ASSOCIATION BETWEEN SERUM URIC ACID LEVELS AND DIFFERENT TAUOPATHIES

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INTRODUCTION

Tauopathies (TAU) are a group of different clinical-pathological neurodegenerative entities characterized by the accumulation of abnormal forms of tau protein. They are currently believed to have a multifactorial pathogenesis but few risk factors have been still identified[1].

Uric Acid (UA) is one of the most prevalent circulating antioxidants and oxidative stress is well known to be deeply involved in the pathogenesis of neurodegenerative diseases. In fact, low serum UA concentrations have been demonstrated to be a significant risk factor for Parkinson's Disease (PD)[2]. Contrariwise, poor and ambiguous data are still available for patients with Tauopathies[3].

SUBJECTS AND METHODS

We retrospectively analysed data from 111 **patients** diagnosed with TAU, 41 with **Progressive Sopranuclear Palsy** (PSP), 45 with **Alzheimer's Disease** (AD) and 25 with **Fronto-Temporal Dementia** (FTD), and a **control group (CTL)** of 130 subjects with non-neurodegenerative conditions (radiculopathies, secondary depression, minor neurological diseases).

Serum UA concentrations were evaluated by indirect uricase UV method, using the dimension Vista System (Siemens) and a bicromatic (293, 700 nm) endpoint technique.

Differences in categorical and continuous variables were respectively calculated with the **chi-square** test and the one-way **ANOVA test** with Bonferroni correction.

The **Odd Ratio** (OR) of serum UA, adjusted for age and gender, was calculated in comparison to CTL for TAU and for PSP, AD and FTD subgroups. A **cut-off value** of serum UA was finally obtained to predict subjects at risk for TAU.

Table 1: Study population

	CTL (n=130)	TAU (n=111)	PSP (n=41)	AD (n=45)	FTD (n=25)	
Age (y)	71.1 ± 11.6	70.2 ± 6.7	70.1 ± 5.9	71.3 ± 6.3	67.0 ± 8.0	n. s.
Sex (M/F)	71/59	53/58	24/17	21/23	11/14	n. s.
Disease Duration (y)	---	2.7 ± 2	2.9 ± 1.7	2.3 ± 1.4	3.1 ± 2.9	n. s.
MMSE	---	22.9 ± 3.9	24.3 ± 3	21.8 ± 4.3	22.7 ± 4.1	n. s.
Serum UA (mg/dl)	4.8 ±1.4	4.14 ± 0.9	4.2 ± 0.9	4.18 ± 0.9	4.02 ± 1.1	***p<0.001***

RESULTS

Groups did **not show differences in gender, age, disease duration** and **MMSE score** distribution *(Table 1)*.

Serum UA concentration was significantly **higher** in CTL (4.8 ± 1.4mg/dl) with respect to TAU (4.15 ± 0.9 mg/dl, *p<0.001*) *(Fig.1)* and also to PSP (4.2 ± 0.9 mg/dl), AD (4.18 ± 0.9 mg/dl) and FTD (4.02 ± 1.1 mg/dl) considered separately (p<0.05) *(Fig.2)*.

Serum UA concentration was significantly **inversely associated** with TAU (OR = 0.61; p<0.001) and all different tauopathies, PSP (OR = 0.53; p<0.05), AD (OR = 0.52; p<0.05) and FTD (OR = 0.37; p<0.01).

The **cut-off value** has been set at 4.35 (AUC = 0.655) to discriminate TAU from CTL, although with poor specificity (57,1%) and sensitivity (62,1%) *(Fig. 3)*.

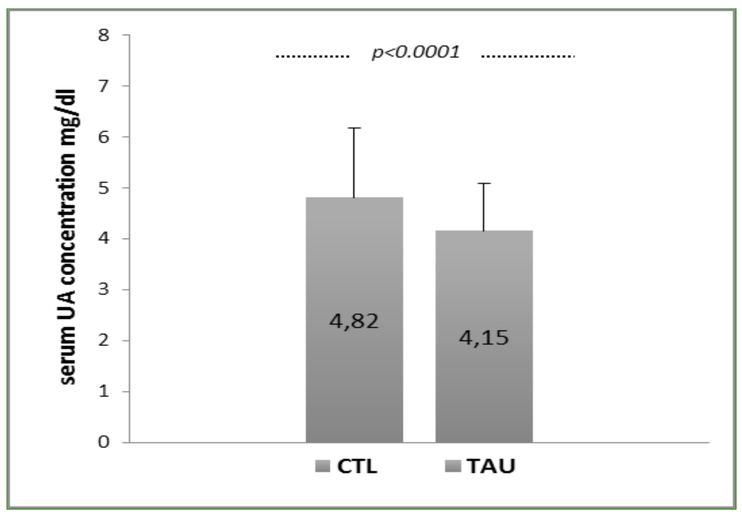

Fig. 1. Serum UA concentrations in CTL vs TAU

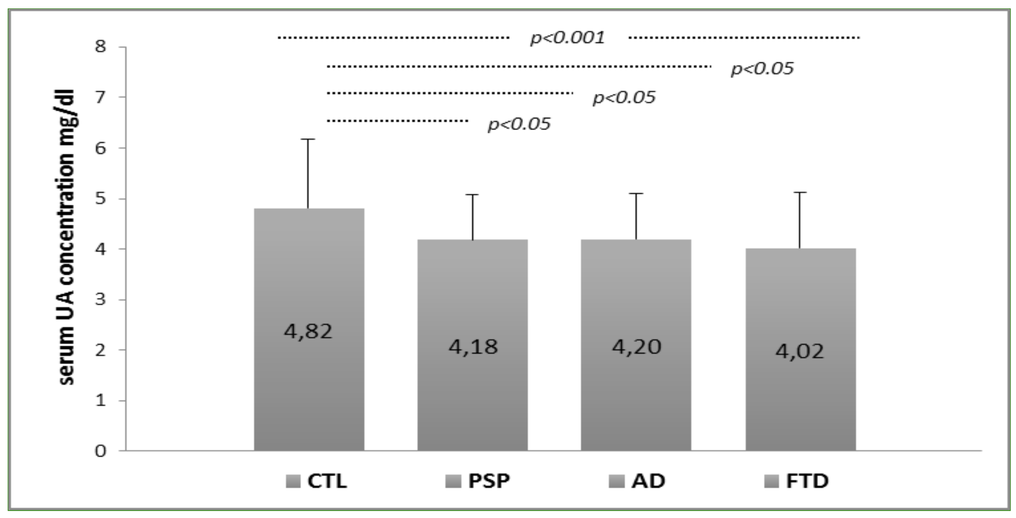

Fig.2: Serum UA concentrations in CTL and distinct tauopathies

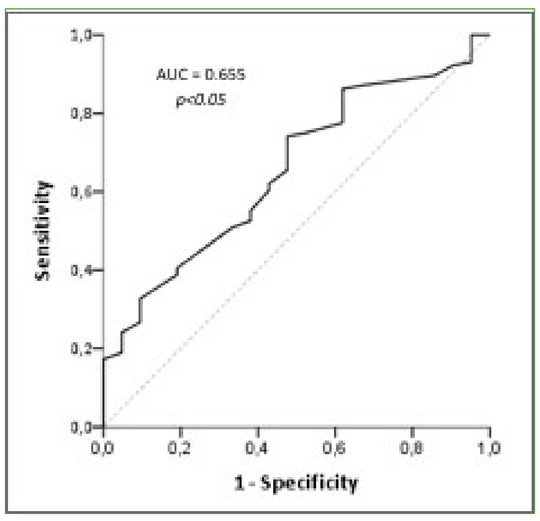

Fig.3: ROC curve analysis for serum UA in TAU vs CTL

DISCUSSION

In this study we found that patients with different tauopathies (PSP, AD and FTD) presented **reduced serum UA concentrations** with respect to controls. In addition, our findings clearly show an inverse correlation between serum UA concentrations and the risk of developing tauopathies, irrespectively of the diagnosis; indeed, along the increasing of **serum UA concentration, the risk** (OR) of PSP, AD or FTD **decreased**.

According with urate antioxidant properties, our data suggest that **low levels of serum UA** represent an **independent risk factor** for three different tauopathies (PSP, AD and FTD). The identified cut-off value might represent a valid tool to identify a **population at risk** which could benefit of novel therapies targeting UA or preventing strategies.

References:

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