The Relationships between Executive Dysfunction and Frontal Hypometabolism in Alzheimer’s Disease.

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Abstract. A series of tasks assessing executive functions was administered to patients with Alzheimer’s disease and control subjects. Two groups of Alzheimer patients were examined: patients with hypometabolism restricted to the posterior (temporal and parietal) cerebral areas and patients with hypometabolism in both posterior and anterior (frontal) cerebral areas. The performance of the Alzheimer patients was inferior to control subjects on all executive tasks. However, the two groups of Alzheimer patients did not differ from each other on all tasks except one. These data indicate that frontal lobe hypometabolism is not necessary to produce executive impairment in Alzheimer’s disease. Consequently, executive dysfunction could be the consequence of a disconnection process between posterior and anterior cerebral areas.

Introduction. The presence of executive dysfunction relatively early in Alzheimer’s disease is now well established (e.g. Collette et al., 1999a). However, there exists at present some debate concerning the neurobiological substrates of these deficits. Indeed, for some authors, executive impairment is specifically related to frontal lobe impairment (e.g. Shallice, 1988) but frontal lobe dysfunction does not seem to be a prominent feature in the earlier stages of the disease (Kennedy & Frackowiak, 1994). In addition, other authors suggest that executive control requires the integration of information coming from different cerebral areas (e.g. Collette et al., 1999b). Consistent with that interpretation, recent studies described Alzheimer’s disease as a disconnection process between different cerebral areas (Morris, 1994). Consequently, the aim of this study was to explore the executive functioning of Alzheimer patients with hypometabolism restricted to posterior (temporal and parietal) cerebral areas or hypometabolism in both posterior and anterior (frontal) cerebral areas. Indeed, the existence of a larger executive impairment in Alzheimer patient with posterior and frontal hypometabolism than in patients with only posterior hypometabolism would be
consistent with the main involvement of frontal areas in executive processes. On the contrary, the existence of similar performances in the two groups of patients would be more consistent with the hypothesis of executive functioning depending on more diffuse cerebral areas.

**Method.** Fourteen subjects meeting the NINCDS-ADRDA criteria for probable Alzheimer's disease (AD) and twelve elderly control subjects (CS) were evaluated on different tasks assessing executive functions. The patients included in this study were selected from a pool of 21 AD patients who underwent PET scan at rest. The brain metabolism distribution of these patients was visually analysed and rated by three clinicians in order to isolate (a) patients with hypometabolism restricted to posterior (parietal and temporal) cerebral areas and (b) patients with both frontal and posterior hypometabolism. The presence of hypometabolism was assessed on a scale ranging from 0 (no hypometabolism) to 3 (large hypometabolism) in several left- and right-sided areas: orbital frontal, lateral prefrontal, temporal, parietal. Two criterions were used to determine the presence or absence of frontal hypometabolism in supplement to posterior hypometabolism. The first criterion, termed as **diffusion**, considered existence of frontal hypometabolism when two of the four frontal measures are superior to 0.5. The second criterion, termed as **intensity**, considered existence of frontal hypometabolism when the sum of the four frontal measures is superior to 2. With this procedure, seven patients showing isolated posterior hypometabolism (P AD, without frontal hypometabolism on the two criterions) and seven patients with posterior and anterior hypometabolism (FP AD, with frontal hypometabolism on the two criterions) were selected. The two groups of AD patients did not differ from CS with regard to their age \[H(2, 26)=0.18, p>0.5\] and their schooling level \[H(2, 26)=0.24, p>0.5\]. The two groups of AD patients did not differ with regard to the level of posterior hypometabolism \[U=11.5, p=0.1\] and the FP AD patients exhibited larger frontal hypometabolism than the P AD patients \[U=0, p<0.005\].

Five executive tasks were administered: (1) the **Go/No-go task** requiring to respond as quickly as possible following the presentation of a stimulus “A” but to inhibit the response when a stimulus “B” is presented; (2) the **Stroop interference task** in which subjects are confronted with words written in different colors and are asked to name the colors as quickly as possible while ignoring the words themselves. The performance of the subjects in that condition was compared to a condition in which subjects have to name colored squares; (3) a **selective attention task (“D2”)** in which subjects have to detect letters *d* surrounded by two lines in a page filled with *d*’s and *p*’s (also surrounded by one, two, three or four lines); (4) a **verbal**
phonemic fluency task requiring to generate a list of words beginning with the letter p; (5) a verbal semantic fluency task requiring to generate as many as possible exemplars of the animal category.

**Results** (see Table 1). Overall performance on the Mattis dementia rating scale was significantly lower for the two groups of AD patients than for control subjects [AD FP vs CS: U=2, p<0.0005; AD P vs CS: U=2.5, p<0.0005], but that performance was not different in the two groups of patients [U=8.5, p>0.1]. On the Go/No-go task, the response time of the P AD was significantly slower than that of the FP AD [U=6, p>0.05] and (marginally) CS [U=19, p=0.05], while the response time of the FP AD and CS did not differ [U=40, p>0.5]. With regard to the Stroop interference task, the interference score (measured as the difference in response time when subjects have to name the colored squares and to name the color of words of color) was not different in the two groups of patients [U=11, p>0.5] and that measure was different between the control subjects and P AD patients [U=2, p<0.005] and (marginally) FP AD patients [U=13, p=0.07]. The two groups of AD patients had a similar performance on the selective attention task [U=11, p>0.1] and that performance was lower than that of CS [FP AD vs CS: U=13, p<0.05; P AD vs CS: U=11, p<0.05]. The number of words generated on semantic fluency was similar in the two AD groups [U=11, p>0.1] but was inferior to that given by CS [FP AD vs CS: U=6, p<0.005; P AD vs CS U=11.5, p<0.05]. With regard to phonemic fluency, both AD groups generated a similar number of words [U=7, p>0.05]. Moreover, the fluency score of the CS was superior to that of FP AD but similar to P AD [FP AD vs CS: U=3, p<0.005; P AD vs CS: U=17, p>0.08].

**Discussion.** Taken as a whole, these results confirm the existence of executive deficits in Alzheimer’s disease. Moreover, these executive deficits were found both in the group with only posterior hypometabolism and in the group with posterior and frontal hypometabolism. These data suggest that executive dysfunction in Alzheimer disease is not related to the presence of frontal lobe impairment but rather to the existence of a disconnection process between anterior and posterior cerebral areas. More generally, these data are in agreement with the hypothesis that executive processes are not dependent only on frontal cerebral areas.
References


Table 1. Performance [mean (standard deviation)] of the control subjects (CS) and Alzheimer patients with (FP AD) and without (P AD) frontal hypometabolism.

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<th>CS</th>
<th>FP AD</th>
<th>P AD</th>
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<tr>
<td>Mattis (total score)</td>
<td>140.5 (3.90)</td>
<td>118.33 (9.83)</td>
<td>124.20 (9.52)</td>
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<tr>
<td>Semantic fluency (number of words)</td>
<td>25.33 (6.37)</td>
<td>14 (4.57)</td>
<td>17 (4.86)</td>
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<tr>
<td>Phonemic fluency (number of words)</td>
<td>21.33 (6.02)</td>
<td>8.67 (4.50)</td>
<td>15.5 (7.50)</td>
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<tr>
<td>Go / No-go (response time)</td>
<td>482.33 (74)</td>
<td>464.14 (93)</td>
<td>589.14 (126.90)</td>
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<tr>
<td>D2 (number of correct items)</td>
<td>283.25 (73.49)</td>
<td>194.33 (132.21)</td>
<td>208.6 (54.97)</td>
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<tr>
<td>Stroop (interference score)</td>
<td>0.29 (0.09)</td>
<td>0.47 (0.21)</td>
<td>0.37 (0.51)</td>
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