# ALZHEIMER'S DISEASE:
## AGE AT ONSET AND SPECT IMAGING

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# INTRODUCTION

[99m Tc]HM-PAO/SPECT technique has been proposed as a routine method for the assessment of brain regional perfusion in Alzheimer's disease (AD)(1,2,3). One of the controversial issue in AD is progresion and severity of the disease. It is, however, generally held to be more rapid and severe when the clinical onset is early (pre-senile AD). Recently Jagust et al.(4) compared SPECT profile of pre-senile (PSAD) and senile AD (SAD), matched for education and disease duration, but not for cognitive impairment. They concluded that, although no asymmetry of cognitive function was noted in both groups, PSAD had relative left-frontal hypoperfusion. The aim of the present study was to ascertain whether the same conclusions can be drawn when PSAD and SAD subjects are matched for severity of cognitive decline, educational level and disease duration (Table 1).

# METHODS

SPECT IMAGING: subjects were injected with 550-750 MBq of [((mTc] HM-PAO, with eyes and ears unoccluded. For each subjects two levels were considered: basal ganglia (G) and mid-ventricular level (V) at 4 and 5.6 cm respectively above the OM line. At each level, four regions of interest (ROI)(6.2x6.2 pixels) were symmetrically located on each hemisphere:inferior frontal (IF)(level G), superior frontal (SF)(level V), anterior temporo-parietal (aTP), posterior temporo-parietal (pTP) and occipital (O). The semiquantitative assessment of rCBF was obtained as a ratio of activity distribution in the cortical ROIs to the activity in the cerebellar ROI.

NEUROPSYCHOLOGICAL ASSESSMENT: all patients underwent the following tests: MMSE (5), BBDM (6) which includes tests of verbal and visual memory, attention, verbal reasoning and orientation and tests of constructional apraxia.

# RESULTS

Tables 2-3-4 show the profiles of the groups for each hemisphere and for each level and ROI. The main factors for the analysis of variance were group, level, ROI and hemisphere.
Multivariate repeated measures analysis of variance revealed significant effects of: a)level ($F= 43.914$; $df= 1,38$; $p<.0001$); b) ROI ($F= 31.341$; $df= 3,114$; $p<.0001$); c) hemisphere ($F= 15.632$; $df= 1,38$; $p<.0001$). Group was not significant ($F= 0.018$; $df= 1$; $p= 0.894$).
Level x ROI interaction was also significant ($F= 12.419$; $df= 3,114$; $p<.0001$).
The means of level x ROI interaction for level V were: F= .78; aTP= .78; pTP= .79; O= .83 and for level G: F= .80; aTP= .81; pTP= .83; O= .90. Post-hoc analysis performed on each region showed no difference among the first three ROI ($F= 1.93$; $df= 2,38$; $p= .15$) and a significant difference between the first three ROIs and the occipital ones ($F= 423.5$; $df= 2,38$; $p<.0001$).

# CONCLUSION

1. When severity and duration of the disease were controlled no significant differences emerged between pre-senile and senile AD subjects on physiological measures as SPECT imaging. This finding raises questions about the controversial issue of the differences between the two subgroups and support the hypothesis that AD is a unitary disease process regardless of age of onset (7,8).

2. A relative LH hypoperfusion was found in both groups of AD, thus confirming previous reports (4,9). The fact that the predominant LH impairment is not specific to AD (10), might suggest several considerations:
a) LH is more vulnerable than the RH to any dysfunction and this vulnerability could be related to the greater complexity of the LH.
b) AD process affects cortical neurons with specific marker and such neurons are more numerous in the LH than in the RH (11).

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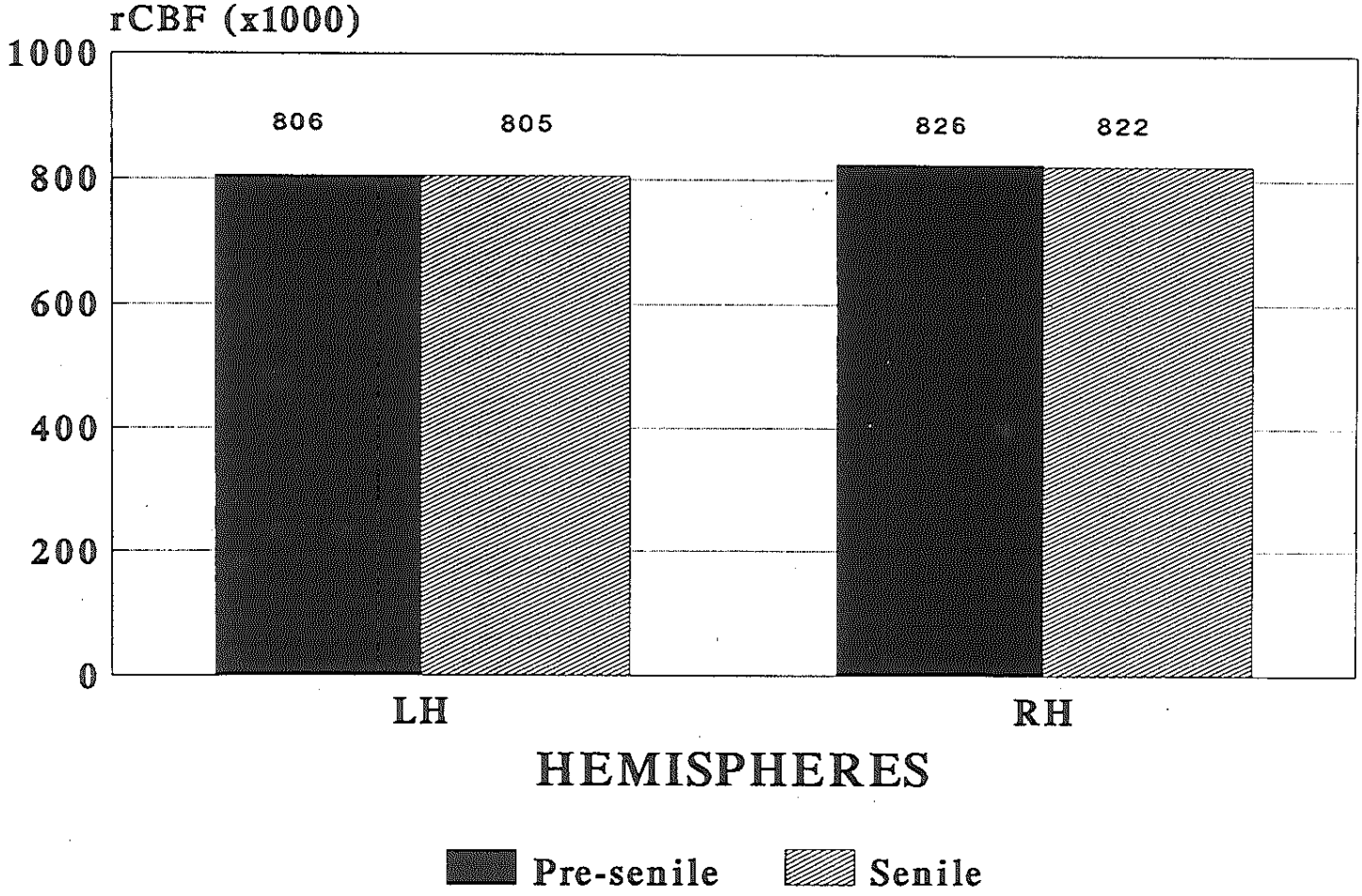
# TABLE 1

## CHARACTERISTICS OF PRESENILE AND SENILE AD

| | Presenile | Senile |
|---|---|---|
| Number | 20 | 20 |
| Age | 61 (6.68) | 72.2 (3.88) (*) |
| Education | 5.6 (2.47) | 4.3 (1.30) |
| Disease duration | 3.3 (1.53) | 2.3 (2.18) |
| MMSE | 18.6 (6.37) | 17.2 (4.21) |
| Gender (M/F) | 5/15 | 7/13 |

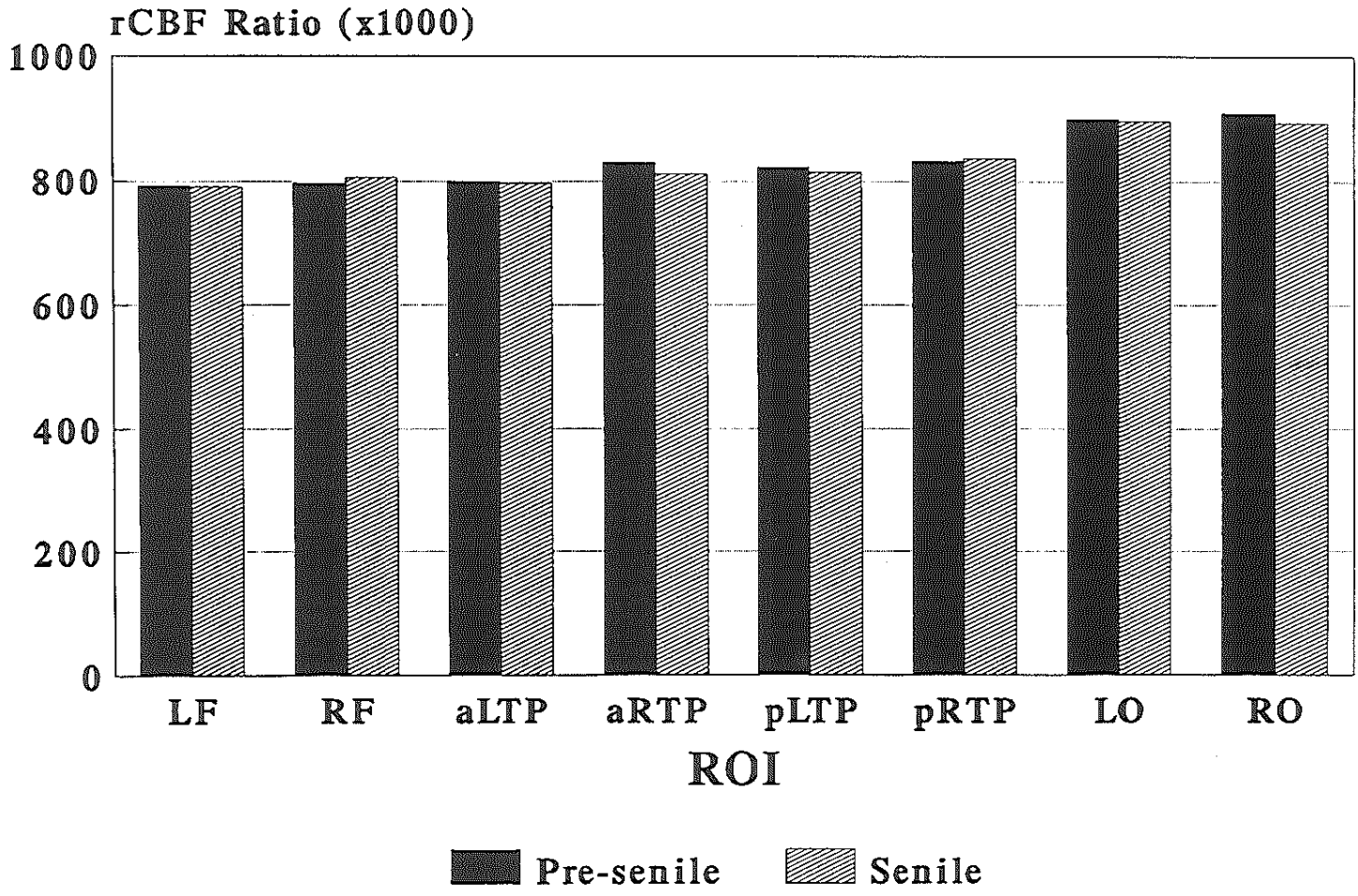
$p<.0001$

# TABLE 2



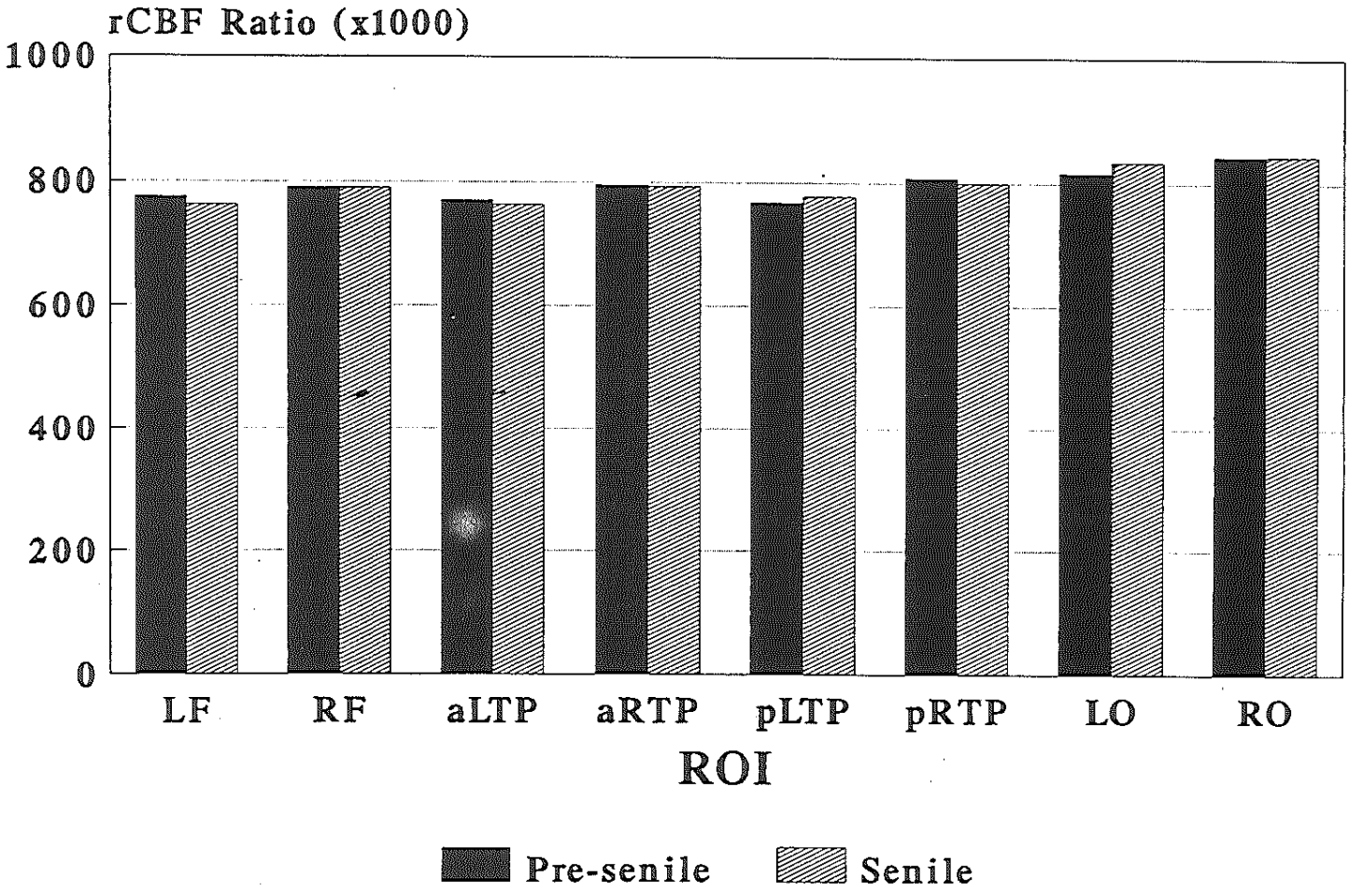

L=left; R=right

# TABLE 3

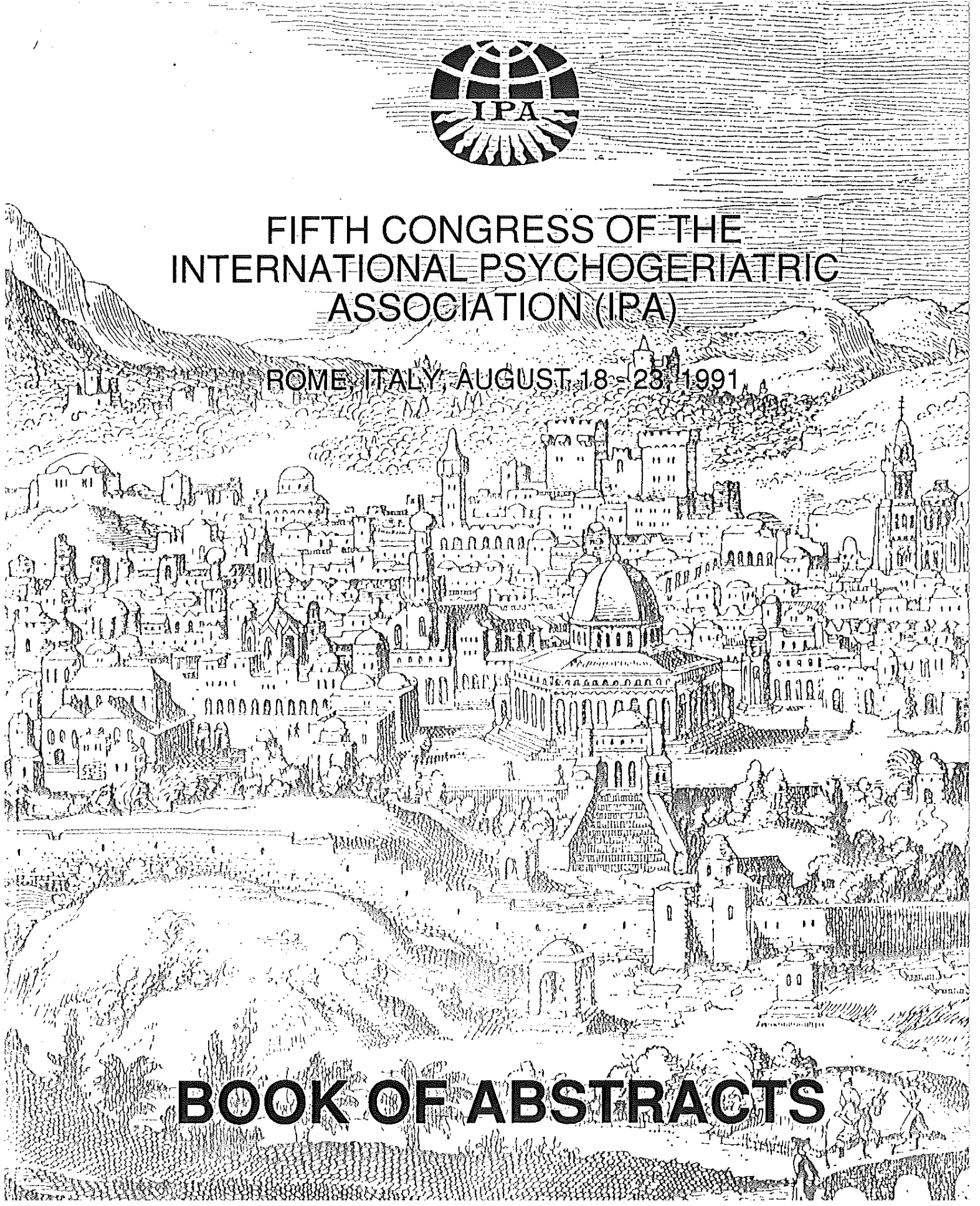



Basal ganglia level (G)L=left;R=right

# TABLE 4




Mid-ventricular level (V)L=left;R=right



# FIFTH CONGRESS OF THE INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION (IPA)

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# BOOK OF ABSTRACTS

## ALZHEIMER'S DISEASE: AGE AT ONSET AND SPECT IMAGING

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Recently Jagust et al (1990) using Single Photon Emission Tomography (SPECT) have demonstrated a greater reduction of regional blood flow in early-onset Alzheimer's Disease (AD) subjects than in late onset patients. The aim of the present report was to test the same hypotesis using 99mTc HM-PAO as tracer and a population not differing in terms of Mini Mental State (MMS). 20 pre-senile subjects (mean MMS: 17.52; SD:6.56) and 17 senile AD patients (mean MMS: 17.62; SD: 4.66) entered the study. Data acquisition were obtained from basal ganglia and mid-ventricular levels. No significant differences were observed between pre-senile and senile group on SPECT profile.

## CELL CULTURE MODELS FOR STUDYING NEUROFIBRILLARY PATHOLOGY OF ALZHEIMER'S DISEASE

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Neurofibrillary degeneration constitutes a diagnostic histopathologic criterion of Alzheimer's disease (AD). It is difficult to examine how neurofibrillary pathology of AD develops in human autopsy brains. This has thus prompted us to explore the possibility of using neuron-like cultures as models to study cellular and molecular mechanisms leading to the development of neurofibrillary degeneration in the affected neurons. We have screened 10 different culture media to study whether by these manipulations certain characteristics of neurofibrillary degeneration could be elicited in three human and one murine neuroblastoma cultures. Of the three human lines, IMR32K was the only one that accumulated epitopes associated with neurofibrillary tangles (NFT) and developed twisted fibrils reminiscent of, though not identical to, paired helical filaments (PHF) when grown in a differentiation medium (DM). Both immunocytochemical and immunoblotting analyses revealed that after incubating IMR32K cells with DM, production of the heavy subunit of neurofilament triplets, in contrast with other intermediate filament components, appeared selectively augmented in the cell body and elaborate neurites. And, immunogold analyses indicated that this elicited immunoreactivity was associated with accumulated fibrillar aggregates. Following a similar culture manipulation, murine neuroblastoma S20Y cells also developed NFT-associated immunoreactivity and fasciculated 10-nm filaments without exhibiting ultrastructural attributes of PHF. These models may provide a useful and convenient means for delineating cytoskeletal aberrations leading to the development of neurofibrillary pathology and significant insights into the pathogenesis of AD.

## WHITE MATTER ABNORMALITIES ON MRI IN "PROBABLE ALZHEIMER'S DISEASE"

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The clinical significance of white matter abnormalities on MRI still remains uncertain. In the present study, we evaluated deep white matter hyperintensity (DWHI) on T2-weighted MRI (0.5T) and clinical features in 80 patients with clinically diagnosed " probable Alzheimer's disease" ( NINCDS-ADRDA, M:F=25:55, a mean age of 70.5 years). The DWHI were graded absent through severe (F. Fazekas et al, 1987). We found 38.8% of patients had abnormal DWHI( moderate to severe). The prevalence of abnormal DWHI in patients with late-onset Alzheimer disease was higher than that in patients with early-onset Alzheimer disease (26/53, 49.0% vs 5/27, 18.5% ; $P<0.01$) In addition, abnormal DWHI were related with hypertension, age and serum triglyceride level. However, there were no significant relation between abnormal DWHI and other clinical features (MMSE, Hachiski ischemic score, etc). These results suggest that patients with "probable Alzheimer's disease " ( NINCDS-ADRDA criteria ), especially late-onset patients, have abnormal DWHI with high frequency and these abnormal DWHI are related with hypertension, high serum triglyceride level and age. DWHI may indicate arteriosclerotic change of deep white matter.

## RELATIONSHIP BETWEEN P300 AND THE LESIONS OF CHRONIC CEREBRO VASCULAR DISEASE.

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The purpose of this study is to investigate the relation between P300 and the lesions of cerebro vascular disease(CVD).
[Subjects] Sixty six cases with chronic CVD (later than one month after onset) and 8 cases of dementia of Alzheimer type(DAT).
[Methods]
EEG activity was recorded at the FZ and CZ sites. Auditory stimulation was presented with odd ball paradigm. The lesions were detected by T1 weighted images of MRI. The sectional areas of periventricular white matter lesions(PVWM) and those of corpus callosum were measured by digitizer.
[Results] There were relationship neither between total number of lesions and P300 latency, nor between laterality of lesions and P300 latency. Subjects who had more than two lesions in thalamus showed longer P300 latency than subjects who had no lesions in thalamus. But no other relation was found with the localization of lesions. Cerebral atrophy showed positive correlation with P300 latency. Sectional areas of corpus callosum showed negative correlation with P300 latency. In DAT cases, the sectional areas of PVWM showed no linear correlation with P300 latency. But, in CVD cases, diffuse PVWM group showed longer P300 latency than localized PVWM group. This result was thought to be derived from the fact that the mental state of Multi Infarct Dementia was associated with PVWM whereas that of DAT was not.
[conclusion]The P300 latency showedsignificant correlation not with total number of lesions but with cerebral atrophy and PVWM.