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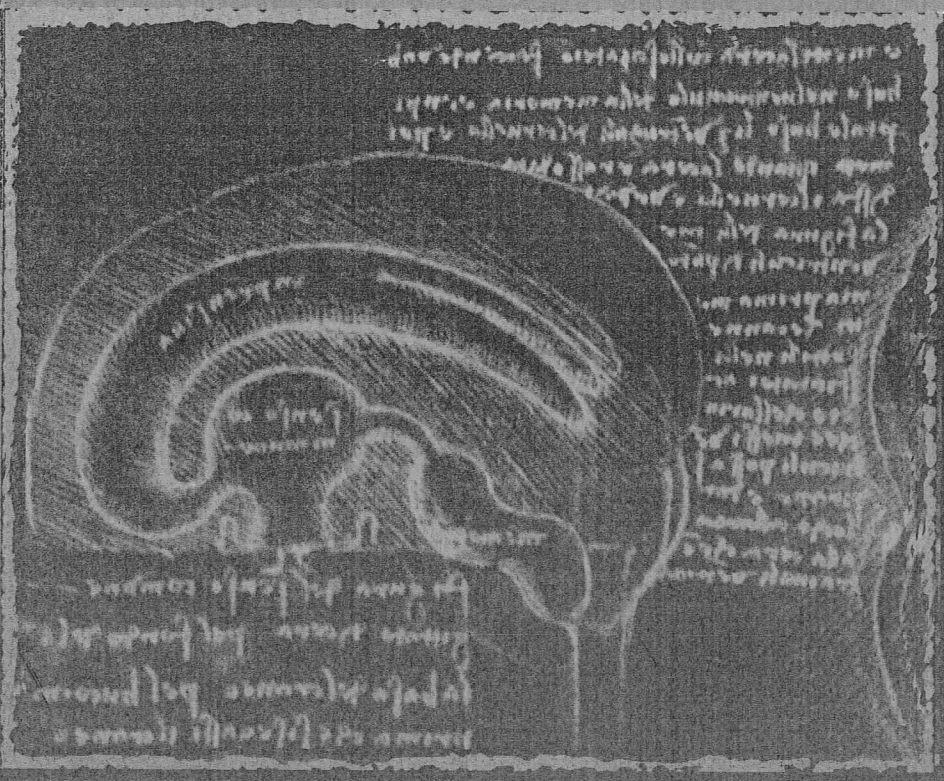

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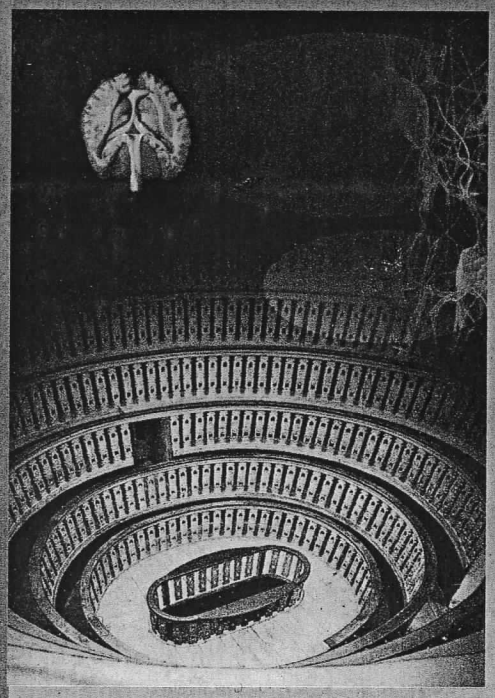

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ABSTRACTS

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SERUM LEVELS OF MONOCYTE CHEMOATTRACTANT PROTEIN-1 IN AMYOTROPHIC LATERAL SCLEROSIS PATIENTS

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Background: Immunological derangements have been implicated in the pathogenesis and pathophysiology of amyotrophic lateral sclerosis (ALS). Monocyte chemoattractant protein-1 (MCP-1) is involved in the recruitment of inflammatory cells of monocytic lineage after inflammation or injury in the central nervous system. Significantly increased cerebrospinal fluid MCP-1 levels have been found in patients with ALS compared to control subjects; [1,2] on the other hand, studies on ALS sera have produced conflicting results (1, 2). MCP-1 chemokine receptor CCR2 has been reported as decreased on circulating monocytes from ALS patients [3].

Objectives: The aim of our study was to assay MCP-1 concentrations in sera from ALS patients overtime.

Subjects and Methods: Twenty-seven ALS patients (15 men and 12 women; mean age ± SD: 66±12 years) were studied. Disease severity was scored by means of the ALS Functional Rating Scale, and patients subgrouped accordingly into 3 classes: I (scoring between 40 and 31); II (from 30 to 11); and III (between 10 and 0). Blood samples were drawn in the morning, and sera were stored immediately at -20°C. MCP-1 concentrations were measured, repeatedly over a two-year period, by an enzyme-linked immunosorbent assay (R&D Systems). MCP-1 data refer to assays at time of diagnosis (T0) and those at time of the most recent clinical examination (Tn).

Results: Mean MCP-1 levels were higher, in both class II and class III patients, at Tn vs T0. Moreover, ALS patients shifting from class II to class III, namely worsening overtime, showed significantly ($p< 0.01$) increased mean MCP-1 values at Tn vs T0 (475±212 vs 339±175 pg/mL).

Discussion and Conclusions: Our data someway parallel those reported in the scientific literature, by showing clearly enhanced serum MCP-1 levels overtime, along disease progression. Such findings might be related to an increased systemic inflammatory response, mirrored by a progressive increase in pro-inflammatory/anti-inflammatory cytokine level ratios, as already reported in some studies.

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A CONTROLLED HYPOPROTEIC DIET IN SPORADIC ALS PATIENTS

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Aims: To low glutamate and BCAA in the plasma and especially in the brain in the attempt to obtain an amino acid plasma profile in our patients similar to that of non affected familiar case bearing L84F SOD1 mutation (previous study) with an innovative low protein low BCAA diet supplemented with a pharmacologic dose of thiamine that could provide an innovative approach to a nutritional management of ALS patients. The main target of the study was to assess amino acid plasma levels modifications with the diet.

Materials and Methods: We tested 10 ALS patients treated with a low BCAAs concentration (<85 mg/Kg/die) and low protein (0.7 g/protein/Kg/die) diet, that provides a physiological energy content. To enhance alpha-ketoglutarate clearance from Krebs cycle, patients were also provided with 300 mg/die thiamin. The main target of the study was to assess amino acid plasma levels modifications with the diet. Disease course assessment was done with ALSFRS-r applied in every patient every two months.

Results: Three patients decided to exit the study before completion. All the patients presented a similar disease course with an important decreasing of ALSFRS-r in time. Amino acid plasma levels revealed a trend to glutamate increase in all patients and BCAA steady-state level. Moreover, alanine levels appeared increased in all patients. The clinical disease course revealed a faster disease progression in the patients during diet implementation.

Discussion: The protein modification in our diet did not obtain the expected plasma aminoacid profile modification. Glutamine, a possible source of glutamate in different biochemical pathways, released by the liver was observed 73% higher in rats fed with low-protein diet. It is possible that, with a low protein diet hepatic glutamine delivery may be increased to fulfil substrate needs for amino acid metabolism in various organs even for N-salvage in the brain. During the post absorptive period, adaptation to high-protein diets resulted in a sustained catabolism of most glucogenic amino acids (glutamine and glutamate are glucegenic), which accentuated the drop in their concentrations.

Conclusion: These observations taken together could partially explain the results on the a concentrations and the worsening of clinical conditions observed in this preliminary study. The protein modification in our diet did not obtain the expected plasma amino acid profile modification.

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PERIPHERAL OXIDATIVE STRESS BIOMARKERS IN SPORADIC AMYOTROPHIC LATERAL SCLEROSIS

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Background: Among a pathogenic hypotheses on motor neuron degeneration leading to amyotrophic lateral sclerosis (ALS), the reactive oxygen species generation and oxidative stress theory has been put forward. Evidences of accumulation of oxidative damage to proteins,