sequences of words were recalled in each condition. The number of words to be recalled in a sequence corresponded to the subjects' span minus one item. Thus a subject with a span of 6 was tested with sequences of 5 items in both conditions. At the beginning of our study, we tested a few patients with sequences corresponding to their span as will be done in Experiment 2. However under these conditions alphabetical recall was virtually impossible to the DAT patients who tended to withdraw from the task. It was thus decided to test subjects with sequence lengths correponding to their span minus one item. The order of presentation of the direct and alphabetical conditions followed an ABBA design, starting with the direct condition. This allowed to control for possible effects of fatigue or practice. The whole procedure was completed within a single testing session.

RESULTS AND DISCUSSION

As a first step, a preliminary analysis was performed that compared the span size assessed in the pre-experimental phase in young subjects, normal elderlies and DAT patients. There was a significant group effect, $F(2,58) = 14.14$, $P < 0.001$. A post-hoc test with Tuckey HSD ($p < 0.05$) showed that DAT had a smaller average span than aged subjects ($M = 3.74$, $SD = 0.69$; and $M = 4.26$, $SD = 0.54$; in DAT and normal aged subjects respectively) and that young subjects ($M = 4.8$, $SD = 0.56$) differed from aged controls ($p < 0.05$) on the same measure. A second preliminary analysis was done to assess the effect of the order of presentation due to the ABBA design. A 3 (Group: young, old, DAT) x 2 (Order: first, second) x 2 (Recall: direct, alphabetical) ANOVA was thus conducted. The main effect of Order just missed significance, $F(1,58) = 3.66$, $MSE = 0.597$, $p = 0.06$, due to the fact that all subjects slightly improved their performance over trials. More importantly however, there were neither Group by Order nor Group by Order by Recall interaction, $F<1$ in both cases. This indicates that the order of presentation of the conditions had no significant influence on the critical interaction namely, that concerning the Group. For this reason, the data from the two orders of presentation was pooled in the subsequent analyzes.

Figure 1 shows the number of sequences correctly recalled by elderly, young and DAT subjects in both conditions. As expected, alphabetical recall yielded a decreased performance in comparison to direct recall (see Figure 1). More importantly, the reduction in performance with alphabetical recall is much larger in DAT than in the control groups. This is confirmed by a 3 (Group: young, old, DAT) x 2 (Recall: direct, alphabetical) ANOVA. The analysis revealed a significant main effect of Recall,

$\underline{F}(1,58) = 93.74$, $\underline{MSE} = 1.522$, $\underline{p} < 0.0001$, confirming the reduced performance level in the alphabetical condition. There was a significant Group effect, $\underline{F}(2,58) = 10.48$, $\underline{MSE} = 3.300$, $p<0.001$, due to the decrease in recall exhibited by DAT patients relative to young and aged normal subjects. Importantly, the interaction was highly significant, $\underline{F}(2,58) = 13.50$, $\underline{MSE} = 1.522$, $p<0.0001$. Analysis of the interaction effect revealed that the Group difference was only apparent in the alphabetical condition, $\underline{F}(2,58) = 13.50$, $\underline{MSE} = 3.698$, $p<0.0001$. In this condition, DAT patients differed from aged and young subjects ($p<0.01$ in both cases) whereas the latter two did not differ one from another ($p=0.74$). There was no group effect in the direct condition, $F<1$. The Greenhouse procedure was used and did not modify the degrees of freedom.

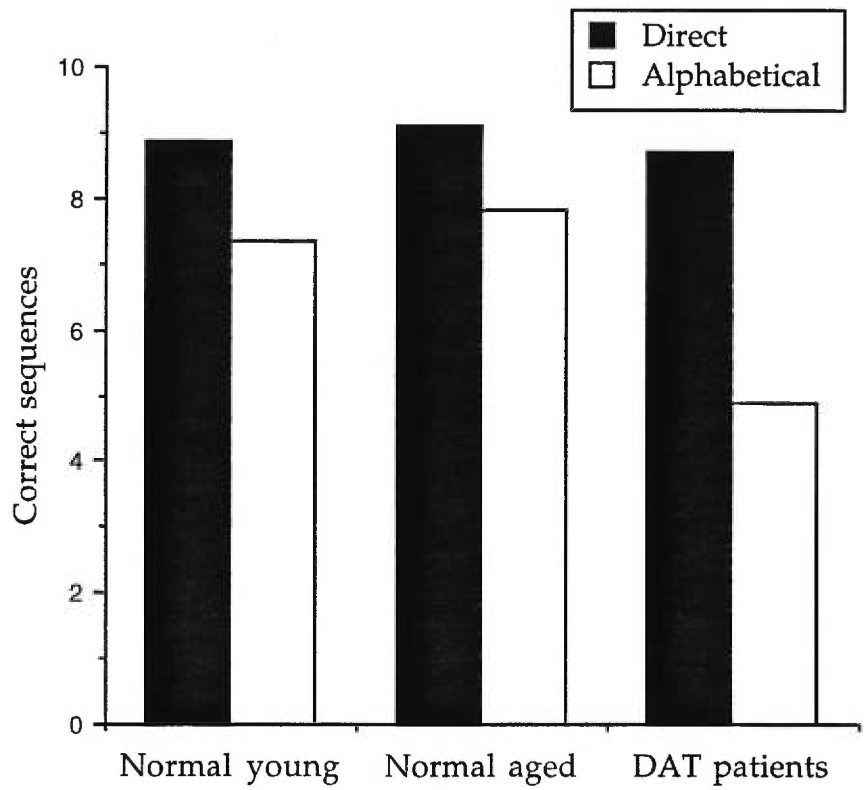

Figure 1: Number of correct sequences in the direct and alphabetical conditions of Experiment 1.

In order to assess heterogeneity, we have derived a manipulation score for each individual subjecs. The score is calculated according to the formula (D-A/D). This represents the memory reduction experienced by each subject when performing the alphabetical recall relative to the direct recall. Figure 2 shows the distribution of manipulation cost for each subject. It is worth noting that the scores for the two control groups (young and elderlies) approximate normal distributions and overlap. In contrast, the distribution of DAT patients'scores has a bi-modal shape. While many patients are severley impaired, a reasonable proportion of them overlaps the distribution of normal elderlies and are thus clearly unaffected. This difference is not merely related to severity of the disease. We performed a split-median on manipulation cost and compared the MMS score of the most and least impaired patients. Patients that were the most impaired on manipulation showed an average MMS score of 21.82 whereas patient that were least impaired patients exhibited a MMS score of 23.25. This difference was not reliable, $t_{(21)} = -1.320$; $p=.2012$, two-tailed.

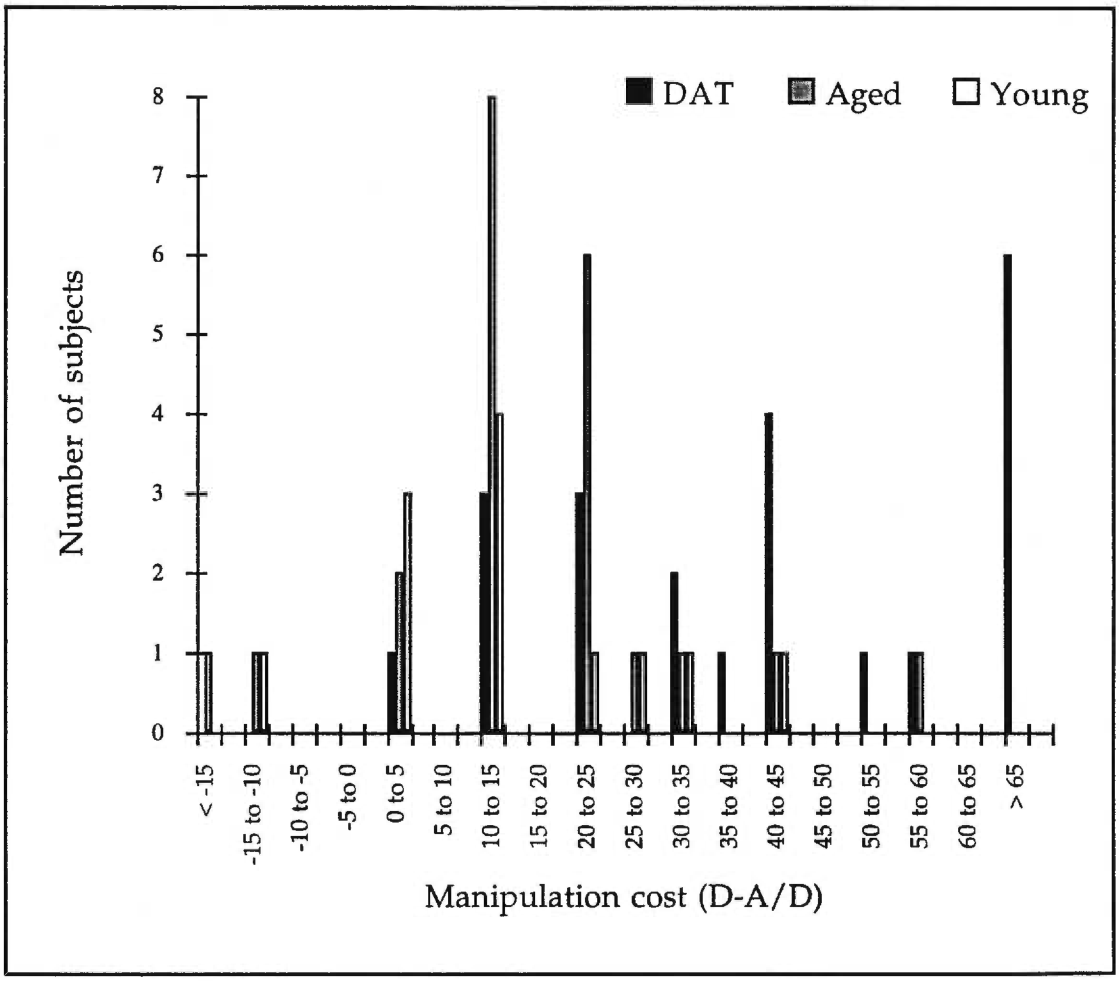

Figure 2: Distribution of the manipulation cost in the three groups of subjects (Experiment 1)

In summary, alphabetical recall yields a decreased performance level in comparison to direct recall, which suggests that there is a cost to the manipulation requirement of the task. Elderly and young subjects, equalized in the direct condition, do not perform differently in the alphabetical condition. This suggests that manipulation is not particularly difficult for normal elderly people as long as basic storage is controlled for. This confirms with a new group of subjects data that we have already reported in normal aging (Belleville, Rouleau & Caza, in press). In contrast, DAT patients are dramatically impaired in the alphabetical condition even if basic storage demand is equated. Examination of individual scores indicates a bi-modal distribution in DAT patients with some subjects overlaping normal elderlies. A substantial subset of DAT patients is excessively impaired on the task. These differences are independent of disease severity.

Experiment 2: Inhibition in working memory

METHOD

Participants

Forty-eight participants, 16 young, 16 old, and 16 patients suffering from Alzheimer's disease took part in the experiment. Of the 16 patients, eleven had taken part in the last experiment. For these eleven subjects, the two experiments were separated by no more than two weeks. The young adults (7 males and 9 females) ranged in age from 19 to 30 years (M = 23.1) and had a mean of 14.0 years of schooling (SD = 1.97). The older adults (7 males and 9 females) ranged in age from 62 to 80 years (M = 70.5) and had a mean of 11.6 years of schooling (SD = 2.5). The patients were diagnosed as suffering from probable dementia of Alzheimer's type, according to the NINCDS-ADRDA criteria (McKhann, 1984). The severity of their disease ranged from mild to moderate on the basis of an extensive neuropsychological assessment. The patients had a mean age of 72.6 years old (SD = 6.5) (range 64-87) and an average of 11.3 years of education (SD = 3.6). Each patient was individually matched with his normal aged control regarding age, sex, and education. There was no significant difference between patients and age-mached controls in terms of age, $t_{(30)} = 1.049$, $p=0.3023$, and formal education, $t_{(30)} = -0.2838$, $p=0.7785$. The difference in formal education between normal youngsters and elderlies was significant, $t_{(30)} = -3.0239$, $p<0.01$. Participants spoke French as their mother tongue and had no knowledge of Romanian, the langage employed in the nonfamiliar speech condition.

Young and normal aged participants were drawn from a pool of volunteers living in the same small community. They had no history of neurological disease, psychiatric disorder, or general anesthesia in the past year. They did not make use of medications known to affect memory or other cognitive functions. Subjects all reported normal hearing and had normal or corrected vision. Older control subjects were subjected to a battery of neuropsychological tests to exclude control participants with early signs of dementia. These tests included the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975) and the Mattis Dementia Rating Scale (1976), two subtests from the Weschler Memory Scale (logical memory and design memory; Weschler, 1945), the Stroop task (Golden, 1976) and the Mill Hill Vocabulary test (Gérard, 1983). None of the normal controls was eliminated following the cognitive assessment. The young participants completed the Mill Hill Vocabulary test. Their score did not differ from those of aged matched controls (34.81/44 (SD = 4.98) and 34.25 (SD = 6.25) on average in aged and young subjects respectively).

Materials

Memory task The experimental task was modeled on the one reported in Rouleau & Belleville (1996). Series of randomly selected digits (1 to 9) were constructed. The length of the series ranged from 2 to 9 digits. Forty lists were constructed for each sequence length, with 10 lists for each experimental condition. Digits were presented on a Macintosh monitor, in the center of the screen, using a program written with SuperLab (version 1.5.9) (Cedrus Corporation, 1992).

Noises and irrelevant speech sources Three types of auditory stimuli were created: white noise (nonverbal), familiar verbal noise, and nonfamiliar verbal noise. The white noise consistedd of electronically generated FM modulations. The familiar noise was an excerpt from Madame de Staël's novel Corinne ou l'Italie read in French, the participant's mother tongue. The nonfamiliar noise was the same text read in Romanian.

Romanian was chosen because, although a Latin language like French, it is unfamiliar to French speakers, unlike other more common Latin languages such as Italian and Spanish. Thus, the two verbal noises used were phonologically akin but differed at the lexico-semantical level in that one was comprehensible to participants. A professional translator produced the Romanian version of the original French text. A female reader fluent in both French and Romanian was used for the recordings in order to have a voice with similar acoustic qualities in both versions, thereby ensuring a better comparison of the verbal conditions. The reader was instructed to read both versions in a steady rhythm without long pauses, while maintaining steady prosody and volume. This last control measure was taken in order to avoid possible orienting responses elicited by sudden variations in prosody or tone of voice. Each version lasted approximately 8 minutes.

The auditory stimuli were played on a Sony tape recorder (TMC-5000) and presented binaurally through Sony headphones (MDR-006). Noise intensity was 75 dB on average, as measured by a noise-level meter. Readings were taken twice each by two different examiners over 30-sec periods. A level of 75 dB is well within the range of normal hearing for both young and older adults (Corso, 1977).

Procedure

Short-term memory (STM) span measure. STM capacity for visually presented digits was measured using a classic span procedure. Digits were presented one at a time for 750 ms, with a 250-ms inter-stimulus interval, in the center of a computer monitor screen. Testing began with sequences of two digits randomly selected from 1 to 9. The length of the sequences was increased by one digit every four trials. A 2-s visual warning (Ready) in the center of the screen preceded each sequence. At the end of a sequence, a table containing the digits 1 to 9 was displayed on the screen. The position of the digits in the table was randomized in order to prevent participants from using spatial cues. Participants were required to reproduce the entire sequence in correct order by pointing to each item serially with a finger. The experimenter recorded the responses. Participants were instructed to point to a question mark appearing on the right of the screen whenever they could not remember a digit. Testing ended once participants failed to report correctly at least two of four same-length sequences. STM span was defined as the longest sequence correctly recalled on 50% of the trials.

Experimental testing. Experimental testing lasted approixmatively thirty minutes, comprising a pause after half of the conditions. The digit recall procedure was the same as the one used in the STM span measure, except that participants were tested only with digit sequences length-adjusted to their individual STM span. In other words, the number of digits a participant had to recall in each condition corresponded to his or her own span. Participants wore headphones in each noise condition, including the silent condition. They were instructed to ignore distracting noises and focus their attention on memorizing digits. Noise began 10 s before presentation of the first digit in a particular condition and continued until participants finished recalling the last sequence in the condition. Ten sequences were presented in each condition. A 10-min break was given after every two conditions.

The experiment thus assessed recall under four auditory backgrounds: silence, non-verbal noise, familiar verbal noise, and non-familiar verbal noise. The effect of order of presentation of the noise conditions was counterbalanced using a Latin Square design.

Phonological loop testing

In addition, all subjects were tested with a task that was meant to assess the phonological loop of WM. The effect of the phonological similarity of words on short-term retention was measured in both the visual and auditory modalities of presentation. Recall of phonologically similar (rhyming such as B-D-G) and dissimilar (non-rhyming) letters was tested separately. Order of presentation of the material was counterbalanced across subjects. Subjects were tested with 10 sequences in each condition. The length of the sequences to recall corresponded to each subject's digit span as measured with the Côte-des-Neiges computerized memory battery (Belleville et al, 1992; Chatelois et al, 1993).

RESULTS

A preliminary analysis was first performed on the digit span data with an one-way ANOVA. There was a main Group effect, $F(2,45) = 22.53$, MSE = 40.646, $p<0.0001$. Post-hoc comparisons with a Tuckey HSD test indicated that young subjects (average span= 7.50) performed significantly better than normal aged subjects (average span= 5.88, $p<0.01$). Normal elderlies showed a better span than DAT patients (average span= 4.31, $p<0.01$). An analysis was also performed to assess the effect of the latin square on performance. An ANOVA was used with the Group as a between subject factor, and Noise and Order as repeated factors. The main effect of Order was not significant, $F(3,36) = 2.04$, MSE = 601.870, $p = .125$. Furthermore, there were neither Group by Order, $F(6,36) = 2.04$, MSE = 601.870, $p = .313$ nor Group by Noise by Order interaction, $F(18,108) = 2.04$, MSE = 77.709, $p = .258$. This indicates that the order of presentation of the conditions had no significant influence on the results. The data was thus pooled across latin square orders.

A 3 (Group) by 4 (noise) one factor repeated ANOVA was then performed using percent correct recall as the dependent variable. The data is represented in Figure 3. Results showed a significant effect of noise, $F(3,135) = 32.27$, MSE = 77.515, $p<0.0001$. Post-hoc comparisons with a Tuckey HSD test indicated that the silence and white noise condition were comparable ($p=0.82$) and that Romanian and French did not differ from each other ($p=0.98$). However both French and Romanian impaired recall relative to white noise (p< 0.0001 in both cases). As expected, the Group effect was not significant, F(2,45)=1.84, MSE = 662.340, p=0.17. Importantly, the Noise by Group interaction was not significant (F<1). Results were not modified when adjusted by the Greenhouse-Geisser procedure for heterogeneous variance.

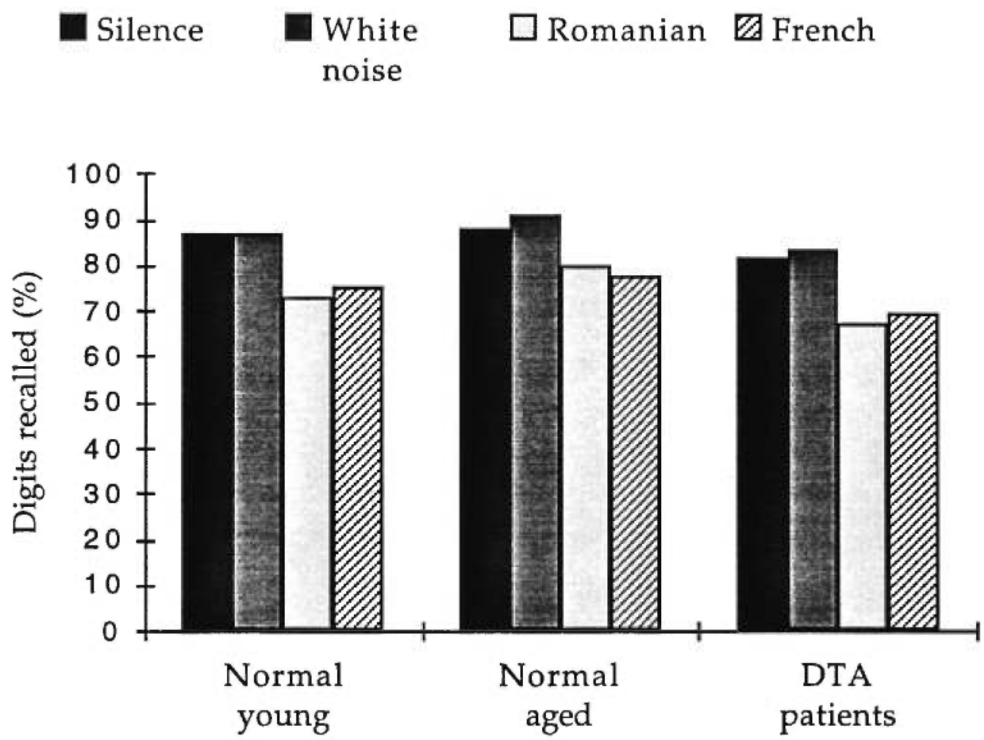

Figure 3: Percent correct recall on the irrelevant speech task of Experiment 2.

The effect of phonological similarity was also assessed by comparing recall of similar to dissimilar letters in both auditory and visual modalities of presentation (Figure 4). A three-way ANOVA was used with Group, Modality and Similarity as factors. Results of the analysis showed a significant Modality effect, F(1,45)= 23.951, MSE =

296.368, p<0.0001 because visual presentation yielded higher recall performance than auditory presentation. As predicted by the working memory model, non rhyming letters were better recalled than rhyming letters, $\underline{F}(1,45)= 12.30$, $\underline{MSE} = 103.27$, $p=0.001$. Inspection of Figure 4 suggests that the phonological similarity effect is much lesser in DAT patients than in the other two groups, particularily with auditory presentation. However, neither the Group by Similarity, $\underline{F}(2,45)= 2.04$, $\underline{MSE} = 103.27$, $p=0.142$, nor the three-way interaction, $\underline{F}<1$, reached significance. However, there was much variability in DAT patients as will be described in the following section.

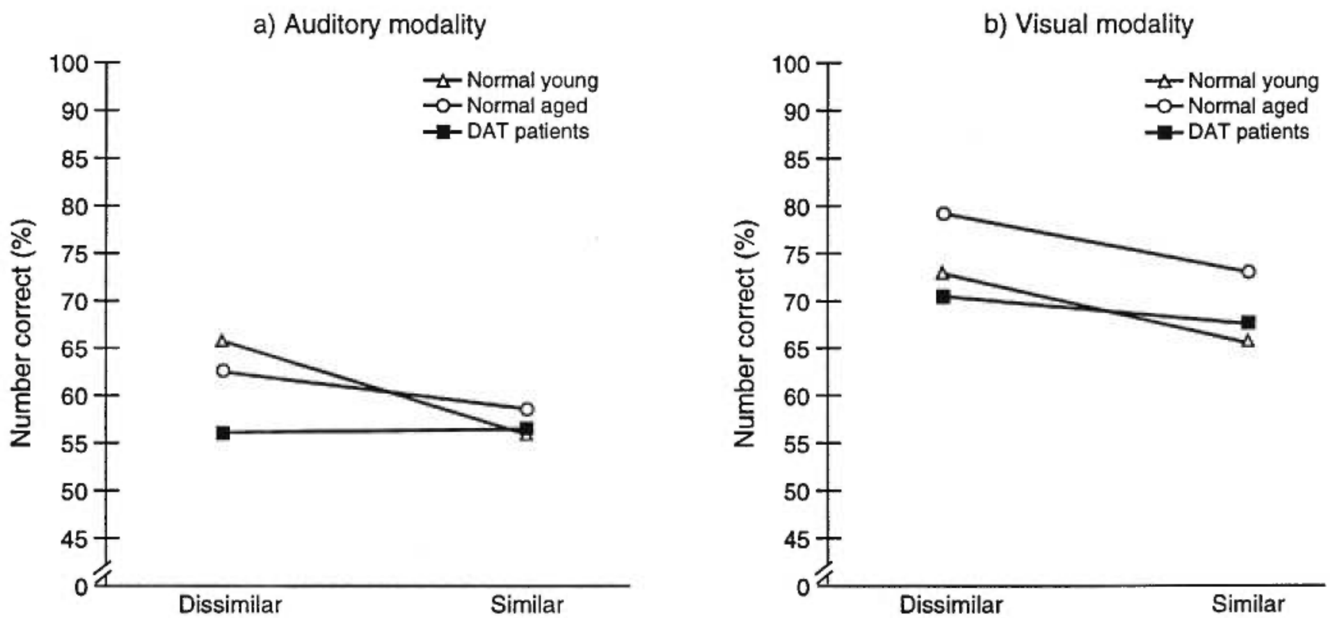

Figure 4: Effect of phonological similarity in the a) auditory and b) visual modality of presentation (Experiment 2)

Individual scores were calculated to assess the level of performance on the inhibition task for each subject. Scores of inhibition costs were determined with the formula ([(Silence - [(Romanian+French)/2]) / [Silence]. This corresponds to the reduction in recall incured by verbal noise relative to silence. The distribution of individual data is shown on Figure 5. The Figure is again eloquent as normal distribution clearly represents normal young and aged performances whereas the distribution of DAT patients is much more scattered. Some of the patient have severe impairment on this task even if as a group no significant differences were evidenced. Again, a median-split was done to compare the MMSE of the most and least impaired patients. Patients with the largest inhibition cost had an average MMSE score of 21.5 whereas patients with the smallest inhibition cost showed a MMSE score of 22.75 on average. This difference was not reliable, $t_{(14)} = -.8704$; $p=.3988$, two-tailed.

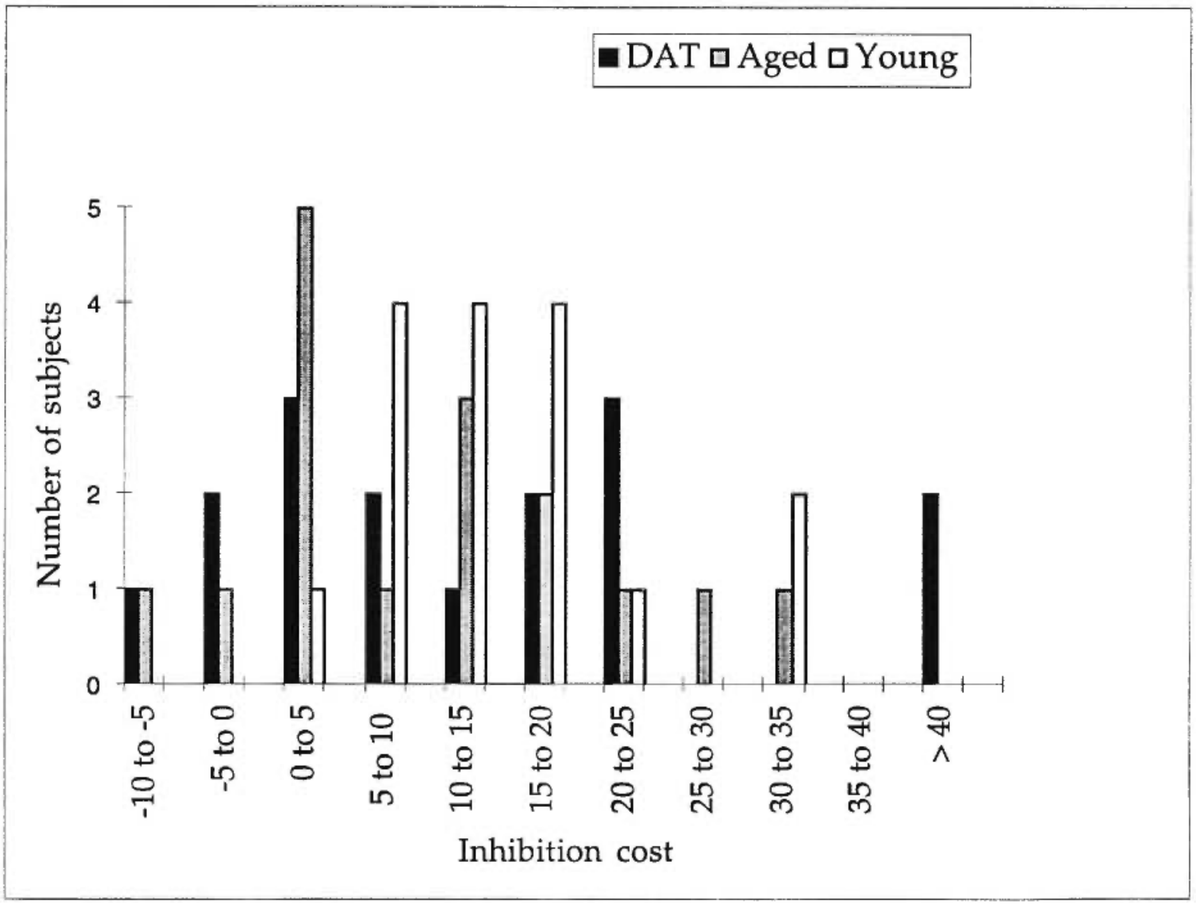

Figure 5. Distribution of the inhibition cost in the three groups of subjects (Experiment 2)

One possibility to explain this heterogeneity is to suggest that some patients have a phonological loop impairment that interferes with their performance on that task. The irrelevant speech effect results from interference whithin the phonological store of WM. Auditory verbal noise have direct access to the store whereas visually presented digits access the store via the rehearsal procedure. Patients with impaired phonological storage might thus exhibit exagerated effect from irrelevant speech due to a reduced storage capacity. Furthermore, patients with rehearsal deficits might fail to show the effect: if digits are not transfered to the phonological store, their retention should not be disrupted by auditory verbal background. This is a reasonable suggestion because we have shown in another group of DAT patients that up to 50 % of them have impaired phonological loop (Belleville et al, 1996). This hypothesis was tested by using the phonological similarity effect. If visual material is not transfered to the phonological store, the effect should not be observed in the visual modality. If the phonological store is impaired, the effect should be absent in both modalities of presentation. The size of the phonological similarity effect was thus measured independantly in each modality and in each patient with the formula Recall of dissimilar letters - Recall of similar letters / Recall of dissimilar letters. We found that six of the 16 patients failed to show a phonological similarity effect in the visual modality and that eight of them did not show the effect in the auditory modality. There was no significant correlation between the inhibition score and the phonological similarity effect score in the visual, $r_{(14)} = .32$, NS, and auditory modalities, $r_{(14)} = -.17$, NS. The phonological similarity effect of patients who were most impaired on the inhibition task was compared in both modalities with the phonological similarity effect of patients least impaired on inhibition. The visual phonological similarity effect was -4.75 and 2.3 in patients who were not impaired and in those who were impaired on the ISE respectively. The auditory phonological similarity effects were 9.2 and -11.8 in patients who were not impaired and in those who were impaired on the ISE respectively. Impaired and non-impaired patients did not differ on either the auditory, $t_{(14)} = 1.36$; $p=0.1955$, two-tailed, or visual phonological similarity effect, $t_{(14)} = -0.405$; $p=0.6911$, two-tailed.

In summary, French and Romanian speech, but not white noise, impairs WM in young and elderly subjects, as well as in DAT patients. Interestingly, the effect is equivalent across groups. DAT patients are not more impaired than normal elderlies nor is normal aging yielding impairment on that task. However, examination of the distribution suggests that a small portion of DAT patients exhibit severe deficit on this task. It was also found that many DAT patients failed to shown the expected phonological similarity effect. Yet, there was no negative correlation between the size of the phonological similarity effect. Patients with larger inhibition deficit appeared to have phonological deficit in the auditory modality because they were less sensitive to the phonological similarity effect. However, this result was not statistically reliable.

Relation between inhibition and manipulation

As was mentionned earlier, a portion of the DAT patients have been tested with both tasks. This provided the opportunity to assess whether the two tasks are related in the patients and whether impairment in any of these tasks is a function of the severity of the disease. Twelve patients have been tested on both tasks. Their performance in terms of manipulation cost is plotted against their performance in terms of inhibition cost on Figure 6. Examination of the function shows no relation whatsoever between the manipulation and inhibition scores in this subset of patients. This is confirmed by a correlation that was weak and non-significant, $r_{(11)} = 0.07$, NS. Furthermore, there are double-dissociations between the tasks. Six patients are much impaired on the alphabetical span but normal on the inhibition task. Two other subjects are impaired in the inhibition task but perform well on the alphabetical task.

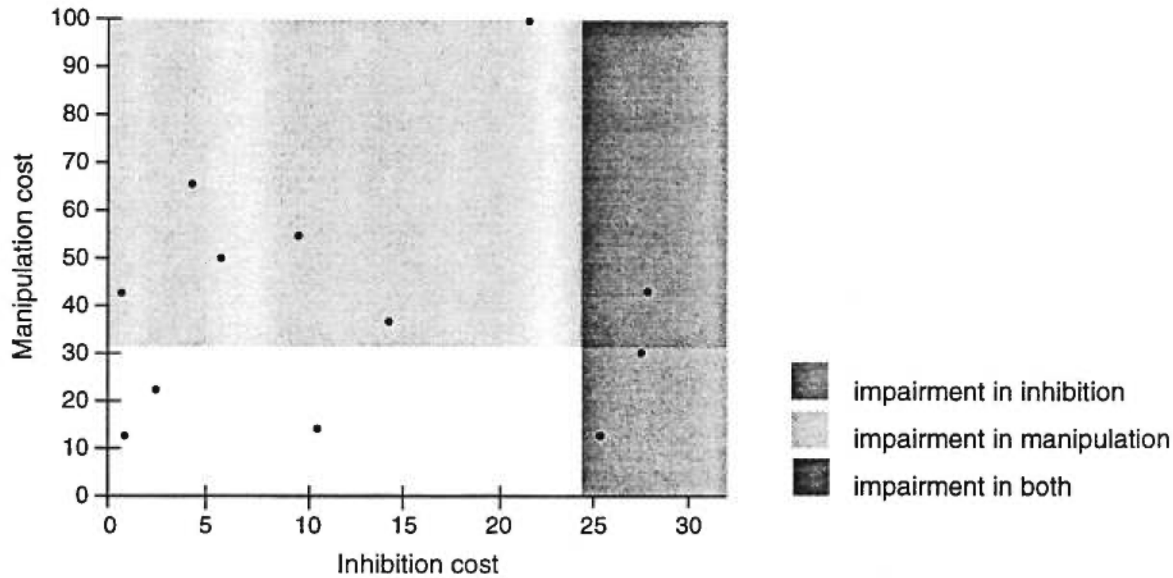

Figure 6. Relation between manipulation and inhibition cost in patients with dementia of the Alzheimer type. Shadows represent the nature of the impairment. Performance is considered to be impaired when it is more than one standard deviation above that of control subjects (mean). The white area indicates no impairment.

DISCUSSION

Three aspects will be adressed in this discussion. First, we will relate our data to the literature on the working memory of DAT patients and discuss how this can contribute to understanding the cognitive decline in this disease. Second, we will discuss the implications of the observed heterogeneity of DAT patients. Third and last, we will argue that our results contribute to a theory of a fractionated central executive component.

Partial central executive impairment in DAT

This study reports two experiments the goal of which was to assess different components of the central executive. Experiment 1 reports impaired manipulation capacities in a group of patients suffering from DAT. Experiment 2 indicates that in contrast to manipulation, phonological inhibition is not affected in the early stages of the disease. Groups of normal aged people were also compared to young subjects which allowed to compare directly the effect of normal aging to that of DAT on working memory. In both experiments, normal aged people did not differ from young controls in their abilities to manipulate or inhibit irrelevant speech. This confirms our previous data which indicated that normal aging did not alter either manipulation or phonological inhibition (Belleville, Rouleau & Caza, in press; Rouleau & Belleville, 1996). In that respect, the manipulation impairment observed here in DAT represents a qualitative difference with normal aging. This could have implications in the clinical practice. Indeed, the most powerful tasks for the diagnosis of DAT should be those that measure processes normal in neurologically intact aged persons. Obviously, the alphabetical procedure responds to this criteria.

Numerous studies have reported impaired WM in DAT patients (for a review, Morris and Baddeley, 1988; Belleville et al, 1996) that was explained by a central executive dysfunction (Baddeley et al, 1986; 1991; Morris, 1986; Greene et al, 1995; Belleville et al, 1996). Our results are congruent with the suggestion of a central executive impairment in this population. However, they also circumscribe it by dissociating two putative functions of the central executive, inhibition and manipulation. This dissociation is found at the group and at the patient level. As a group, DAT patients do not show inhibition deficit, as measured here, but exhibit major difficulties in the on-line manipulation of information. Not all aspects of the central executive is thus impaired in DAT as capacity to inhibit irrelevant auditory material remains functional in a majority of patients.

A second point of interest relates to the selectivity of the central executive impairment across the different WM components. In a review of the literature and based on his own work, Morris proposed that the phonological loop was not impaired in DAT (Morris & Baddeley, 1988). In the present study, abnormal phonological similarity effects is observed in a substantial portion of patients. The finding of impaired phonological loop in a subset of DAT patients replicates previously published data (Belleville et al, 1996). It is conceivable that if only part of the DAT population are phonologically impaired, different studies using different patients and having different statistical power will lead to conflicting results. This relates to the important point of heterogeneity of DAT patients, an aspect that is discussed in the following section.

Heterogeneity in DAT

As mentioned above, heterogeneity in the performance of DAT patients is observed at the level of the phonological loop because a portion of patients fail to show the expected phonological similarity effects. Furthermore, examination of the individual profiles of performance in DAT patients suggests that a general description of impaired manipulation but intact phonological inhibition is true for most but not all patients. Although a majority of them appear to be well accounted for by such a description, some patients are normal in manipulation while others are impaired in the inhibition task. This heterogeneity is not a simple exageration of the deviation in performance that would normally occur in normal aging. Indeed, the distribution of normal elderlies is by far closer to that of young subjects. The bi-modal shape of the DAT distribution is likely to reflect the underlying pathological process as it is not found in normal elderlies.

The presence of substantial heterogeneity in the performance of our DAT patients corroborates numerous recent findings on this disease. However, the heterogeneity usually reported concerns much wider domains of knowledge such as language, perception and memory (e.g.: Neary et al, 1986; Martin et al, 1986). In the present report two different components of the central executive were differently sensitive to the disease across patients. Furthermore, a phonological loop impairment characterizes a reasonable portion of DAT patients. We thus have evidence for the presence of a heterogeneity that extends beyond large modules to their constituents. The extension of heterogeneity to smaller components of cognition is not surprising given the postulates underlying cognitive neuropsychology. The postulate of neurological specificity refers to the fact that independent cognitive components depend on distinct cerebral substrates (Ellis & Young, 1986; Seron, 1994). Many authors suggested that the central executive is located in the frontal lobe whereas the slave systems would rely mostly on posterior lateralized systems (Paulesu, Frith & Frackoviak, 1993). One important hypothesis to explain the presence of heterogeneity in DAT is that different regions of the brain are differently affected by neuropathological alterations (Ritchie & Touchon, 1992). As a consequence, it is no more surprising to observe dissociations in

DAT patients between physically distant components of WM, the phonological loop and the central executive, than it is to observe dissociations between say language and praxis. The same logic applies to the different functions of the central executive in the hypothesis of a frontally located system. The frontal lobe is a large part of the brain with different cytoarchitectonic regions and it is possible that different parts of the frontal lobe are responsible for different executive functions. If DAT leads to heterogeneous pattern of performance, this might also involve dissociations between functions localized in different areas of the brain or of the frontal lobe.

Theoretical implications

Our data also bears relevance to the present theories on the central executive. There is indeed numerous recent papers suggesting that the central executive is not unitary and fractionates in different components (or functions). For example, Baddeley (1996) suggested that the central executive could be examined as a set of component functions: dual task coordination, retrieval switch, selective attention and inhibition, manipulation of information from long term memory. Stuss and collaborators (1996) also suggested to fractionate the central executive into many different components. However, the empirical data on a fractionation of the central executive is very scarce partly because access to frontal lobe patients is rare and partly because the complexity of executive functions has slowed progression of data collection. It appears that the study of normal and pathological aging can provide interesting input to this field as these are subjects in which the central executive has been suspected to be involved. Furthermore, the recent models constitute incentives to do researches in the field of executive functions. In the present study, we have confirmed that normal aging does not lead to major central executive deficits. We have confirmed with new subjects that the manipulation capacity of working memory and that phonological inhibition, as measured in this particular paradigm, are functional in normal aging. This point will not be discussed in much detail since it is not the main focus of our paper. Yet it indicates that the two components are not dissociated in this population.

In contrast, there is clear dissociation in DAT patients. In many DAT patients, severe manipulation impairments were observed whereas inhibition capacities remained intact. There would thus be indications for a fractionation of the central executive at least with respect to these two components - or functions. One possible explanation of this dissociation however could relate to the difficulty of the task. It is indeed possible that our manipulation task was just more difficult than the inhibition task. If the central executive is a single resource component, its impairment is likely to be more apparent on tasks that are more demanding. Whereas this is a logical possibility, we do not think that it explains our results. This is because there was a double-dissociation between the two tasks. We have been able to identify patients who are impaired on the inhibition task but normal on the manipulation task. This pattern of performance would not be possible if a single component was responsible for the two tasks. Furthermore, there was no correlation between the two tasks in DAT patients: impairment in one aspect of the central executive was not necessarily accompanied by impairment in the other aspect. One important question remains and it is whether the phonological inhibition depends on phonological processing systems located in the posterior portion of the left hemisphere. This would be coherent with the suggestion that processing systems (e.g.: spatial, phonological, lexical) possess their own inhibition systems. We have failed to find very convincing evidence in favor of this hypothesis because there is no strict association between a phonological loop deficit and a phonological inhibition deficit. However, this is based on a small number of subjects and further studies would be required to elucidate this question.

Our results thus argue strongly for the presence of at least two components in the central executive, one responsible for actively manipulating on-going information, the other involved in inhibiting irrelevant material that enters phonological WM. Whereas DAT patients would be impaired in active manipulation, they would be able to inhibit phonologically irrelevant information suggesting that not all aspects of central executive is impaired in these patients.

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Footnote

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Article n° 4

Exploration of multiple inhibitory systems and interference in dementia of the Alzheimer type

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Abstract

Three tasks were used to assess the effect of normal aging and dementia of the Alzheimer type (DAT) on interference and inhibition. DAT patients, normal aged controls and young subjects were tested with the negative priming procedure, the Hayling test and the Stroop. In the negative priming, results in normal aged subjects evidenced impaired inhibition of identity and habituation but normal interference effects. Normal aged subjects also showed deficits in the Stroop and Hayling Tests. When compared to their age-matched controls, DAT patients showed strong deficit in all inhibitory conditions of the negative priming and in the Hayling Test. However, interference in DAT was comparable to that of normal older subjects, whether they were tested with the Stroop or the negative priming procedure. These group comparisons evidence dissociations between inhibition components. Furthermore, examination of the individual performance profiles in the DAT group shows double dissociations. Results are discussed in relation with current models of inhibition.

The concepts of inhibition and interference have played a major role in theories of cognition of this century (for a review, see Dempster & Brainerd, 1995). Experimental measures of interference such as the Brown-Peterson or the Stroop test have been used for a few decades. In contrast, inhibition has long remained a theoretical concept without empirical basis because direct experimental tests were not available. Recently, direct tests of inhibition were devised principally in the field of selective attention. As a result, the last few years have witnessed a tremendous increase in the number of studies on inhibition in the fields of cognitive psychology (e.g.: Gérard, Zacks, Hasher, & Ravandsky, 1991; Gernsbacher & Faust, 1991; Tipper, 1985), developmental psychology (e.g.: Arbuckle & Gold, 1993; Bjorklund & Harnishfeger, 1990; Hasher & Zacks, 1988), clinical psychology (e.g.: Pennington & Ozonoff, 1996) and neuropsychology (e.g.: Stuss, 1991). These studies revealed the role played by inhibition in a wide range of cognitive processes, such as reading, discursive abilities, long-term retrieval and so on. Therefore, a better understanding of inhibition and of its dysfunctions in normal and pathological aging is of significant interest. This is the main objective of the present study.

Inhibition

Cognitive inhibition is defined as a mechanism which actively suppresses distracting information (Hamm & Hasher, 1992). Inhibition is classically conceived as a system parallel to activation, the system which processes target informations (e.g. Broadbent, 1958). By suppressing irrelevant informations inhibition would ensure the effective selection of stimuli present in the environment. More precisely, Bjorklund & Harnishfeger (1995) defined inhibition as the "suppression of previously activated cognitive contents or processes, the clearing of irrelevant actions or attention from consciousness, and resistance to interference from potentially attention-capturing processes or contents (page 143)". Inhibition can be exogenous, i.e. directed toward external distractors like noises or objects, or endogenous, i.e. directed toward internal distractors like unrelated thoughts, or daydreams. Inhibition would occur on the mental representations that are activated by irrelevant events (Tipper, 1985). However, only specific properties (location, color, identity, shape, etc.) of those representations would be inhibited (Tipper et al., 1994). Inhibition would suppress the properties of the distractors which are in direct competition with the information relevant to the subject's goals, so as to prevent inappropriate actions (Tipper, Weaver & Houghton, 1994). Thus a distractor is not intrinsically disturbing, but becomes interfering when it is both related and irrelevant to the intended goal. Inhibition thus seems to be a flexible mechanism, which can adapt to the nature of distractors and to the action at hand, rather than an invariant one as it was first proposed by Houghton & Tipper (1994). There has been recent evidence for the existence of at least two major inhibitory systems. One inhibitory system would act on irrelevant "semantic-meaning-bearing" information and the other on spatial information (Connelly & Hasher, 1993).

Fractionation and characterization of inhibition depends on experimental paradigms devised to evidence inhibition. Several experimental tasks have been used to assess inhibition. The negative priming procedure (Neill, 1977; Tipper, 1985), which is considered a classic index of inhibition, is certainly the most widely used (May, Kane & Hasher, 1995; Tipper, 1985). In the negative priming procedure, subjects are simultaneously shown two letters of the alphabet, one red (the target) and the other green (the distractor). Subjects are instructed to name the red letter as fast as possible and to ignore the green one (see Figure 1). The observed effect (called *"negative* priming") is that response time increases when the letter serving as the distractor in one trial (prime) is used as the target in the very next trial (probe). The explanation for this

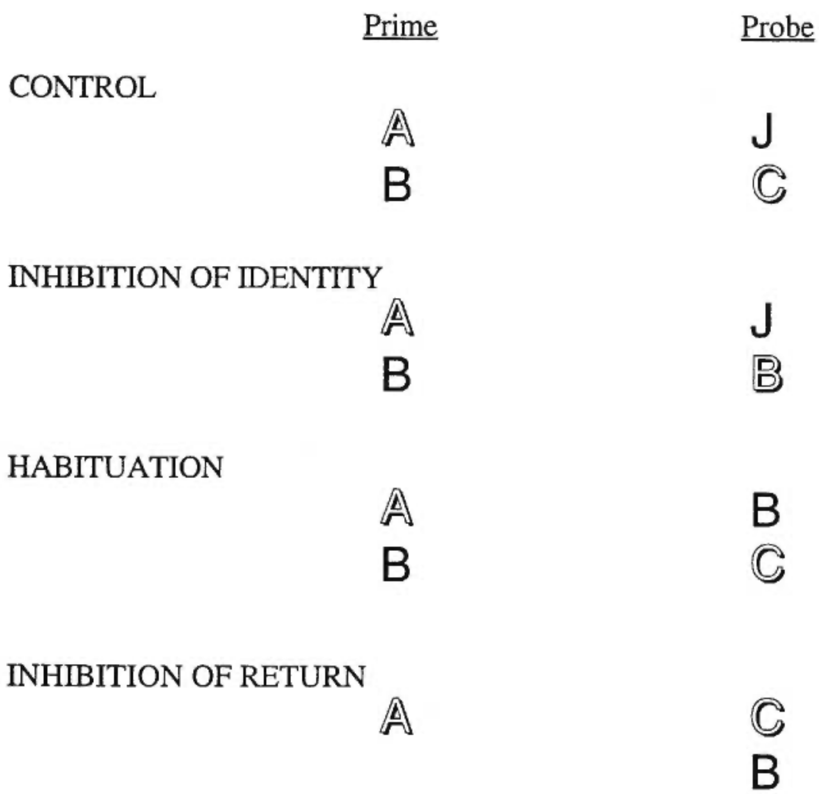


Figure 1. Examples of trials in the four experimental conditions of negative priming (letters in white represent the target).

effect (called *"suppression effect"*) is that the distractor is actively inhibited in the prime trial. Thus, when this distractor becomes the target in the subsequent trial, its selection is delayed because of residual inhibition. This inhibition effect is central and acts upon representations: it does not depends on the modality of response (Tipper, MacQueen, & Brehaut, 1988) and it concerns semantically related stimuli (Tipper & Driver, 1988). This effect has been suggested to reflect inhibition of the lexico-semantic identification of the item and has thus been labelled *inhibition of identity.*

The negative priming procedure allows inclusion of conditions that measure other aspects of inhibitory processes: inhibition of return, habituation to distractors and interference (see Figure 1). *Inhibition of return* refers to the increase in reaction time when the subject has to process a target presented in the same spatial location as the previous one. There is strong suggestion that this delay reflects a spatial inhibitory process (Connelly & Hasher, 1993). When a locus has been explored in a trial, it would be temporarily inhibited. This would attract attention away from the location already explored and would promote a continuous exploration of the visual scene. *Habituation* is measured in the negative priming procedure with the "repeated distractor" condition (Kane, Hasher, Stoltzfus, Zacks & Connelly, 1994). In this condition, the letter-to-be-ignored is the same in the prime and in the probe trials. Usually, this condition induces a facilitation effect, i.e. a faster reaction time in habituation probe trials than in control probe trials (in which distractors differ). Habituation has been interpreted as a result of inhibitory processes (Tipper & Cranston, 1985). The distractor is inhibited in the prime trial. The target is more rapidly detected in the subsequent probe trial if the distractor is the same as in the prime trial because the distractor is still under suppression. If this interpretation is true, a decreased inhibition should yield decreased habituation. However, Tipper, Bourque, Anderson & Brehaut (1989) showed that habituation is observed in children in the absence of inhibition which does not support the view that habituation depends on inhibition. Habituation and inhibition might therefore rely on different mechanisms, in line with a multiple-inhibitory-systems view.

Although negative priming is a very useful tool in the examination of inhibitory processes, it measures inhibition in a restricted context. The inhibition investigated in this paradigm 1) is automatic (as opposed to controlled or volontary); 2) is fast (measured in millisecond differences); 3) reflects visual selective attention; 4) uses lexical material (but picture stimuli were also used, see Allport, Tipper, & Chmiel, 1985). Furthermore, the negative priming task can yield facilitation effects under particular experimental conditions (Connelly & Hasher, 1993; Park & Kanwisher, 1994). This has led some authors to propose different interpretations of negative priming effects which do not rely as heavily on inhibitory processes (for a review, see Fox, 1995). Thus, negative priming by itself can hardly give a comprehensive picture of the general action of inhibitory processes in cognition. It therefore seems essential to compare negative priming to other tasks measuring inhibition.

Burgess & Shallice (1996) have used a very interesting task, the Hayling Test, to study inhibition in frontal-lobe injured patients. In this task, subjects are asked to complete, as fast as possible, sentences in which the last word is missing. The sentences provide a semantically constrained context, i.e. they are selected to rapidly and automatically induce a particular ending-word (e.g. Most cats see well at ? - night -). In the first condition (automatic), subjects are asked to complete the sentences in the way they should end. In the second condition (inhibition), they are asked to refrain from using the automatically-activated word and to complete the sentence with an entirely unrelated word. This task taps inhibition of semantic activation, as subjects have to inhibit the activated word and its semantic associates in order to perform correctly. According to network models of long-term memory, the processing of words or sentences automatically activates interconnected items. Attentional processes, presumably with the help of inhibition, therefore determines the direction and strength of activation upon items in the semantic network (McDowd, Oseas-Kreger, & Filion, 1995).

Interference

As it was mentioned earlier, inhibition is defined as a mechanism which actively suppress task-irrelevant information. A related concept, interference, refers to the susceptibility to decreased performance in the presence of distracting stimuli (Brainerd & Reyna, 1989; Harnishfeger, 1995) and to the slowed selection induced by concurrent possible targets (Sullivan, Faust & Balota, 1995). As interference can be confused with inhibition, Sullivan et al. (1995) proposed a distinction in which the interference task is described as the measure of the selection's slowing time. He described the inhibition task as the measure of the amount of inhibition directed toward a distractor. The well-known and widely used Stroop test was often employed to study the sensitivity to interference caused by the presence of distracting stimuli (Harnishfeger, 1995; Stroop, 1935). Other measures of interference are speed of response and dual-tasks (Harnishfeger, 1995). The negative priming procedure also allows to measure interference, as the reaction time to respond to a target-alone can be compared to the reaction time to respond to a target-with-distractor. The attentional cost (in time) associated with the presence of a distractor therefore represents interference.

The distinction between inhibition and interference is a controversial point in the field. Some authors use inhibition and interference in an interchangeable manner, whereas others describe those mechanisms as being dissociable (Dempster, 1995; Sullivan et al., 1995). The independence between inhibition and interference effects has been empirically assessed by measuring correlations between interference and inhibition scores in negative priming tasks. One position is to suggest that inhibition is used to reduce interference (Tipper, 1985). From this point of view, a negative correlation between inhibition and interference scores is hypothesized: the more subjects can inhibit, the less they show interference. The other position (Stoltzfus et al, 1993) dissociates both mechanisms and thus does not predict any relationship. The matter remains unresolved, as some studies indicate a correlation between interference and inhibition (Tipper, 1991; Tipper, Bourque, Anderson & Brehaut, 1989), whereas others do not (Driver & Tipper, 1989; Tipper et al., 1991; Stoltzfus et al., 1993).

Inhibitory processes in normal aging and in dementia of the Alzheimer type

The advances in neuroscience had an important impact on models of inhibition and interference, particularly studies of patients with frontal cortical lesions who show a deficit in executive and interference tasks (Luria, 1966; Shallice, 1988; Stuss, 1991). It has been suggested that inhibition is under the control of the pre-frontal lobes (Dempster, 1991; Fuster, 1989; Shallice, 1988; West, 1996). This has provided a biological support to the concept and has helped circumbscribing clinical populations at risk for deficits of inhibition.

These include aged individuals and patients with dementia of Alzheimer type (DAT) because their cognitive impairments are frequently interpreted as resulting from a decline in functions associated with the frontal lobes (West, 1996; Moscovitch & Winocur, 1996). The study of inhibition and interference in normal aging and DAT can contribute to further our understanding of these processes as components of inhibition and/or interference are impaired in these populations. This provides the opportunity to explore the nature of inhibition and/or interference impairment in clinical populations. Furthermore, it provides the possibility to examine the relationship between the different components of inhibition. From a clinical point of view, this study should contribute to the characterization of DAT and normal aging. A major difficulty in the diagnosis of DAT is to distinguish its early manifestations from normal aging. If the impaired inhibition processes are different in DAT and normal aging, assessment of inhibition could contribute to the clinical diagnosis of DAT.

Hasher & Zacks (1988) have proposed that impaired inhibitory processes are key factors in normal aging. According to their model, older adults perform less efficiently in cognitive tasks because of a general decline in inhibitory processes. Decreased inhibition leads to distractors remaining active, entering working memory (WM) and interfering with its functionning. This disturbance in the efficiency of WM subsequently affects linguistic processing and other related cognitive performances. Age-related changes would thus result from inadequate control of WM access. Empirical arguments, such as those described below have been provided to support this hypothesis.

Inhibition in aging has been studied with the negative priming procedure. In this task, smaller or absent negative priming effects have often been observed in older adults, hence providing empirical evidence for their inhibition deficit (Connelly & Hasher, 1993; Hasher et al. 1991; McDowd & Filion, 1992; Tipper, 1991, but see Sullivan & Faust, 1993 for normal negative priming in aged subjects). However there is evidence for a dissociation between inhibitory processes in normal aging, as spatial inhibition remains unaffected (Connelly & Hasher, 1993). These results confirm a multiple inhibitory systems view (Connelly et al., 1993; Rouleau & Belleville, 1996). However, further investigations are required to confirm the hypothesis of the co-existence of multiple inhibitory systems since the other components of inhibition have rarely been explored.

Dementia of Alzheimer's type (DAT) is a degenerative disease of the brain, affecting a wide range of cognitive functions including memory, attention, and langage. Surprisingly, studies of inhibition in DAT are virtually inexistant. Nonetheless, the distractibility of DAT patients and their tendency to make numerous intrusion errors in memory and retrieval tasks are suggestive of deficient inhibitory processes. Furthermore, there is strong indications for a deficit of the attentional component of working memory in DAT (Baddeley, Logie, Bressi, Della Sala, & Spinnler, 1986; Belleville, Crépeau, Caza & Rouleau, 1995; Belleville Peretz & Malenfant, 1996; Morris, 1986). The attentional component of working memory, the central executive, would rely heavily upon the inhibition of automatic and conflicting schemas. This suggests inhibition deficits in DAT patients. In fact, only one recent study has adressed inhibition in this clinical population (Sullivan et al., 1995). The authors (Sullivan et al., 1995, Experiment 1) showed impaired inhibition, yet normal interference, in DAT patients. There are therefore indications for inhibition deficits in DAT patients, but the nature and the extent of this deficit remains to be replicated and documented.

The present study aims at assessing the different aspects of inhibition and interference by using the negative priming and two independent tasks in a within-subject experimental design. The study compares inhibitory performances of young, normal older, and DAT subjects. Subjects are tested with a negative priming procedure that includes conditions to measure inhibition of identity, inhibition of return, habituation and interference. The protocol also includes the Hayling test (Burgess & Shallice, 1996) and the Stroop test (Stroop, 1935). The Hayling seemed a sound measure of semantic inhibition but performance of normal aged or DAT persons on that test have never been reported. The Stroop is a classical interference task widely used in clinical neuropsychology.

METHODS

Participants

Thirty-seven participants, 12 young, 12 old, and 13 patients suffering from Alzheimer's disease took part in the experiment. The young adults (6 males and 6 females) ranged in age from 19 to 30 years (M = 22.0) and had a mean of 13.8 years of education (SD = 1.7). The older adults (4 males and 8 females) ranged in age from 68 to 83 years (M = 72.7) and had a mean of 11.0 years of education (SD = 2.0). The DAT patients had a mean age of 72.5 years old (SD = 5.99) (range 64-85) and an average of 10.1 years of education (SD = 1.9). Each patient was individually matched with his normal aged control with respect to age, sex, education, and profession when possible. The difference in formal education and mean age between old subjects and Alzheimer's was not significant, $t(11) = 2.11$, $p = .0586$, and $t(11) = -0.39$, $p = .7195$, respectively. All subjects were french-speaking. Young and normal aged participants were drawn from a pool of volunteers. They had no history of neurological disease, psychiatric disorder, or general anesthesia in the past year. They did not use medication known to affect memory or other cognitive functions. Alzheimer's patients were recruited from three different hospitals in Liège (Begium) and Montreal (Canada). Subjects all reported normal hearing and had normal or corrected vision.

The patients were diagnosed as suffering from dementia of Alzheimer's type (DAT), according to the NINCDS-ADRDA criteria (McKhann, 1984) (10 probable and 3 possible diagnosis). The severity of their disease ranged from mild to moderate, according to the Clinical Dementia Rating scale (CDR, Hughes, Berg, Danziger, Coben, & Martin, 1982). The patients were submitted to an extensive medical examination to confirm absence of any other major neurological condition. Furthermore, most of them were submitted to neurological examination including a nuclear magnetic resonance and a positron emission tomography (PET-scan). Seven patients were beginning a pharmacological procedure with the E2020 molecule (Tacrine), an acetylcholinesterase inhibitor. However, treatment was in its early stage, (i.e. from 2 to 8 weeks in all but one patient who was treated for 5 months). In this phase, patients were given only weak doses of medication. At the time of testing, no modifications due to medication were observed on the neuropsychological performance of patients.

Aged subjects were subjected to a battery of neuropsychological tests, in order to exclude control participants with early signs of dementia. For control subjects, these tests included 1) the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975), used to screen for major cognitive defects, 2) the Mattis Dementia Rating Scale (Mattis, 1976) which estimates functionning of attention, initiation, construction, concepts, and memory, 3) two subtests from the Weschler Memory Scale (logical memory and design memory) (Weschler, 1945), and 4) the French-version of the Mill Hill Vocabulary Test (Gérard, 1983), a multiple-choice synonym test reflecting the general verbal level of subjects. Normal aged subjects performed normally on this neuropsychological assessment and none were excluded from the study on the basis of this neuropsychological assessment. On the Mattis Dementia Rating Scale, they obtained a mean score of 140.17 (over 144), which is well within normal limits according to the most recent norms (Schmidt et al., 1994). Thus, aged people included in the control group do not show signs of early dementia. Patients were examined with the same battery but additional neuropsychological tests were used in some of them. Young participants were not tested as extensively as elderly controls since they are not at risk for dementia. Nevertheless, they completed the Mill Hill Vocabulary Test and a short-term memory span (Batterie d'Évaluation de la Mémoire, Côte-des-Neiges, Chatelois et al., 1993), on which they performed within normal range.

Material and Procedure

1. Negative Priming

The procedure is modelled on the classicial negative priming from the literature. The only difference is the presentation time. We used longer presentation time than the average one in the literature because older subjects show reduced processing speed (Salthouse, 1985). This was made to optimize their processing of the stimuli, target and distractor.

There were four experimental conditions: 1) *Control* (C), a neutral condition in which all stimuli differed, 2) *Inhibition of identity* (ID), where the distractor of the prime became the target in the probe, 3) *Habituation* (H), in which the distractor was identical in both the prime and the probe displays, 4) *Inhibition of Return* (IR), in which the spatial location of the target remained the same in both prime and probe.

Materials

Twelve capital letters (A, B, C, D, E, J, K, N, O, S, T, V) each in green and in red color, served as stimuli. Stimuli were about 6 mm high and wide. Stimuli were vertically presented, one on top of each other with a distance of 2 mm between stimuli. The horizontal visual angle of the total display was 1.39°. A fixation cross measuring 2 mm high and wide was presented in the space between the two locations of stimuli. A warning signal was also created ("Êtes-vous prêt?" - "Ready?"), in order to self-pace the experiment. Stimuli were produced with the software MacDraw 1.1 and were presented on the center of a Macintosh color monitor, using the SuperLab 1.5.9 software (Cedrus Corporation, 1992).

Procedure

Subjects were individually tested in a quiet room. They sat 50 to 75 cm from the screen. The experimenter told them that one or two letters, one green and one red, would appear rapidly on the center of the screen. They were asked to name the red letter as fast as possible, and ignore the green letter. Response times were taken with a microphone, directly plugged into the computer. Subjects were asked to talk loud enough to ensure registration of their reaction time by the microphone.

A warning signal was presented at the beginning of each trial ("Ready?"). The trial was started when the subject responded and was thus self-paced. Each trial was composed of a prime and a probe display. A fixation cross appeared for 500 msec between each display. Displays appeared on the screen for 350 msec. The interval between trials was individually determined by the speed of response of subjects to the warning signal, as the experiment is self-paced. The time between the prime response and the presentation of the probe was 500 msec. Subjects responded to 192 trials. Thus, the experiment required a total of 384 responses from subjects. There were 48 trials for each of the four experimental conditions. Trials were presented pseudo-randomly, with the constraint that no condition occured on more than three subsequent trials. For each experimental condition, every stimuli appeared four times as a target (in red) and four times as a distractor (in green), and this equally for the prime and for the probe displays. Moreover, stimuli were counterbalanced in both possible spatial locations on the screen (top or bottom). The dependant measure was the reaction time associated with the naming of each probe target letter. Furthermore, the examinor recorded subjects' responses. Trials were presented into eight blocks separated by a short pause. Testing lasted approximatively 45 minutes.

2. The Hayling Test

Materials

We used an adaptation of a task reported by Burgess and Shallice (1996). The original version was in English. It was thus necessary to translate and adapt the sentences to French. Thirty sentences in which the final word is missing were constructed. Four sentences were directly translated from Burgess and Shallice, and twenty-six were entirely new sentences more suited to the French culture and language. A pilot study was conducted to ensure that the sentences that were chosen were completed with a similar word by a majority of subjects. In this pilot study, twenty young subjects (half were from Quebec and half from Belgium since the patients were recruited from both countries) were asked to provide the final word of 50 incomplete sentences. From this set, thirty sentences were chosen. Each of these 30 sentences was completed by a word common to all subjects in the pilot study. Sentences were randomly assigned to one of two conditions, automatic or inhibition. Four additional sentences were used for examples (see Appendix A for sentences).

Procedure

There were two conditions (Automatic and Inhibition), each comprising 15 sentences. The first condition was labelled "Automatic". The experimenter read aloud each sentence to the subject. The subject was told to listen to the sentence and, as fast as possible, complete it with the appropriate word. Two practice sentences were first given. Response latencies were recorded by stop-watch, beginning when the last word was pronounced by the examinor, and finishing when subject began to respond. Response accuracy was also recorded (see result section for detailed scoring). In the " Inhibition " condition subjects had to give a response completely unrelated to the sentence. Subjects were told to give a word which makes no sense at all with the sentence, and this, as fast as possible. Two examples were also given to the subjects. If subjects gave an appropriate response (related to the sentence, or the automatically-activated word), the examinor repeated the instructions and told the subject that his response was too related to the sentence. This was done on every trial where an error was made. In DAT patients, instructions could thus be repeated on every sentence. No time limit was given for responding. However, most responses (whether correct or incorrect) was given within 60 sec. The dependent measures were response latency and response accuracy.

3. The Stroop test

Materials

The task employed was the one adapted by Golden (Golden, 1976), and largely employed in clinical pracice. Stimuli were presented on three different cards, one for each of three conditions. On the first card the words *bleu* (blue), *rouge* (red), and *vert* (green) were written in black ink. On the second card, the symbols *xxxx* were presented in red, blue or green ink. On the third card, the words *bleu* (blue), *rouge* (red), and *vert* (green) were written in blue, red, or green ink. On this last card, the three color words always differ from the color ink (e.g. the word green written in a red ink). One hundred stimuli were presented on each card.

Procedure

Three conditions were used. In the "Word" condition, subjects are asked to read aloud as fast as possible the words from the first cards (color names written in black ink). In the "Color" condition, subjects are asked to name as fast as possible the ink color of the stimuli from the second card (the x's written in color). In the "Interference" condition (Stroop-effect) subjects are asked to name the inkcolor of the stimuli from the third card (color names written in color). In this last condition, subjects have to inhibit the written word in order to correctly name the color ink since the two always differ. Conditions are presented in the following order: Word, Color, and Interference. In this version of the Stroop, the dependent variable is the number of items correctly read in a forty-five-sec interval. Scores for each condition are age-corrected when needed, and then translated into a t-score.

4. Experimental design

Each subject performed all experimental tasks. Testing was completed in one session of approximately two hours. The negative priming test was first completed followed by the Hayling Test and the Stroop test. A fixed order of presentation was chosen to allow comparison across subjects.

RESULTS

1. Negative priming

The first dependant variable was the median reaction time associated with verbal responses under each of the four experimental condition. Furthermore, an interference score was used as a dependent variable. The score was calculated by comparing the reaction time for prime composed of a target-and-distractor (control prime) versus prime composed of a target only (inhibition of return prime). The difference between these two reaction times indicates the attentional selection cost associated with the presence of a concurrent distractor. A second analysis was performed with percent error in the same conditions as the dependant variable. It was important to know wether any subject was aware of the relationship between the prime and probe trials since it has been shown that knowledge of the relationship can prevent occurrence of the negative priming effect (Hasher et al., 1991). Subjects were thus asked at the end of the session if they perceived the goal of the experiment. None of our subjects reported being aware of the relationship between the prime and probe. Nevertheless, the data from three subjects were discarded from analysis of the negative priming task. One young subject was eliminated because of a technical problem with the software, one DAT patient was discarded because of high error rate (90%) and one DAT patient could not complete the task because of a visual problem.

Analyses on reaction time

Erroneous trials were rejected from the reaction time analysis. In these cases, both prime and probe were excluded even if the error occured on only one of these. Reasons for exclusion were the following 1) a technical problem (with the microphone or with the computer); 2) presence of any vocal noise produced before the response (even if the following response was correct) because it initiated reaction time measure; 3) an incorrect response. Exclusion occured whether the problem arose on the prime or probe. The percentage of excluded trials was approximately the same in young and aged subjects (11.3% and 12.8%, respectively). It reached 33.2% in DAT patients. Most of the rejected trials in patients were due to their reading (instead of responding "yes") of the "ready" (Êtes-vous prêt?) warning signal.

An analysis of variance (ANOVA) with Group as a between-subject factor (Young, Aged, Alzheimer) and Condition as a repeated factor (Control, Inhibition of identity, Habituation, Inhibition of return) was first used. Analysis were performed on the median reaction time associated with the probe trial of each condition. Table 1 shows the mean reaction time for each group in each condition. The ANOVA revealed a significant main Group effect, F (2, 31) = 9.07, MSE = 23759.50, $p < .001$. The power for the Group effect was .961. The main Condition effect also reached significance, F (3, 93) = 6.13, MSE = 551.81, $p < .001$. The power for the Condition effect was .955. Importantly, the Group by Condition interaction was significant, F (6, 93) = 3.35, MSE = 551.81, $p < .01$, with a power of .924. Analysis of the simple effects showed that Condition was significant in DAT, F (3, 93) = 6.96, MSE = 551.81, $p < .001$, and young subjects, F (3, 93) = 4.58, MSE = 551.81, $p < .01$, but not in elderly persons, $F < 1$.

Table 1. Mean naming latencies (msec).

	Young	Older	Alzheimer
Control			
Prime	468.0 (41.8)	512.4 (57.2)	615.5 (120.5)
Probe	465.9 (42.3)	504.1 (53.8)	604.7 (128.3)
Inhibition of identity			
Prime	468.1 (44.5)	508.5 (52.2)	619.3 (142.3)
Probe	487.2 (44.8)	506.7 (50.4)	621.1 (117.5)
Suppression	21.3 *	2.6	16.3
Inhibition of return			
Prime	439.2 (45.7)	474.3 (52.4)	581.9 (135.9)
Probe	456.3 (50.9)	514.2 (71.4)	576.2 (109.8)
Suppression	-9.6	10.1	-28.5 *
Habituation			
Prime	468.6 (99.8)	500.2 (60.7)	624.9 (103.9)
Probe	453.9 (42.9)	498.5 (49.9)	605.3 (117.8)
Facilitation	-12 *	-5.63	0.6
Interference effect	28.8 *	38.1*	33.6*

Note: Standard deviations in parenthesis

Since we had hypotheses on the nature of the effects we performed planned contrasts separately for each condition and for each group. In line with the current literature on negative priming, this was done by comparing reaction time (RT) to the probe control with RT's to the probe of each inhibition condition. Furthermore, we computed a suppression effect score for each condition in order to quantify the size of the different inhibition effects (see Table 1). This score was obtained by substracting the probe RT of a given condition from the median reation time associated with the control probe. A positive score represents a suppression (or inhibition) effect. A negative score indicates a facilitation effect (i.e. positive priming).

In young subjects, planned contrasts indicated a slower reaction time on inhibition of identity trials than on control ones, $t(10) = -3.87$, $p < .005$, with a suppression effect of 21.3 msec. There was also a significant difference between the habituation condition and control probe trials RT, $t(10) = 2.70$, $p < .05$, with an habituation effect (or facilitation) of -12 msec. There were no significance difference between the inhibition of return and control trials $t(10) = 1.74$, $p = .113$. Older subjects showed no difference between inhibition of identity and control trials, $t(11) = -0.34$, $p = .738$, indicating no inhibition of identity effect. Furthermore, they showed neither inhibition of return, $t(11) = -1.03$, $p < .324$, nor habituation effect, $t(11) = 0.956$, $p = .359$. In DAT patients both the inhibition of identity, and habituation effects failed to reach significance, $t(10) = -1.63$, $p = .134$ and $t(10) = -0.037$, $p = .971$, respectively. Surprisingly, they showed faster RT in the inhibition of return than in control trials, $t(10) = 3.459$, $p < .01$, with a facilitation effect of -28.5 msec.

Planned contrasts were also used on interference scores. Young subjects, elderly controls, and DAT patients showed significant interference ($\underline{t}$ (10) = 5.358, $\underline{p}$ < .005; $\underline{t}$ (10) = 4.62, $\underline{p}$ < .001, and $\underline{t}$ (10) = 3.21, $\underline{p}$ < .01, respectively). A one-way ANOVA was conducted to verify if the size of the interference effect differed according to group. The analysis failed to show any group difference, $\underline{F}$ < 1.

Analyses on error rate

The stastistical analysis on error rate were performed with percent incorrect naming responses. A 3 by 4 analysis of variance (ANOVA) was first performed with Group (Young, Aged, Alzheimer's) and Condition (Control, Inhibition of identity, Habituation, Inhibition of return). Table 2 shows the mean error rate for each group on each condition. The ANOVA indicates no significant main Group effect, $\underline{F}$ (2, 31) = 2.44, $\underline{MSE}$ = 22.63, $\underline{p}$ = .104. The power of the group effect was moderate (.453). The main Condition effect was significant, $\underline{F}$ (3, 93) = 18.57, $\underline{MSE}$ = 4.28, $\underline{p}$ < .001, with a power of 1.000. However, the Group by Condition interaction did not reach significance, $\underline{F}$ < 1, and showed a very small power index (.128).

Table 2. Percentage of error.

	Young	Older	Alzheimer
Control	11.4 (7.4)	12.3 (8.1)	14.4 (7.0)
Inhibition of identity	11.7 (6.4)	12.5 (4.6)	15.7 (9.6)
Inhibition of return	3.9 (3.0) *	6.3 (4.1) *	10.0 (6.7) *
Habituation	6.6 (4.1) *	7.5 (3.5) *	11.6 (6.6) *
Total percentage of error	8.4	9.6	12.9

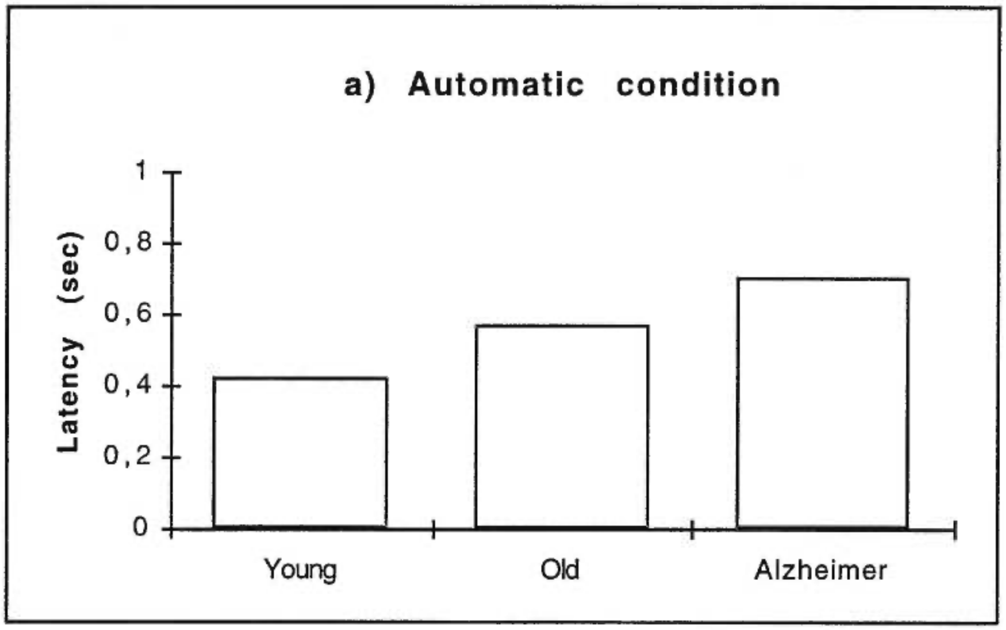
Note: Standard deviations in parenthesis

Since there were specific predictions associated with each condition, planned contrasts were performed separately for each condition and for each group. This was done by comparing errors made on the control probe with errors made on the probe of each inhibition condition. In young subjects, there were no reliable difference in error rate between inhibition of identity trials and control ones, $\underline{t}\ (10) = -0.225$, $\underline{p} = .826$. However, young subjects produced significantly less errors in the inhibition of return, $\underline{t}\ (10) = 4.24$, $\underline{p} < .005$, and habituation trials, $\underline{t}\ (10) = 2.768$, $\underline{p} < .05$, than in control ones. Older subjects showed no difference between inhibition of identity and control trials, $\underline{t}\ (11) = -0.075$, $\underline{p} = .942$. They produced less errors in the inhibition of return, $\underline{t}\ (11) = 2.46$, $\underline{p} < .05$, and habituation condition, $\underline{t}\ (11) = 2.785$, $\underline{p} < .05$, than in the control one. In DAT patients, there were no difference between the control condition and inhibition of identity, ($\underline{t}\ (10) = -0.603$, p = .559, and habituation, t (10) = 1.42, p = .184. However, DAT patients made less errors on the inhibition of return than on control condition, t (10) = 3.272, p < .01.

2. Hayling Test

Two dependent measures were used in the Hayling test: response latency and error rate. For latency, the median (in sec) was calculated in each condition for each subject. In the inhibition condition, responses were scored according to criteria proposed by Burgess & Shallice (1996). The subject obtained an error score of three points on each sentence for which the automatically-activated word was given. For example in the sentence "The captain wanted to stay with the sinking ?", the response "boat" would yield a score of 3. One point was given when a subject gave an antonym, a semantically related word, a word that made vague reference to the sentence, as well as obscenities or other inappropriate words. The subject received no error point when an unrelated response was provided. In the automatic condition, an error score was computed following the reversed correction criteria: three error points were given when subject gave an unrelated word, one point when the word was semantically connected to the target or semantically relevant to the sentence, and no error point for the target.

A 3 (Group) by 2 (Condition) ANOVA was conducted separately for latencies and inhibition errors. Figure 2 illustrates the latencies data. Their analysis indicated a significant Group effect, F (2, 33) = 21.686, MSE = 0.867, p < .001, a significant effect of the Condition, F (1, 33) = 114.782, MSE = .871, p < .001, and a Group by Condition interaction, F (2, 33) = 15.278, MSE = .871, p < .001. Analysis of the interaction revealed that groups did not differ significantly in the Automatic condition, F (2, 33) = 2.890, MSE = 0.082, p = .07, but differed in the Inhibition condition, F (2, 33) = 19.251, MSE = 1.655, $p < .001$. Post-hoc pairwise comparisons (Sheffe) indicates that this is due to the fact that DAT patients were slower than both aged ($p < .01$) and young ($p < .001$) subjects. Moreover, aged subjects were slower than young ones ($p < .05$). All subjects were affected by the experimental condition but the effect was larger in DAT patients, F (1, 33) = 103.680, MSE = .871, $p < .001$, than in normal aged controls, F (1, 33) = 36.034, MSE = .871, $p < .001$ and young subjects, F (1, 33) = 5.624, MSE = .871, $p < .05$.



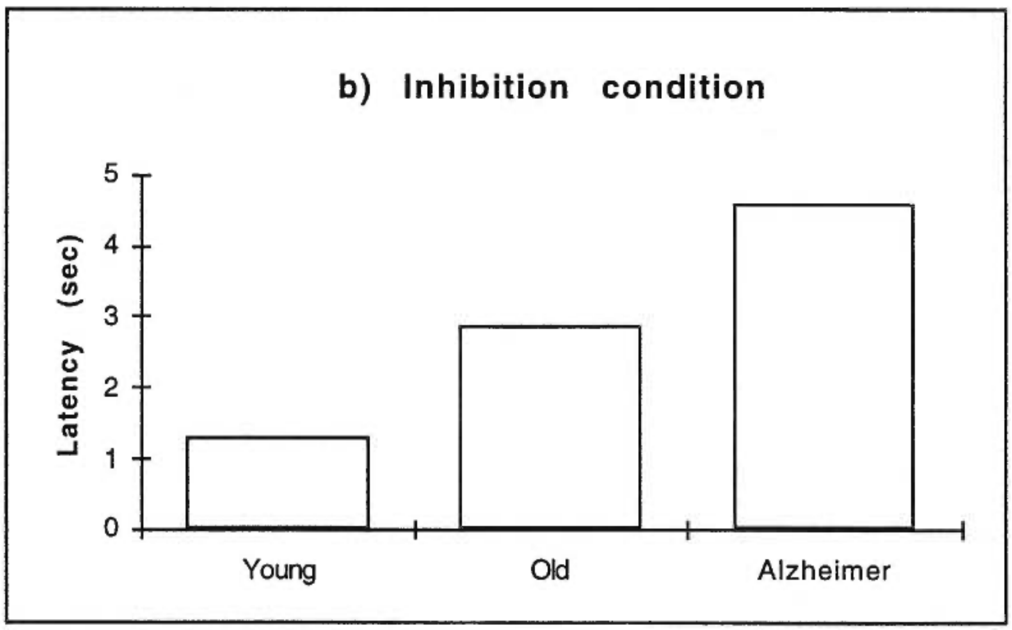


Figure 2. Latencies of response in the Hayling Test. a) Automatic condition, b) Inhibitory condition

A 3 (Group) x 2 (Condition) anova was also performed on error scores (Figure 3). The analysis showed a main Group effect, F (2, 33) = 29.756, MSE =

573.29, $p < .001$. The effect of Condition also reached significance, $F(1, 33) = 51.753$, $MSE = 12.176$, $p < .001$. Importantly, the Group by Condition interaction was significant, $F(2, 33) = 20.352$, $MSE = 12.176$, $p < .001$. Analysis of the simple effects revealed that the performance of young and aged subjects did not differ in the automatic and inhibition conditions, $F(1, 33) = 1.971$, $MSE = 12.176$, $p = .170$ and $F(1, 33) = 2.878$, $MSE = 12.176$, $p = .099$, respectively. However, DAT patients were more impaired in the inhibition than automatic condition, $F(1, 33) = 87.608$, $MSE = 12.176$, $p < .001$. Additionnaly whereas groups differed in both conditions, the effect was more significant in the inhibition, $F(2, 33) = 28.391$, $MSE = 27.720$, $p < .001$, than in the automatic condition $F(2, 33) = 9.157$, $MSE = 3.722$, $p = .05$.

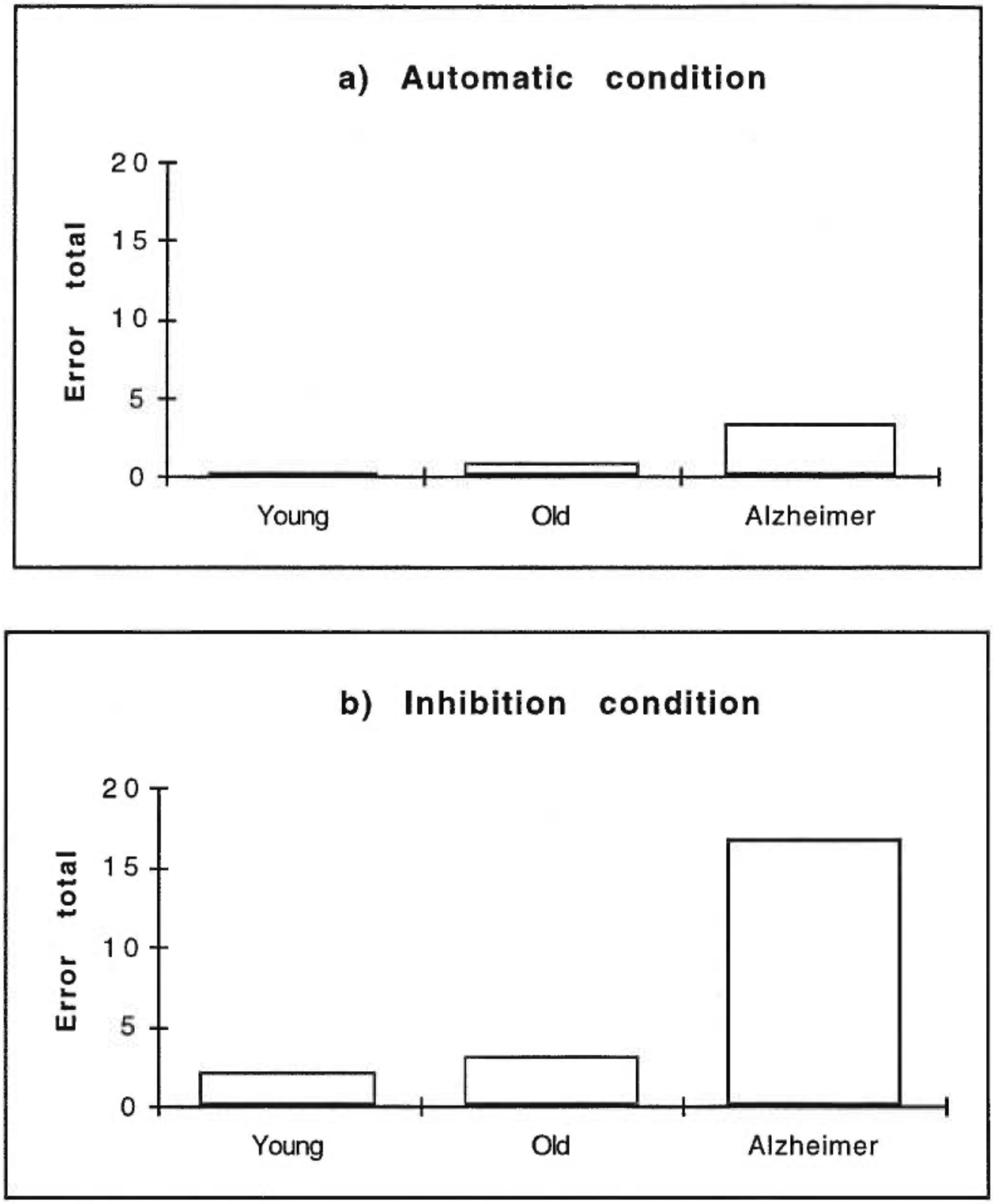


Figure 3. Number of errors in the Hayling Test. a) Automatic condition, b) Inhibition condition.

3. Stroop Test

An "interference score" was calculated for each subject according to the following formula: Interference - [(Word x Color) / (Word + Color)] (Golden, 1976). The results of the formula is translated into a t-score. This formula takes into account processing speed (an important aspect in aging samples) and quantifies sensitivity to interference. Subjects with greater sensitivity to interference have lower (negative) interference scores when compared to normative data. These scores are presented in Figure 4. A one-way ANOVA was used to test any Group difference on these interference scores. The ANOVA revealed a significant Group effect, F (2, 33) = 5.924, MSE = 48.392, $p < .01$. Sheffe's test indicated that young subjects were less sensitive to interference than both normal aged subjects ($p < .05$), and DAT patients ($p < .05$). However, there was no difference between normal aged subjects and DAT patients.

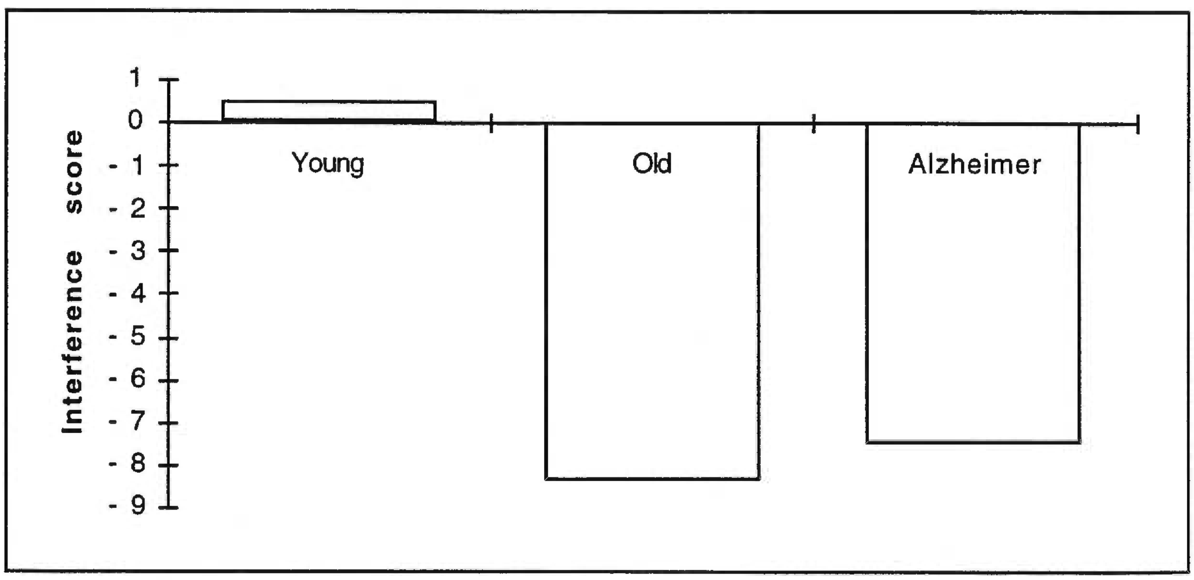


Figure 4. Interference score (Interference - [(Word x Color)/(Word + Color)]) on the Stroop Test. A negative score represents a sensitivity to interference.

4. Correlation analyses

Correlational analyses were used to examine the relationship between the different interference and inhibition tasks. They were performed with the three suppression effects and the interference measure derived from the negative priming procedure (see Table 1), the error score in the Inhibition condition of the Hayling test and, the interference score of the Stroop test.

In young subjects, there was a negative correlation between the inhibition errors on the Hayling and the suppression effect on inhibition of identity in the negative priming task, $r = -0.6016$, $p < .05$. That is, inhibition in the Hayling was related to identity inhibition on the negative priming task. There were no other significant correlation in young subjects including that between the interference and identity inhibition scores of the negative priming, $r = 0.4142$, N.S..

There were a few significant correlations in aged subjects which differed from those found significant in young subjects. Results in older individuals indicated a solid negative correlation between inhibition errors on the Hayling and the habituation effect on negative priming, $r = -0.8047$, $p < .01$. That is, subjects with inhibition failures on the Hayling tended to habituate less on negative priming. Furthermore, there was a negative correlation between the interference and inhibition of return scores of the negative priming, $r = -0.7041$, $p < .05$. In DAT patients, no significant correlations were observed.

DISCUSSION

In the present study, various aspects of inhibition were assessed in young subjects, older adults, and patients with DAT. At this point, it appears important to first summarize and discuss the pattern of results observed in normal aging. Then the results observed in DAT will be reviewed and their clinical implications discussed. Finally, the contributions of the present results to theories of inhibition will be discussed.

Normal aging

Two tasks were used to measure inhibition: the negative priming procedure and the Hayling test. Both tasks evidenced inhibition deficits in normal aged individuals. In the inhibition condition of the Hayling Test, older subjects were not impaired when considering response accuracy. Yet they were slower than young subjects in this particular condition. In the negative priming procedure, reation time and percent of error revealed that aged subjects showed deficits in the inhibition of the identity of distractors. This replicates the identity-inhibition deficit previously reported with this task. Interestingly, the present study yielded larger inhibition effects than in previous studies when young subjects were tested (21.3 msec as compared to approximately 10 msec in previous studies). This might be related to the proximity of stimuli, which was considerably greater in the present study and which might have increased the selection complexity of the task. If selection is increased in complexity, more inhibition of distractors is required. One might conclude that this would leave more room for an effect, however small, to occur in aged subjects but it was not the case. Therefore, the results obtained in both tasks of the present study are in line with the hypothesis of a decreased lexico-semantic inhibition in normal aging.

However, alternative explanations can be proposed to account for some of those results. The first involves the inhibition deficits observed in the Hayling Test. As it was proposed by McDowd (1995), this decrement on the Hayling test could be related to the fact that older adults have a richer semantic structure, which creates more difficulties in inhibiting semantic information. However, this explanation could not account for their performance on the negative priming task. Secondly, an explanation for the absence of inhibition in aging was that older subjects do not process distractors. Obviously, unprocessed stimulus would not require inhibition. However, this interpretation is unlikely because of the interference effect observed in aging. If older subjects indeed would not process distractor, they should not be affected by them, which was not the case here.

The negative priming procedure included a condition measuring spatial inhibition with the inhibition of return (IR) phenomenon. Results indicated no inhibition of return in aged subjects. However, this effect was also absent in young subjects. Methodological aspects of our tasks could have prevented the effect to occur in both groups: 1) As other studies examining IR used four spatial locations (Connelly & Hasher, 1993), it should be considered that the use of only two spatial locations was instrumental in the absence of effect. However, there is no theoretical reason to suspect an effect of the number of stimuli on spatial inhibition. 2) Explicit processing of the spatial aspects of the stimuli might be necessary for the effect to occur. Tipper (1994) claimed that inhibition is goaloriented, which means that distractors are inhibited when their features are interfering with the action at hand. As our paradigm requires a response to the identity of distractors and not to their location, there might have been no need to inhibit their spatial location. However other studies have found spatial inhibition in conditions where the response did not require spatial processing (Connelly & Hasher, 1993). Further research will thus be required to determine the optimal conditions to put the IR phenomenon in evidence.

Older subjects show indications of habituation deficit when reaction times are considered but not when percent of error are taken as criterion. It is thus possible that aged people experience a modest habituation deficit which can be slightly compensated for by a slowing in response time. Only one study directly adressed habituation in normal aging (Kane, Hasher, Stoltzfus, Zacks & Connelly, 1994). In this article, the authors used a procedure similar to ours, with the exception that words rather than letters were used. They failed to show habituation in aged subjects but their paradigm did not evidence any habituation effect in young subjects either. Kane et al. (1994) claimed that habituation effects are only observed with a block-presentation of stimuli (in contrast to randomized presentations) and that several successive habituation trials are needed to observe habituation. Our results do not confirm this explanation, since we used a randomized procedure and few habituation trials. It also remains possible that unknown methodological differences between the two studies account for the different data. Nonetheless, the present results indicate that, aged persons have a slightly impaired habituation. This would handicap their capacity to suppress irrelevant stimuli which are repetitive in their environment. This impairment could possibly be due to their inhibition deficit.

In addition to inhibition processes, interference was measured with the Stroop test and the negative priming procedure. These two measures showed different results in normal aging. The Stroop evidenced greater sensitivity to interference in aged than in young subjects. In contrast, the interference condition of the negative priming failed to show any age effect. An explanation for this difference might lie in the different sensitivity of the two interference tasks. In the negative priming, interference is related to the mere presence of external distractors, which are not intrinsically incompatible and do not compete significatively for response with the target. The Stroop yields an activation of an inappropriate word that competes for response with the correct word. The strong activation of two possible responses could thus create more interference.

Dementia of Alzheimer type

As compared to age-matched controls, DAT patients exhibit major differences on two conditions of the negative priming procedure. First, DAT patients show less habituation than normal aged individuals who themselves already habituate less than young subjects. Second, they differ from controls on the IR condition. The performance on the inhibition of return condition is intriguing: not only do DAT patients fail to show the inhibitory effect, but they exhibit a large facilitation one. This means that when they have processed a location in a trial, they tend to respond much more rapidly to this same spatial location in the next trial. In similar conditions normal subjects are usually slower to respond (Connelly & Hasher, 1993). This facilitation probably reflects a deficit in visual selective attention, since it indicates some form of attentional grasping or disengagment deficit. The DAT patients' attention would not disengage from previously processed positions so that when the same spatial information has to be processed, the response is more rapid. This interpretation is coherent with the data of Parasuraman et al. (1992). They showed spatial disengagment deficits with no engagement impairment in DAT patients when using the Posner experimental procedure.

The negative priming procedure also allows to measure identity inhibition. However, one major problem with applying the negative priming procedure to DAT was that aged people showed no identity inhibition effect. It was thus not very likely that DAT patients would differ from aged individuals. However, the Hayling test provides informative data in this regard. Indeed, DAT patients were slower than older adults on the inhibition condition of the Hayling test and also made more errors. These results reflect a semantic inhibition deficit in DAT that is more severe than in normal aging. One explanation of the decreased performance shown by DAT patients on the Hayling test could be related to the lexical access deficit which is often reported in these patients (Puel, Démonet, Ousset & Rascol, 1991). However, a lexical access impairment should have the opposite effect, i.e. to slow the access to the automatically activated word and consequently facilitate inhibition. It is thus not likely that deficient lexical access explain the semantic inhibition deficit observed in DAT patients.

DAT patients show interference effects in both the Stroop and the negative priming, but only to the same extent as their age-matched controls. Results are therefore consistent: there is no increase of sensitivity to interference in DAT and this in spite of their deficient inhibition. If the role of inhibition is effectively to decrease interference, as it was proposed (Tipper, 1985), greater interference would be expected in subjects.

This study reveals that DAT affects aspects of inhibition, but in a different way than does normal aging. Some of these differences are quantitative, such as habituation and semantic inhibition which are mildly affected in normal aging and severely affected in DAT. In contrast, inhibition of return appears to be qualitatively different in DAT and in normal aging, being intact in the latter yet severely impaired in the former.

DAT is known to be heterogeneous (Habib, Joanette & Puel, 1991; Martin et al., 1986; Neary et al., 1986), leading to different cognitive impairments across patients. This was only partially confirmed in the analyses of individual profiles of DAT patients on the different inhibition tasks. The data of individual patients was fairly consistent with the group description: all DAT patients were within normal range on the Stroop test, and only two were impaired on the interference condition of the negative priming procedure. In the Hayling Test, all but one patients were impaired. Given the relative homogeneity within patients and the severity of their impairment on some tasks, our study could have clinical contributions. For exemple, the Hayling Test or the IR effect could be interesting tools for the early diagnosis of DAT.

Theoretical contributions to the conceptualization of inhibition

Our study can have significant theoretical consequences. One important data in this regard is the dissociation between impaired inhibition and intact interference in DAT patients, when their performance is compared to that of aged controls. Furthermore, interference is not correlated with inhibition. There are two implications of this dissociation. Firstly, it suggests that interference and inhibition effects are truly distinct, as proposed by Stoltzfus et al. (1993). Secondly, it confirms the theoretical position according to which inhibition occurs late in selection (see May et al., 1995). Currently, two different hypothesis are described in literature for explaining the relationship between inhibition and interference. The first one, the *pre-selection,* (Tipper, 1985; Tipper & Baylis, 1987), suggests that inhibition acts during the selection of stimuli, in order to reduce the interference caused by the presence of distractors. The second hypothesis (Stoltzfus et al., 1993; Tipper et al., 1991) claims that the function of inhibition is *post-selection.* Inhibition and interference would thus not be related and inhibition would serve to prevent distractors to reactivate and disturb the task at hand. As DAT patients do not show an increased interference effect but show a deficient inhibition, our data support the view that inhibition acts after the selection is made. If inhibition would effectively serve to reduce interference, a deficient inhibition would lead to an increased amount of interference.

Another interesting data is the association of impairment between the negative identity priming and the Hayling Test. This suggests that both tasks measure a common mechanism, possibly a lexico-semantic inhibition. This weakens alternative explanations of the negative priming effect, such as the *feature mismatching* (Park & Kanwisher, 1994) or the *episodic retrieval hypothesis*

(Neill & Valdes, 1992) in which authors interpret negative priming effects without using inhibition. The performance on the Hayling Test can not be easily explained by any of those two hypothesis as they both refer to incompatibility between two events that occured in succession.

In conclusion, our results seem to indicate that inhibition can be fragmented into different systems differently impaired by neurological pathology. Apparently, interference and inhibition effects are distinct because they are dissociated in DAT, and resistance to interference does not appear to depend on inhibitory processes. Furthermore, inhibition of return can be impaired in a way that suggests disengagement deficits of spatial attention in DAT patients. Our work suggests that inhibition and interference can represent fruitful concepts in neuropsychology. It would be interesting to investigate them in other neurologicaly impaired populations, particularily frontal lobe injured patients, in order to address their anatomical substrates and to assess whether other patterns of impairment can be found.

Appendice A

Sentences used in the Hayling Test (French-version)

1. Automatic Condition

Exemples:
1: Les prisonniers se sont évadés de la__________ (prison).
2: La neige est de couleur __________ (blanche).

1. Le facteur s'est fait mordre par un__________________________ (chien).
2. Les pompiers ont éteint le________________________________ (feu).
3. J'ai jeté mes déchets dans la ______________________________ (poubelle).
4. Avant de manger, lavez-vous les ___________________________ (mains).
5. Les enfants adorent le gâteau au ___________________________ (chocolat).
6. En courant, je me suis foulé la _____________________________ (cheville).
7. La poule a pondu un _____________________________________ (oeuf).
8. Pour l'appeler, il me faut son numéro de ____________________ (téléphone).
9. Le fermier doit traire les __________________________________ (vaches).
10. Pour prévenir la carie, il faut se brosser les __________________ (dents).
11. La vache donne du _______________________________________ (lait).
12. Pour se détendre, on écoute de la __________________________ (musique).
13. On dit que les loups sortent les soirs de pleine__________________ (lune).
14. Avant de traverser la rue, il faut regarder des deux______________ (côtés).
15. Dans le journal, on voit sa photo en première__________________ (page).

2. Inhibition condition

Exemples:
1: Quand ils se sont rencontrés, ce fut le coup de__(foudre).
2: On se mouche le __________ (nez).

1. Lorsqu'elle a appris la mauvaise nouvelle, elle a versé des__________________.
2. Les deux mariés sont partis en voyage de__________________________.
3. Il a posté la lettre sans y mettre un______________________________.
4. Pour se protéger de la pluie, il a ouvert son________________________.
5. Le bébé pleure pour appeler sa____________________________________.

6. Le menuisier a cloué un clou avec un ______________________________.
7. Pour améliorer sa vision, il porte des ______________________________.
8. Après sa journée de travail, il rentre à la______________________________.
9. Il était tellement bizarre, on aurait dit qu'il venait d'une autre ______________.
10. Il est bon de manger trois fois par______________________________.
11. Le chat court après la ______________________________.
12. Avant d'aller au lit, on éteint la______________________________.
13. Il y a beaucoup de livres dans la ______________________________.
14. On dépose notre argent à la ______________________________.
15. Pendant le repas, toute la famille est assise autour de la________________.

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Footnote

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Chapitre III:

DISCUSSION GÉNÉRALE

Cette thèse avait deux objectifs généraux: 1) évaluer l'effet du vieillissement normal sur les capacités d'inhibition et de manipulation de l'AC en égalisant le niveau de base des sujets jeunes et âgés; 2) caractériser les atteintes des fonctions de manipulation et d'inhibition dans la DTA et les distinguer de celles associées au vieillissement normal. Dans le cadre de cette discussion générale, nous résumerons d'abord les principaux résultats obtenus dans nos différentes études. Par la suite, nous en discuterons les implications cliniques et théoriques.

1. Résumé des résultats obtenus

1.1 Vieillissement normal

Nous avons évalué les capacités de manipulation en utilisant une tâche exigeant que le sujet modifie la position des items à retenir et les rapporte selon l'ordre de l'alphabet (Article n° 1 et Article n° 3). Le paradigme utilisé contrôlait pour d'éventuelles différences entre les sujets dans les capacités de stockage. Trois expériences ont montré que le vieillissement normal n'altérait pas les capacités de manipulation en MdeT. Une quatrième expérience a démontré la validité de cette tâche comme mesure de l'AC puisqu'une mobilisation de l'AC chez des sujets jeunes perturbait leur rappel alphabétique.

Quatre paradigmes ont été utilisés pour évaluer les processus d'inhibition: l'amorçage négatif, le Hayling Test, le Stroop et l'ISE ("irrelevant speech effect"). Les données obtenues à la tâche d'amorçage négatif montrent un déficit associé au vieillissement normal, particulièrement en ce qui concerne l'inhibition de l'identité des distracteurs (Article n° 4). Le Test de Hayling dans lequel le sujet devait produire un item qui ne correpondait pas au contexte induit par une phrase a permis de montrer des difficultés d'inhibition sur la mesure des temps de réponse mais non sur la mesure des erreurs (Article n° 4). En revanche, trois expériences ont rapporté des capacités intactes à inhiber des distracteurs ambiants lors de la réalisation d'une tâche de MdeT (Tâche de ISE, Article n° 2 et Article n° 3). L'habituation aux stimuli distracteurs dans la procédure d'amorçage négatif apparaît moins efficace chez les sujets âgés (Article n° 4). Enfin, la résistance à l'interférence n'est que partiellement atteinte puisque les personnes âgées montrent des déficits d'interférence au Stroop mais pas à la condition d'interférence de la procédure d'amorçage négatif.

1.2 La démence de type Alzheimer

Les épreuves mesurant les capacités de manipulation et d'inhibition ont été utilisées auprès de patients souffrant de DTA et leur performance a été comparée à celles de sujets âgés neurologiquement sains. Les résultats chez les patients DTA font état de déficits marqués à plusieurs de ces tâches. D'abord, les capacités de manipulation de l'information en MdeT sont sévèrement touchées et ce, même en égalisant la demande en terme de stockage (Article n° 3). L'examen des performances individuelles met en lumière une relative homogénéité des performances à cette tâche mais certains patients DTA ont néanmoins des performances normales. Dans la tâche d'amorçage négatif, la condition d'inhibition de retour entraîne non seulement une absence d'inhibition, mais un effet inverse de facilitation chez les DTA. De même les capacités d'habituation sont atteintes dans la DTA. L'inhibition de distracteurs sémantiques mesurée par le Test de Hayling est particulièrement touchée chez les patients (Article n° 4). Par ailleurs, comme cela est le cas des sujets âgés normaux, les patients DTA ne montrent pas une performance déficitaire sur la totalité des épreuves. Ainsi, l'inhibition de distracteurs phonologiques dans une tâche de MdeT semble intacte au niveau de la moyenne de groupe, même si l'analyse des profils individuels montre un déficit chez un sous-groupe de patients (Article n° 3). De plus, la résistance à l'interférence est comparable à celle observée chez les sujets contrôles (Article n° 4).

2. La nature du vieillissement cognitif

Une des motivations de ce travail était de contribuer à une meilleure compréhension du vieillissement cognitif. Nous discuterons d'abord d'un facteur méthodologique pouvant rendre compte de nos résultats négatifs, soit la procédure d'égalisation, puis d'un facteur pouvant expliquer nos résultats positifs, soit l'utilisation de la vitesse comme variable dépendante. Nous verrons ensuite comment nos résultats contribuent à l'hypothèse d'un trouble de l'AC ou de l'inhibition dans le vieillissement normal.

2.1 Procédure d'égalisation des performances

Plusieurs études antérieures suggéraient une atteinte de l'inhibition et de la manipulation dans le vieillissement normal (Connelly & Hasher, 1993; Craik, 1986; Dobbs & Rule, 1989; Hasher et al., 1991; Tipper, 1991). Nos travaux n'ont pourtant montré d'effet liés à l'âge ni dans la tâche de rappel alphabétique ("alpha-span"), ni dans celle d'inhibition de bruits non-pertinents (ISE). Or ces tâches comportaient une méthode d'égalisation des performances. Plusieurs arguments nous portent à croire que la procédure d'égalisation est responsable de l'absence d'un effet lié à l'âge. D'abord, les travaux antérieurs portant sur les capacités de manipulation et qui ne contrôlaient pas pour les différences en terme de stokage ont observé des effets liés à l'âge. L'analyse des données de la littérature portant sur l'attention divisée suggère un phénomène comparable puisque plusieurs auteurs montrent que l'égalisation des niveaux de base élimine l'effet lié à l'âge (Belleville et al., 1982; Salthouse et al., 1995; Somberg & Salthouse, 1982). Enfin, il est intéressant d'observer que les trois tâches touchées ici par le vieillissement normal soit l'amorçage négatif, le Hayling Test et le Stroop, sont celles pour lesquelles l'égalisation n'a pas été faite. Il semble donc que des différences dans les niveaux de base puissent être responsables d'interactions observées ultérieurement entre l'âge et le facteur à l'étude comme le proposaient Loftus (1978) et Salthouse (1985).

Dans des travaux ultérieurs, il pourrait être intéressant de modifier les protocoles expérimentaux afin de permettre l'égalisation des performances des sujets. Par exemple, l'ajustement individuel du temps de présentation des stimuli (en fonction du temps de dénomination du stimulus, par exemple) pourrait être envisagée dans la procédure d'AN, ce qui assurerait le même traitement des stimuli par tous les sujets.

Par ailleurs, il est important de reconnaître les limites de la procédure d'égalisation. Comme le souligne Salthouse (1985), le fait de modifier les conditions d'évaluation à travers les sujets pourrait altérer la façon dont le matériel est traité. Il est ainsi possible que jeunes et âgés n'aient pas recours au même système cognitif pour compléter la tâche. Toutefois, nous croyons que l'objection peut aussi s'appliquer à des protocoles qui utilisent des tâches dont le niveau de difficulté à la base diffère chez les deux groupes. De plus, Salthouse (1985) propose pour répondre partiellement à ce type d'objections de mesurer la performance des sujets à différents points de la fonction reliant le comportement et le processus. Par exemple, il faudrait pour cela évaluer les deux groupes de sujets, jeunes et âgés, avec des temps de présentation lents et rapides plutôt que de tester les jeunes avec des temps rapides et les âgés avec des temps lents. Une telle stratégie est coûteuse bien sûr mais pourrait s'avérer fructueuse car elle permettrait de vérifier que la procédure expérimentale ne modifie pas les comportements de façon qualitative.

Malgré les risques inhérents à la procédure d'égalisation, nous croyons que l'impact de cette procédure sur la nature des données, soit le fait qu'elle annule la plupart du temps l'effet du vieillissement normal, est fondamental et appelle à une plus grande vigilance dans l'élaboration ou l'interprétation de protocoles expérimentaux qui ne tiennent pas compte des différences dans les niveaux de base.

2.2 Vitesse de traitement de l'information et vieillissement

Les sujets âgés sont reconnus comme ayant une vitesse de traitement ralentie (Salthouse, 1991) ce qui conséquemment pourrait influencer leur performance aux tâches sollicitant la vitesse (e.g. temps de réaction, vitesse de lecture, tâches chronométrées). Il est donc possible que les différences d'inhibition liées à l'âge soient causées par ce facteur cognitif général.

Dans nos études, l'atteinte des sujets âgés se manifeste de façon particulièrement marquée sur les tâches prenant en compte la variable vitesse. Par exemple, au Hayling test, les sujets âgés sont ralentis mais ne commettent pas plus d'erreurs que les jeunes. De la même façon, l'inhibition est touchée à l'amorçage négatif, une tâche ne considérant que la vitesse, mais pas dans l'ISE, une tâche ne considérant que les erreurs. Ce patron d'atteintes pourrait donc s'expliquer par un trouble ne touchant que la vitesse et se manifestant de façon secondaire dans certaines tâches mesurant l'inhibition. Les personnes âgées étant généralement ralenties, les tâches exigeant plus d'opérations pourraient être celles sur lesquelles ce ralentissement se manifeste avec le plus d'ampleur. Il ne s'agirait donc pas d'une atteinte première de l'inhibition. La présence d'un tel facteur général pourrait éventuellement expliquer les corrélations obtenues chez les sujets âgés entre les différentes tâches sollicitant la vitesse (Article n° 4). Une réduction de la vitesse de traitement pourrait diminuer la performance sur toutes ces tâches, lesquelles pourraient corréler à cause de ce facteur commun.

Notons toutefois qu'il est aussi possible que la vitesse soit tout simplement une variable plus sensible que le nombre d'erreurs et moins sujette aux effets plancher ou plafond. Elle serait donc plus à même de révéler des différences d'inhibition liées à l'âge.

Quoiqu'un facteur important à considérer, un ralentissement du traitement ne peut rendre compte de la totalité de nos résultats. Par exemple, le ralentissement explique moins facilement la présence de dissociations observées à l'intérieur d'un même paradigme, par exemple entre l'interférence et l'inhibition de l'identité dans l'amorçage négatif. De plus, nous avons tenté de contourner le ralentissement des sujets âgés à traiter les distracteurs dans la tâche d'amorçage négatif en augmentant le temps de présentation des stimuli. Malgré cela, les sujets âgés ne montrent pas d'inhibition de l'identité.

Il est aussi possible que l'absence d'effet d'inhibition de l'identité soit causée par délai dans l'apparition de cette inhibition dû au ralentissement (Stoltzfus et al., 1993). Comme l'inhibition prend un certain temps à se développer, elle pourrait ne pas avoir atteint suffisamment d'ampleur lors de l'apparition du test pour être expérimentalement mesurable chez les âgés. Il s'agit là d'une hypothèse intéressante mais une étude a montré que l'utilisation d'un intervalle plus long entre l'amorce et le test afin de permettre à l'effet de se développer n'entraînait pas davantage d'inhibition chez les personnes âgées (Stoltzfus et al., 1993). L'atteinte de l'inhibition par le vieillissement normal ne peut donc s'expliquer entièrement pas un simple ralentissement cognitif.

2.3 L'hypothèse du trouble de l'administrateur central et de l'inhibition dans le vieillissement normal

Nos travaux découlaient de l'hypothèse selon laquelle les personnes âgées souffrent d'une difficulté à inhiber des stimuli non pertinents, difficultés occasionnant une surcharge en mémoire de travail. De façon plus éloignée, nous souhaitions évaluer l'hypothèse d'une dysfonction de l'AC dans le vieillissement normal. D'abord, il est clair à partir de nos résultats que le vieillissement normal n'affecte pas de façon massive l'administrateur central (AC) de la MdeT et que certaines de ses fonctions sont préservées. Ainsi, la manipulation et l'inhibition de bruits ambiants apparaissent normales.

Il est néanmoins assez clair que le vieillissement normal affecte au moins certaines fonctions inhibitrices. Ainsi, l'inhibition de l'identité des distacteurs et l'inhibition d'associations sémantiques fortes sont déficitaires. De plus, l'interférence et l'habituation aux stimuli distracteurs sont perturbés par le vieillissement normal. Dans ce sens, nos données confirment l'hypothèse selon laquelle les sujets âgés normaux se caractérisent par une diminution de leur capacité d'inhibition (Hasher & Zacks, 1988). Par ailleurs, nos résultats permettent de qualifier la façon dont cette inhibition agit sur le fonctionnement cognitif. En effet, Hasher & Zacks (1988) proposaient que le trouble d'inhibition agissait en introduisant une surcharge de la MdeT par les différents stimuli y ayant accès de façon inutile. Un des rôles majeurs de l'inhibition était de bloquer l'accès à la MdeT ou de désactiver toute information non pertinente y ayant eu accès. Cette hypothèse était entièrement spéculative bien sûr dans la mesure où elle ne reposait pas sur des données empiriques évaluant directement le contenu de la MdeT. Or il est important de souligner que dans notre première étude, les sujets âgés accomplissant une tâche faisant appel à leur MdeT pouvaient sans difficulté inhiber des stimuli ambiants non-pertinents ayant directement accès à cette mémoire. Ces résultats vont donc tout à fait à l'encontre de l'explication de Hasher & Zacks (1988) voulant que c'est par le biais d'une surcharge de la MdeT que l'inhibition perturbe le fonctionnement cognitif des sujets âgés. Même si certains processus inhibiteurs sont bel et bien touchés dans le vieillissement, la façon dont cette atteinte se répercute sur le fonctionnement cognitif général reste donc à être clarifiée.

2.4 Impact clinique pour l'évaluation de la démence de type Alzheimer

Un des objectifs de ce travail était de contribuer à une meilleure compréhension des conséquences cognitives de la DTA, particulièrement en ce qui concerne l'inhibition. Nous souhaitions également contribuer aux outils cliniques utilisés en neuropsychologie du vieillissement pour dissocier le vieillissement normal et pathologique. Pour cela, il nous paraissait important d'identifier des tâches associées à des différences qualitatives. Les atteintes des patients DTA pourraient en effet se diviser en deux catégories: celles qui sont de nature quantitative et celles qui sont de nature qualitative. Une atteinte quantitative se définit par le fait qu'elle soit présente chez des sujets âgés normaux (par rapport aux sujets jeunes) et chez des patients DTA bien que de façon plus prononcée chez ces derniers. Les atteintes qualitatives concernent les tâches pour lesquelles les personnes âgées non porteuses de la maladie performent normalement alors que les DTA sont déficitaires. La plupart des travaux portant sur la DTA ne peuvent déterminer si les atteintes qu'ils observent sont qualitatives ou quantitatives car ils n'incluent pas de sujets jeunes. Cela n'est pas le cas de nos travaux qui utilisent des groupes de jeunes adultes et permettent donc d'identifier directement les effets liés au vieillissement normal.

Des différences quantitatives sont observées au Hayling Test. Dans cette tâche, le vieillissement normal augmente le temps de latence nécessaire pour effectuer la tâche, mais sans perturber le type de réponses fournies. Les DTA, en plus d'être ralentis, commettent un très grand nombre d'erreurs d'inhibition. L'habituation aux distracteurs s'avère aussi être affectée dans le vieillissement normal et la DTA bien que plus sévèrement chez ces derniers. Par ailleurs des différences quantitatives se manifestent dans la condition d'inhibition de retour de la procédure d'amorçage négatif où un trouble de désengagement est observé chez les patients DTA. La tâche de rappel alphabétique indique une atteinte des capacités de manipulation chez les patients DTA, capacités qui demeurent intactes dans le vieillissement normal. Par ailleurs, la tâche d'inhibition phonologique (ISE) permet de montrer des différences qualitatives entre les personnes âgées et un sous-groupe de patients DTA.

Nos travaux fournissent donc des épreuves ayant un bon pouvoir discriminatif entre les effets du vieillissement normal et ceux liés à la DTA. De telles tâches sont rares dans la littérature, la plupart des études montrant des différences quantitatives. Les épreuves d'ISE, d'inhibition de retour et d'empan alphabétique pourraient donc éventuellement s'avérer utiles au niveau du diagnostic clinique de la DTA. L'atteinte de l'AC dans la DTA pourrait s'expliquer par une anomalie des régions frontales. Toutefois, il est aussi possible que cette atteinte résulte de déconnexions dans un réseau cérébral plus large. Morris (1994) a en effet suggéré que les fonctions de l'AC sollicitent la coordination de l'ensemble du cerveau. Cette proposition est compatible avec la diminution du nombre de synapses associée à la DTA (De Kosky & Scheffe, 1990) et suggère une relative déconnectivité chez ces patients.

Plusieurs auteurs ont rapporté la présence d'hétérogénéité chez les patients souffrant de démence de type Alzheimer (Belleville et al, 1996; Habib, Joanette & Puel, 1991; Martin, 1990; Martin et al., 1986; Neary et al., 1986). De façon relativement surprenante, notre échantillon de patients DTA se montre assez homogène à la majorité des épreuves utilisées et les moyennes de groupes réflètent généralement assez bien les performances des individus. Par exemple, le Stroop a été réussi adéquatement chez tous les patients, aucun d'entre eux ne montrant de déficit d'interférence supérieur à celui observé chez les sujets âgés contrôles. Pour sa part, le Hayling Test a aussi mesuré un déficit chez tous les patients, à l'exception d'un seul. Nous avons aussi observé que l'amorçage négatif est une tâche dans laquelle les performances varient considérablement entre les sujets mais cela est vrai qu'ils soient normaux ou DTA. L'empan alphabétique montre aussi une certaine variabilité inter-patients bien que la plupart soient touchés à cette tâche. La tâche d'inhibition phonologique (ISE) est en fait la seule tâche pour laquelle nous observons une hétérogénéité manifeste puisque les patients montrent une distribution clairement bi-modale. Compte tenu du caractère relativement homogène des performances de nos patients, les épreuves pour lesquelles des effets qualitatifs sont rapportés pourraient présenter encore plus d'attrait pour le clinicien dans l'évaluation précoce d'une DTA.

De nombreuses autres questions d'intérêt clinique sont soulevées par ce travail. Par exemple, il serait important de savoir comment évoluent les patients souffrant de DTA et si les composantes intactes en début d'évolution le demeurent dans les stades plus avancés. De plus, la relative homogénéité de ces patients pourraient s'estomper avec l'évolution de la maladie et certains patients pourraient présenter des profils plus divergents. Dans un autre ordre d'idée, la mise en évidence de capacités intactes dans la DTA pourrait avoir des conséquences pour la prise en charge de ces patients. Ainsi, les DTA en début d'évolution montrent une bonne capacité d'inhibition de stimuli distracteurs lorsqu'ils effectuent une tâche de MdeT et ils ne sont pas plus sensibles à l'interférence que des sujets âgés sains. Voilà une donnée intéressante qui pourrait modifier la façon dont on intervient auprès de ces patients, ce que l'on croit possible pour eux de faire, et l'aménagement de leur quotidien.

2.5 Contributions théoriques au modèle de l'administrateur central et de l'inhibition

Une des questions à la base de la thèse concernait le fractionnement possible de l'AC. Nos résultats permettent de proposer l'existence de fonctions distinctes au sein de cette composante de la MdeT. En premier lieu, les processus d'inhibition apparaissent dissociés de ceux de manipulation. Dans l'Article n° 3, des doubles dissociations ont été observées chez les patients DTA entre les capacités de manipulation et d'inhibition phonologique. L'existence d'une double-dissociation est un argument empirique appuyant le fait que deux fonctions soient distinctes, neurologiquement et psychologiquement. Ces résultats appuient les auteurs proposant de fractionner l'AC en différentes sous-composantes (Baddeley, 1996; Stuss et al., 1995). Deux d'entre elles pourraient être la manipulation de l'information et l'inhibition des distracteurs.

En second lieu, nos travaux visaient à vérifier l'hypothèse de systèmes inhibiteurs multiples (Connelly & Hasher, 1993). Selon cette hypothèse, l'inhibition pourrait s'effectuer via différents processus spécialisés. Une distinction possible concerne le type d'information devant être inhibée. Certains auteurs ont montré que les personnes âgées sont en mesure d'inhiber la position spatiale mais non l'identité d'un distracteur (Connelly & Hasher, 1993). Une conséquence théorique de cette dissociation était de proposer l'existence de deux système inhibiteurs, l'un agissant sur l'identité (le Quoi) l'autre agissant sur l'information spatiale (le Où) (Connelly & Hasher, 1993). Dans le même ordre d'idée, une explication de la dissociation entre l'inhibition de bruits non-pertinents (ISE) et l'inhibition de l'identité d'un distracteur (amorçage négatif) est de proposer l'existence d'un processus d'inhibition phonologique intact dans le vieillissement normal et distinct de l'inhibition de l'identité. L'habituation pourrait aussi être un système distinct de celui d'inhibition puisqu'elle agirait en diminuant l'interférence causée par des distracteurs stables et répétitifs. Par ailleurs, l'habituation et l'interférence sont dissociées dans la DTA. Ces derniers ont une résistance à l'interférence normale mais une habituation à l'interférence diminuée.

De la même façon, l'inhibition et la résistance à l'interférence paraissent distincts. L'interférence a été définie comme réflétant l'augmentation du temps de traitement des stimuli en présence de distracteurs, ou le "coût attentionnel" associé à la présence de distracteurs. L'inhibition pour sa part, concernerait la suppression active dirigée directement vers la représentation d'un distracteur identifié afin de diminuer son intensité. Dans le dernier article, nous avons montré que l'inhibition n'agissait pas pour réduire l'interférence et que les deux effets expérimentaux pouvaient être dissociés. Nous avons observé un déficit des processus inhibiteurs chez les patients DTA, lesquels ne montraient aucune sensibilité accrue à l'interférence. Il semble donc que les tâches mesurant l'interférence ne sollicitent pas obligatoirement les processus inhibiteurs et que les deux effets bénéficieraient d'être évalués séparément.

L'hypothèse d'une distinction possible entre l'inhibition et l'interférence entraîne obligatoirement un questionnement par rapport à la contribution relative de chacun des phénomènes à nos épreuves expérimentales. Il demeure possible que certaines tâches utilisées dans notre protocole expérimental mesurent davantage l'interférence et d'autres, l'inhibition. Par exemple, les tâches d'inhibition pourraient être celles où la représentation d'un distracteur est activement inhibée, soient les tâches dans lesquelles le distracteur est identifié par le sujet comme le Hayling et l'AN. Cependant, la tâche d'inhibition phonologique, l'ISE, pourrait possiblement être mieux définie comme une tâche d'interférence, puisqu'elle évalue la diminution de la performance mnésique en présence de distracteurs phonologiques ou verbaux. Effectivement, dans cette tâche, le sujet n'inhibe pas une représentation active d'un distracteur qu'il a spécifiquement identifié, mais ce sont plutôt les différents codes phonologiques contenus dans le registre phonologique de la MdeT qui interfèrent entre eux et diminuent le rappel. Comme l'ISE n'est pas affectée chez les sujets âgés et les patients DTA, une hypothèse pourrait être que le vieillissement normal et pathologique affecte l'inhibition et non la résistance à l'interférence. Cette interprétaion est compatible avec la performance relativement normale de ces sujets aux autres mesures d'interférence (Stroop et condition d'interférence de l'amorçage négatif).

Par ailleurs, les tâches pourraient se distinguer par le lieu d'action de l'inhibition, selon qu'elle soit exogène ou endogène. L'inhibition endogène agirait sur des distracteurs internes (par exemple, des associations sémantiques), tandis que l'exogène agirait sur les distracteurs externes (par exemple, les bruits de l'environnement). Le vieillissement normal et pathologique pourrait donc affecter l'inhibition endogène (comme dans le Test de Hayling) et laisser intacte l'exogène (comme dans l'ISE). De plus amples travaux sont évidemment nécessaires afin de clarifier ces différentes hypothèses explicatives.

Finalement, nos résultats contribuent à la controverse existant entre les hypothèses *pré-* et *post-* sélection de l'inhibition dans l'attention sélective. Comme nous l'avons déjà mentionné, un point de vue propose que l'inhibition agit sur les distracteurs avant la sélection des stimuli, afin d'assurer une réponse efficace. L'autre suggère que l'inhibition agit après la sélection des stimuli, lesquels pourraient affecter la tâche en cours s'ils étaient non-inhibés et réactivés. Nos résultats appuient davantage l'hypothèse selon laquelle l'inhibition agit après la sélection. Le fait que l'inhibition et l'interférence semblent être distinctes et non reliées affaiblit l'hypothèse selon laquelle l'inhibition servirait à diminuer l'interférence des distracteurs et appuie conséquemment l'idée que l'inhibition survient après l'interférence et la sélection. Si les deux phénomènes étaient reliés, un déficit d'inhibition conduirait inévitablement à une interférence accrue. Cela n'est pas le cas dans nos travaux. En effet, les sujets âgés neurologiquement sains et souffrant de DTA ne montrent pas d'inhibition mais ont néanmoins une sensibilité à l'interférence comparable à celle des sujets jeunes.

En conclusion, de nombreuses interrogations demeurent quant à la nature de l'inhibition, quant à l'interdépendance entre les différents processus qui y sont reliés et quant à son lien avec les système cognitifs. Par ailleurs, la notion d'inhibition s'est avérée fructueuse tant pour la compréhension du vieillissement normal que pour la caractérisation de la DTA. Il ne fait aucun doute que l'inhibition devrait faire partie de l'évaluation neuropsychologique de patients cérébrolésés. Les travaux du type de ceux présentés dans cette thèse pourraient contribuer à l'élaboration d'outils d'évaluation cliniques arrimés aux modèles théoriques actuels.

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