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# Vitamins, metals and routine bloodchemistry in normal aging

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We have examined SER functioning (a) by measuring basal and stimulated concentrations of intraplatelet free calcium ($[Ca^{2+}]_i$) in response to thrombin (1 unit/ml), using fura-2 and (b) by measuring the specific activities of calcium regulating enzymes such as, $Ca^{2+}/Mg^{2+}$-ATPase, $Mg^{2+}$-ATPase and $Ca^{2+}$-ATPase, using malachite green reagent for determination of inorganic phosphate. Our results (Table 1) show that, there was a significant increase in the percentage of $[Ca^{2+}]_i$ released above the basal levels with thrombin stimulation in AD platelets compared to controls. This was partly due to to a lower basal and a higher stimulated $[Ca^{2+}]_i$ in AD platelets compared to controls. We have also found that, the specific activities of $Ca^{2+}/Mg^{2+}$-ATPase, $Ca^{2+}$-ATPase but not $Mg^{2+}$-ATPase were significantly reduced in AD platelets compared to controls (Table 1).

These data suggest that calcium homeostasis is altered in AD platelets. This is comparable to the findings in AD fibroblasts[3] and might be important in the CNS pathophysiology of this disorder.

Table 1.

| | Basal [Ca2+]i (nM) | Stimulated [Ca2+]i (nM) | %increase | Mg2+ ATPase | Ca2+/Mg2+ ATPase (nmole/min/mgprot) | Ca2+ ATPase |
|---|---|---|---|---|---|---|
| ALZ | n=19 | n=19 | | n=24 | n=24 | n=24 |
| | 149±21 | 545±50 | 305±19** | 7.4±0.4 | 9.6±0.6* | 2.2±0.3* |
| CON | n=10 | n=10 | | n=18 | n=18 | n=18 |
| | 198±23 | 476±70 | 134±8 | 8.8±1.2 | 13.3±1.8 | 4.5±0.9 |

Values are the Means ± SEM.
*$p<0.05$, **$p<1x10^{-5}$; Significantly different from controls (unpaired t-test).

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## 343

DIFFERENT PATTERNS OF CSF MONOAMINE METABOLITES IN OLD-AGE DEMENTIAS. L. Parnetti, A. Gaiti^, *P. Mecocci, D. Cadini, M. Brunetti^, U. Senin. Chair of Gerontology and Geriatrics; ^Chair of Biochemistry, Perugia University, Ø6100 Perugia, ITALY.

Many investigations have been carried out in recent years in an attempt to clarify the ethiopathogenetic role of neurotransmitter deficiencies in dementia disorders. With regard to "ex vivo" studies on biogenic amines, which have importance in regulating cognitive and motor functions, attention has been focused on CSF levels of the key breakdown products of these neurotransmitters: homovanillic acid -HVA- for dopamine, 5-hydroxy-indoleacetic acid (5-HIAA) for serotonin and 3-methoxy-4-hydroxyphenyl-ethylglycol (MHPG) for norepinephrine, since they reflect the central monoaminergic activity. With the aim of better understanding the pathogenetic usefulness of these biological markers in dementia disorders,we have thus measured CSF levels of the main metabolites of monoamines (HMPG, 5-HIAA and HVA) in patients with early-onset Alzheimer's disease (e-AD, n. 12), late-onset AD (l-AD, n. 13), vascular dementia (VD, n. 13), simple senile dementia (SSD, n.9) and twelve elderly controls. Psychobehavioural assessment was also carried out by means of MMSE and GBS Rating Scale for Dementia. Mean HMPG levels did not differ from controls among the groups considered, while 5-HIAA was slightly lower ($Ø.1Ø>p>Ø.Ø5$) in e-AD, l-AD and VD; HVA was consistently decreased ($p<Ø.Ø2$) in e-AD and l-AD, showing a slight reduction ($Ø.1Ø>p>Ø.Ø5$) in VD. No variation was found in SSD. Negative and differently distributed correlations between neurochemical and psychobehavioural parameters were observed in l-AD, VD and SSD groups while no relationship between these variables was documented in e-AD. These results confirm that CSF levels of monoamine metabolites are of scarce diagnostic value but reinforce the evidence of the clinical heterogeneity of old-age dementias and the potential importance of these clinical-biological studies in view of differentiated therapeutical treatments.

## 344

VITAMINS, METALS AND ROUTINE BLOODCHEMISTRY IN NORMAL AGING: RESULTS FROM A MULTIPLE COHORT STUDY. *N. Bohnen, J. Jolles and C. Degenaar. Dept of Neuropsychology & Psychobiology; Limburg University; Box 616; 6200 MD Maastricht; The Netherlands.

Up till now, there is a very limited number of studies into blood parameters in normal aging: there are only few reports on a reasonably representative sample from the normal population who include young as well as old subjects. This restricts the possibilities to study pathogenetic factors with respect to blood parameters in age related diseases such as Alzheimer's disease, because reference values from healthy control subjects are needed for that purpose. The present research project aims at, first, providing objective information on age-dependent changes in blood levels of vitamins, metal ions and routine chemical parameters. The second objective was the establishment of objective norms for a comparison with AD, and depression. The study was performed on 4 cohorts of healthy subjects who had undergone a rigorous healthscreening in order to exclude biasing factors such as risc factors for brain dysfunction and dysfunctions in the realm of internal medicine. The cohorts were 20 (±3), 40 (±3), 60 (±3) and 80 (±3) with 10 males and 10 females per cohort. Venous blood samples were collected after an overnight fast between 8.00 and 9.00 am. The parameters under investigation were: vitamins, metals, hormones and routine blood biochemistry. The effects of age and sex were evaluated for each variable by ANOVA. From the 19 routine parameters (Na, K, Cl, Ca, Ca-ion, P, Fe, Mg, plasmaosmolality, total protein, albumin, triglycerids, cholesterol, BUN, creatinin, liver enzymes and alcaline phosphathase), 11 demonstrated significant abnormalities related to age and these included Ca, P, Albumin, Cholesterol, BUN, creatinin, liver enzymes and alcaline phosphase. In addition there were sex related differences in aging (for example Fe, albumin and BUN) Further results in this disease-free population are that there is no evidence of a decline of blood vitamin levels (B1, B2, B6, B12 and C) with aging. Furthermore nutrition dependant elements change in normal aging (such as zinc). The results with respect to trace-metals, neurotoxic elements and hormones will be reported at a later occasion. The findings may have an important impact in that they provide norms for a well characterised healthy aging population. In addition, this population appears characterised by age related changes in several blood parameters without change in vitamins. Age related decreases in vitamins found in earlier studies may be the result of inclusion of non-healthy individuals in the sample.

## 345

CORRELATIONS BETWEEN AND AMONG PURINES AND PURINE METABOLITES IN ALZHEIMER'S DISEASE. * P.E. Milbury[1], E.A. Ryan[1], M.F. Beal[2], W.R. Matson[1], [1]ESA, Inc., Bedford, MA 01730 USA and [2]Massachusetts General Hospital, Dept. of Neurology, Boston, MA 02114 USA.

Through the utilization of large, multiparameter data bases containing sufficiently reliable information, data which may seem chaotic can be used in the definition of normal metabolism and the altered state metabolism associated with specific disorders. Studies of patients with neuropsychiatric disorders suggest that dietary levels of tryptophan and tyrosine profoundly affect the levels of various neurotransmitters. Deficiencies in purine metabolism have been linked to neurochemical lesion in Parkinson's Disease, while variations in purine metabolites have been implicated in Alzheimer type dementias.

A multiparameter data base has been created utilizing a Coulochem® Electrode Array System. Approximately 1000 Alzheimer, Huntington, Parkinson, control tissue and CSF samples comprise this data base. We have analyzed these data for potential metabolic interactions between the purine, tyrosine and tryptophan pathways. A strong correlation has been observed between levels of tyrosine and xanthine. Tyrosine/xanthine ratios were found to be significantly decreased in the putamen and A4 of the Parkinson samples. Guanosine levels in putamen, A20, A21, A9, and A4 in Alzheimer samples were decreased approximately 50 percent of control values. Alterations in the metabolism of purines were associated with changes in the tyrosine/tryptophan pathways. These data suggest a relationship between purine and aromatic amino acid metabolism in certain central disease disorders.

## 346

THE EEG SPECTRA OF ALZHEIMER'S DISEASE. *D. Giannitrapani, J. Collins and D. Vassiliadis. Department of Veterans Affairs Medical Center, Perry Point, MD. 21902 USA.