AGE AT ONSET AND SPECT IMAGING IN ALZHEIMER'S DISEASE

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OBJECTIVES

It has been reported that patients with pre-senile AD have faster disease progression and severer cognitive impairment than subjects with senile AD (1,2,3). Nevertheless Grady et al.(4) showed no differences between the two groups on neuropsychological measures and only a more parietal metabolic dysfunction in early onset AD. More recently Jagust et al.(5) using [99m Tc] HM-PAO/SPECT technique found a relative hypoperfusion in left frontal pre-senile but not senile AD, providing evidence for a biological difference between the two groups. The present study was aimed to ascertain whether the same conclusions can be drawn, matching the groups not only for disease duration and education, but also for cognitive impairment (Table 1).

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METHODS

SPECT IMAGING: subjects were injected with 550-750 MBq of [99m Tc] HM-PAO, with eyes and ears unoccluded. For each subject two levels were considered: BASAL GANGLIA (BG) and MID-VENTRICULAR level (V) at 4 and 5.6 cm respectively above the orbitomeatal line (OM). At each level, four regions of interest (ROI)(6.2 x 6.2 pixels) were symmetrically located on each hemisphere: inferior frontal (IF; level BG), dorso-lateral frontal (DF; level V), anterior and posterior tempo-ro-parietal (aTP ; pTP) and occipital (O). The semiquanti-tative assessment of rCBF was obtained as a ratio of activi-ty distribution in the cortical ROIs to the activity in the cerebellar ROI.

NEUROPSYCHOLOGICAL EXAMINATION: all patients underwent the following tests: MMSE (6), BBDM (7) which includes tests of verbal and visual memory, attention, verbal reasoning and orientation and tests of constructional apraxia.

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RESULTS

The main factors for the analysis of variance were group, level, ROI and hemisphere. ANOVA showed significant effects of: a)level ($F= 43.914$; $df= 1,38$; $p<.001$; b)ROI ($F= 31.341$; $df= 3,114$; $p<.001$); c)hemisphere ($F= 15.632$; $df= 1,38$; $p<.001$). Group was not significant ($F= 0.0018$; $df= 1$; $p= 0.894$). Level x ROI interaction was also significant ($F= 12.419$; $df= 3,114$; $p<.001$) and a post-hoc analysis performed on each region showed a significant difference only between the first three ROIs and the occipital ones ($F=423.5$ $df= 2.38$; $p<.001$). Same results were obtained by adding MMS as further factor. Furthermore no significant correlations emerged between MMS total score and ROI values. In addition an asymmetry index was calculated accordingly to that previously described by Jagust et al.(5). Negative values for this ratio are indicative of left hypoperfusion. Only level was significant ($F= 4.92$; $df= 1,38$; $p<.03$; mean level GB : -0.0315; mean level V: -0.0148). Pearson correlation index among severity of cognitive impairment (MMS) and asymmetry ratio did not show any significant results.
(see Fig.1,2,3 for mean rCBF values)

CONCLUSIONS

1. When severity of cognitive impairment and duration of AD were controlled, no significant differences emerged between pre-senile and senile AD subjects on physiological measures as SPECT. This finding seems to support the hypothesis that AD is a unitary process regardless of age of onset (8).

2. A relative LH hypoperfusion (especially at cortical level) was found in both groups of subjects and this could suggest several considerations:

a) LH is more vulnerable than RH to symmetrical cerebral disease (9) and this vulnerability could be related to the greater complexity of the LH

b) AD process could affect cortical neurons with specific marker and such neurons are more numerous in left hemisphere than in the right (10).

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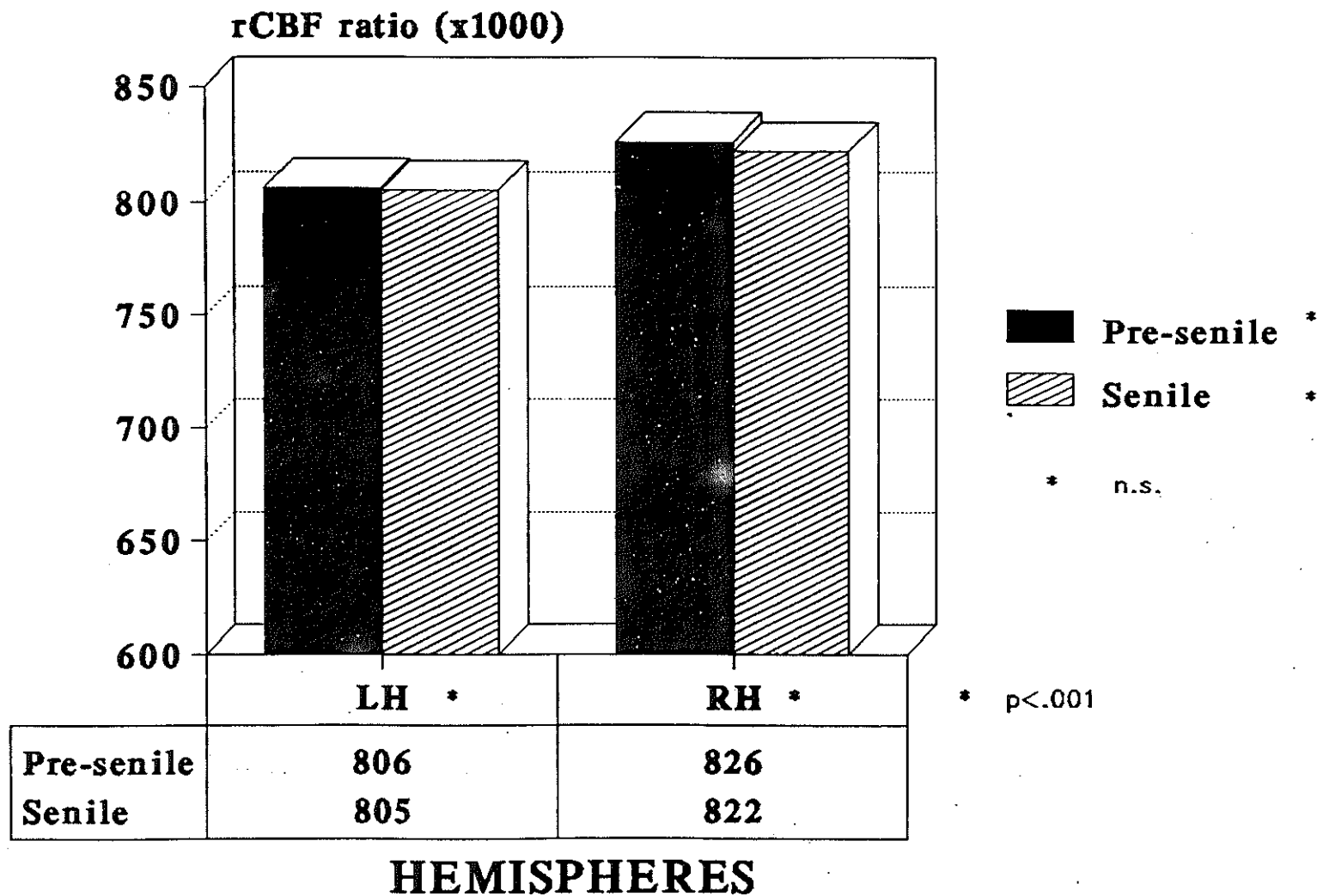10.E.Capitani et al. Cortex 1990;26;133-145.

TABLE 1
CHARACTERISTICS OF SUBJECTS

	PRESENILE AD		SENILE AD	
	Mean	SD	Mean	SD
Number	20		20	
Age*	61	6.7	72.2	3.9
Education	5.6	2.5	4.3	1.3
Disease Duration	3.3	1.5	2.3.	2.2
MMSE	18.6	6.4	17.2	4.2
Gender (M/F)	5/15		7/13	

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*(t=6.5;df=38;p<.001)

FIGURE 1

rCBF ratio (x1000)

	LH *	RH *
Pre-senile	806	826
Senile	805	822

Pre-senile *

Senile *

* n.s.

* p<.001

HEMISPHERES

FIGURE 2

rCBF Ratio (x1000)

Legend:
- ■ Pre-senile *
- ▨ Senile *

* n.s

ROI	LIF	RIF	LaTP	RaTP	LpTP	RpTP	LO	RO
Pre-senile	793	797	801	797	823	833	900	910
Senile	791	806	797	812	823	837	897	894

ROI
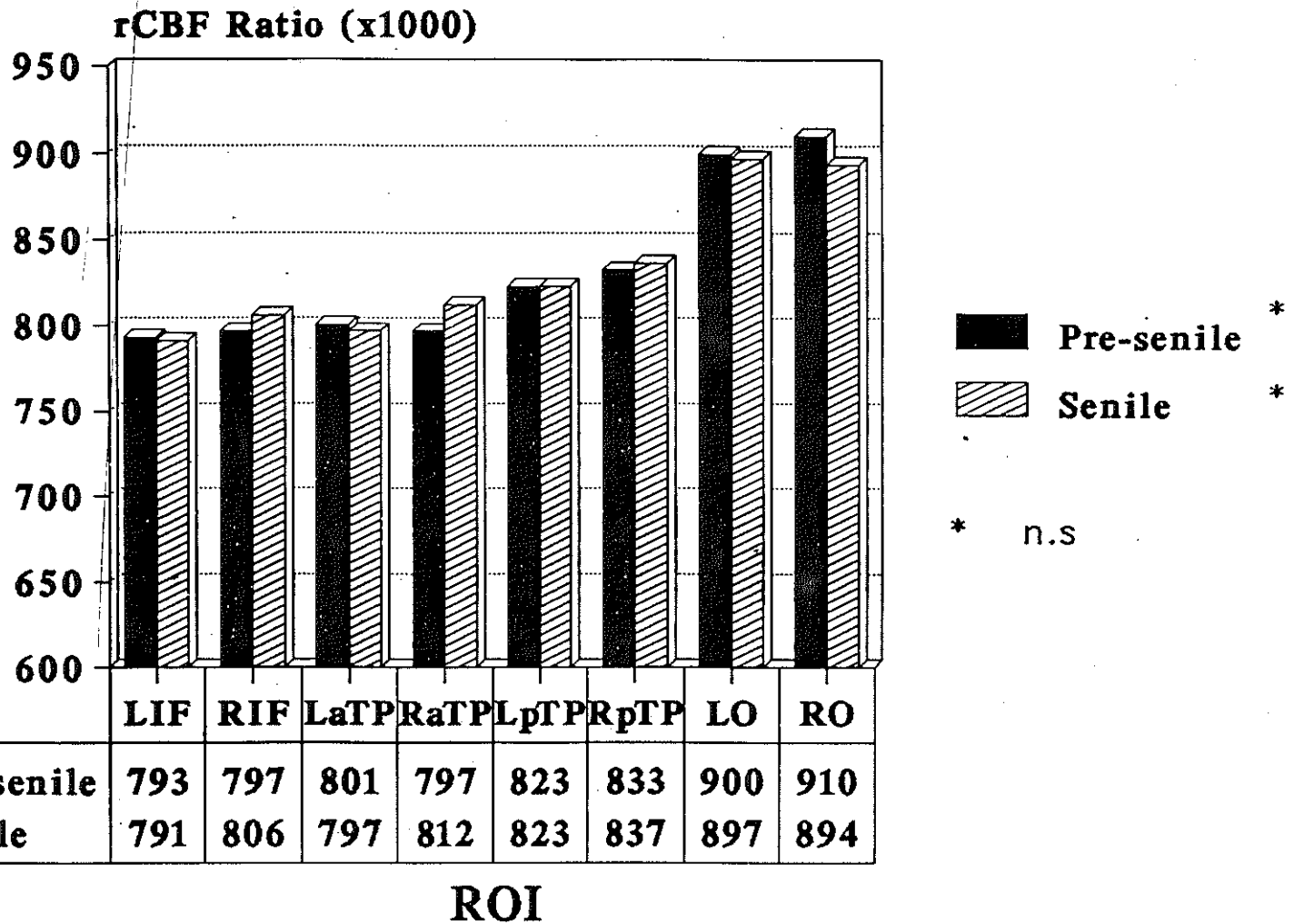
Basal Ganglia level

FIGURE 3

rCBF Ratio (x1000)

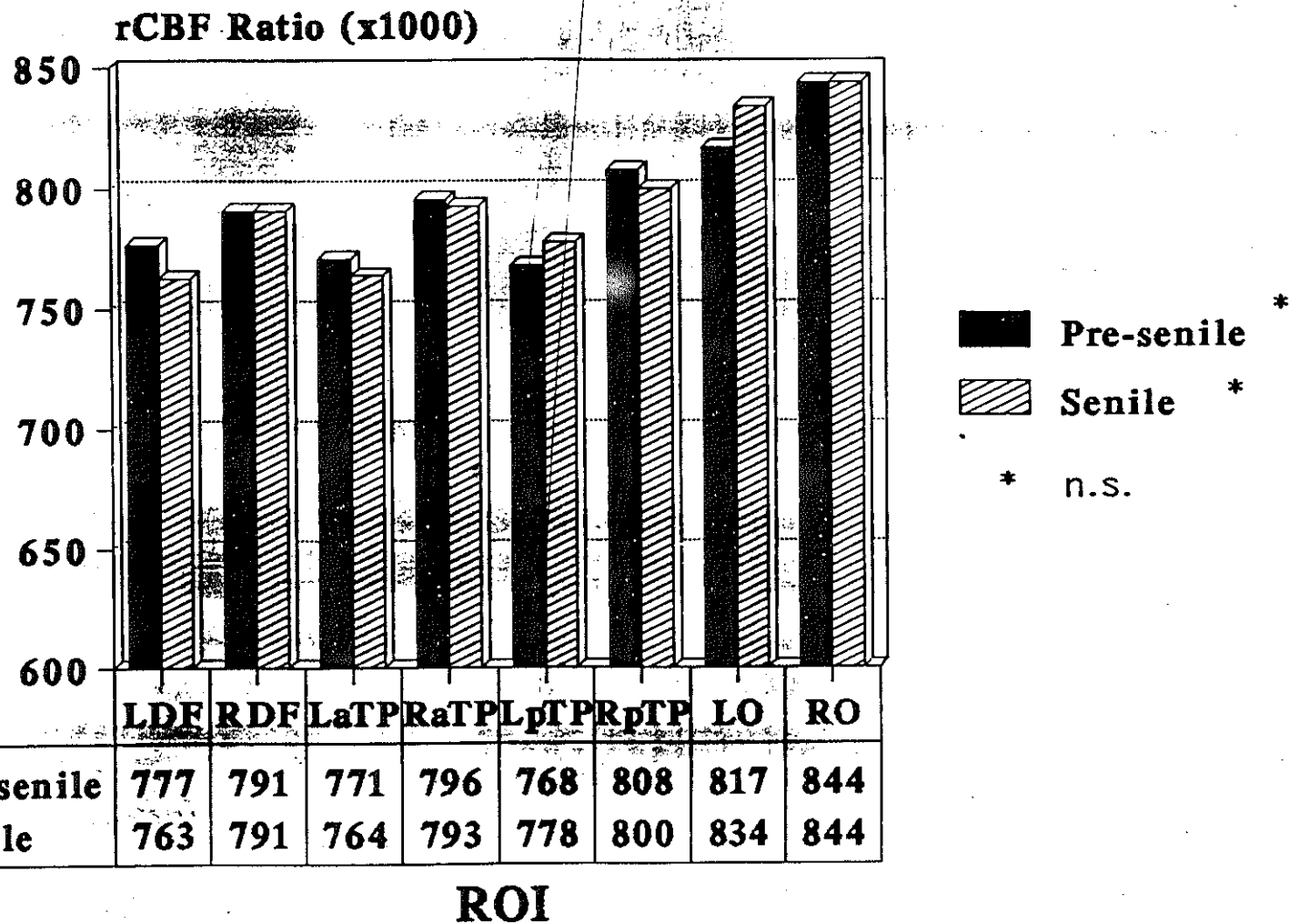| ROI	LDF	RDF	LaTP	RaTP	LpTP	RpTP	LO	RO
Pre-senile	777	791	771	796	768	808	817	844
Senile	763	791	764	793	778	800	834	844

ROI

Pre-senile *

Senile *

* n.s.

Ventricular level

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both apathic and disinhibited groups compared with controls (absolute values: 18 to 38%, normalized values: 8 to 26%). The disinhibited group had significantly lower ($p < 0.05$) normalized rCBF values than the apathic group in the lobar and in the infero-basal frontal regions but not in the superior dorsolateral frontal region.

Conclusion. Disinhibition behavior in Pick's disease seems to be related to more pronounced frontal hypoperfusion, especially in the fronto-basal region.

Age at Onset and SPECT Imaging in Alzheimer's Disease

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Objective. The aim of the present report was to ascertain whether pre-senile and senile AD, matched for educational and cognitive decline, differed in terms of cerebral perfusion, as measured with 99 mTc HM-PAO technique.

Background. One of the controversial issues in AD is progression and severity of the disease. It is however generally held to be more severe in pre-senile than in senile AD. Recently, Jagust et al (1990) found relative left frontal hypoperfusion in pre-senile compared to senile AD, matched for education and disease duration, but not for cognitive impairment.

Design/Methods. Twenty subjects with pre-senile AD (mean education 5.6 yrs; mean MMSE 18.6) and 20 senile AD pts (education 4.3 yrs; MMSE 17.2) were injected with 550-750 MBq of HM-PAO. Two levels were considered: basal ganglia (G) and mid-ventricular (V) where four ROIs were symmetrically located.

Results. MANOVA revealed significant effects of a) level ($p < 0.0001$), b) ROI ($p < 0.0001$) and c) hemisphere ($p < 0.0001$). Group was not significant. Level $\times$ ROI interaction was also significant.

Conclusion. 1) A relative left hypoperfusion was found in both groups; 2) when cognitive profile was controlled, no differences emerged between pre-senile and senile AD, supporting the hypothesis that AD is a unitary disease process regardless of age at onset.

Physostigmine and Scopolamine Effects on Glucose Metabolism Measured with Positron Emission Tomography (PET) in Human Brain

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Objective. Alzheimer's disease (AD) is associated with the degeneration of cholinergic projections from medial forebrain nuclei and a reduction in brain metabolism. To study in humans the relation between these two findings, we compared the effect of drugs that block or stimulate cholinergic function on brain energy consumption using PET and fluorodeoxyglucose.

Methods. Six patients with probable AD were studied with physostigmine (cholinergic agonist) at their maximum tolerated dose, and six age-matched normal volunteers were studied with scopolamine (cholinergic antagonist) at a dose that induces memory impairment. Each subject was studied with placebo and a cholinergic drug on different days in a blind and randomized fashion.

Results. With physostigmine, brain metabolism increased in thalamus and decreased in parietal and occipital cortex ($p < 0.01$). With scopolamine, glucose consumption increased in cerebral cortex regions and decreased in thalamus ($p < 0.001$). Regional variations in glucose metabolism with these oppositely acting drugs showed a significant ($p < 0.001$) negative correlation.

Conclusions. These results suggest that the pattern of metabolic dysfunction occurring in Alzheimer patients cannot be explained by cholinergic denervation alone and thus that alterations in other systems must be contributory.

Primary Progressive Dysarthria: Behavioral and 5-Year FDG-PET Follow-Up

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Objective. To investigate longitudinal patterns of behavioral and FDG-PET metabolic changes in a patient with primary progressive dysarthria.

Background. Primary progressive dysarthria from focal cerebral degeneration has not been previously described; it may be related to the syndrome of primary progressive aphasia.

Design/Method. Five-year follow-up with neuropsychological evaluations and FDG-PET scans in a 57-year-old RH patient with a slowly progressive dysarthria in the absence of aphasia or cognitive abnormalities.

Results. The patient had gradual onset of difficulty with reading aloud. Except for a mild dysarthria, neuropsychologic and neurologic exams were normal. MRI was normal; FDG-PET showed questionable hypometabolism in the left anterior perisylvian region. The dysarthria gradually progressed in severity, and at 5-year follow-up, his speech was nearly unintelligible. However, there was no dysnomia or aphasia, nor any decline of memory or intellect. Neurologic exam was normal, except for a recent sensory neuropathy of unknown significance. Resting FDG-PET showed definite left and possible right perisylvian hypometabolism.

Conclusions. This case appears to be an unusually focal presentation of a slow degenerative process. Its possible etiologies may be similar to those which are thought to cause the syndrome of slowly progressive aphasia.