Beta-amyloid and phosphorylated tau metabolism changes in narcolepsy over time.

Claudio Liguori, Placidi F, Izzi F, Nuccetelli M, Bernardini S, Marciani MG, Cum F, Marciani MG, Mercuri NB and Romigi A

Centro di Medicina del Sonno, Unità di Neurofisiopatologia, Dipartimento di Medicina dei Sistemi, Università degli studi di Roma "Tor Vergata"

XLVI CONGRESSO SOCIETÀ ITALIANA DI NEUROLOGIA

OBJECTIVE

We evaluated CSF biomarkers involved in inflammatory and neurodegenerative processes (beta-amyloid and tau proteins) in a population of narcoleptic drug-naïve patients ranging from early to late phases of the disease in order to determine whether the expression of these biomarkers changes in narcolepsy over time.

METHODS

We analyzed a population of narcoleptic drug-naïve patients compared to a sample of healthy controls. Patients and controls underwent lumbar puncture for CSF beta-amyloid$_{42}$ ($A\beta_{42}$), total tau (t-tau) and phosphorylated-tau (p-tau) levels assessment. Moreover, based on the estimated median disease duration of the whole group, narcoleptic patients were divided in two subgroups: patients with a short disease duration (SdN, <5 years) and patients with a long disease duration (LdN, >5 years).

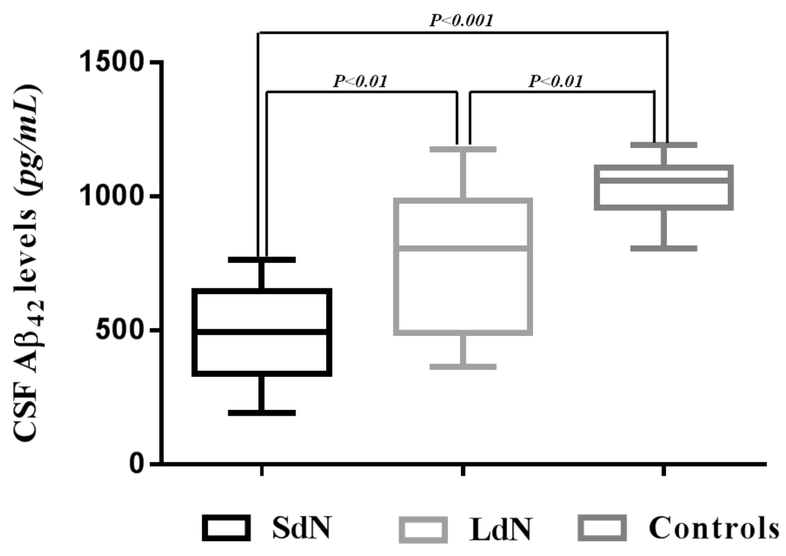
RESULTS

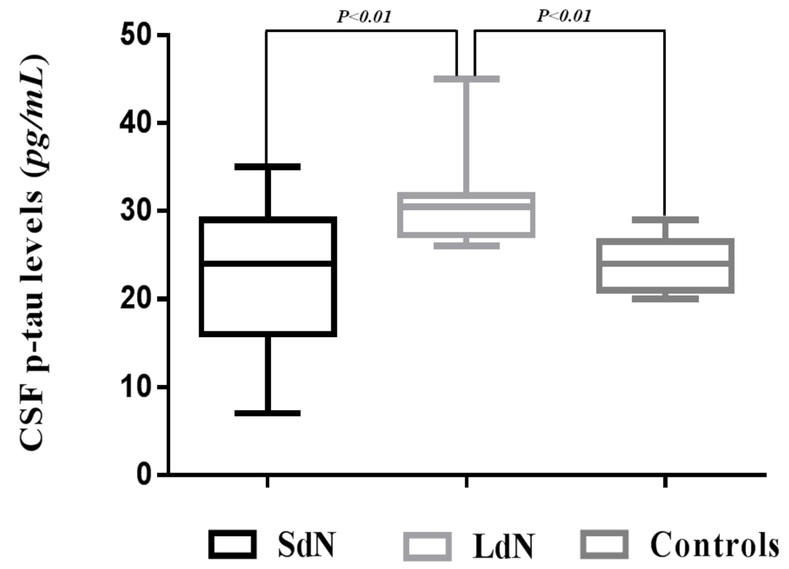
We found significant lower CSF $A\beta_{42}$ levels in the whole narcolepsy group with respect to controls. Taking into account the patients subgroups, we documented reduced CSF $A\beta_{42}$ levels in SdN compared to both LdN and controls. Even LdN patients showed lower CSF $A\beta_{42}$ levels with respect to controls. Moreover, we documented higher CSF p-tau levels in LdN patients compared to both SdN and controls. Finally, a significant positive correlation between CSF $A\beta_{42}$ levels and disease duration was evident.

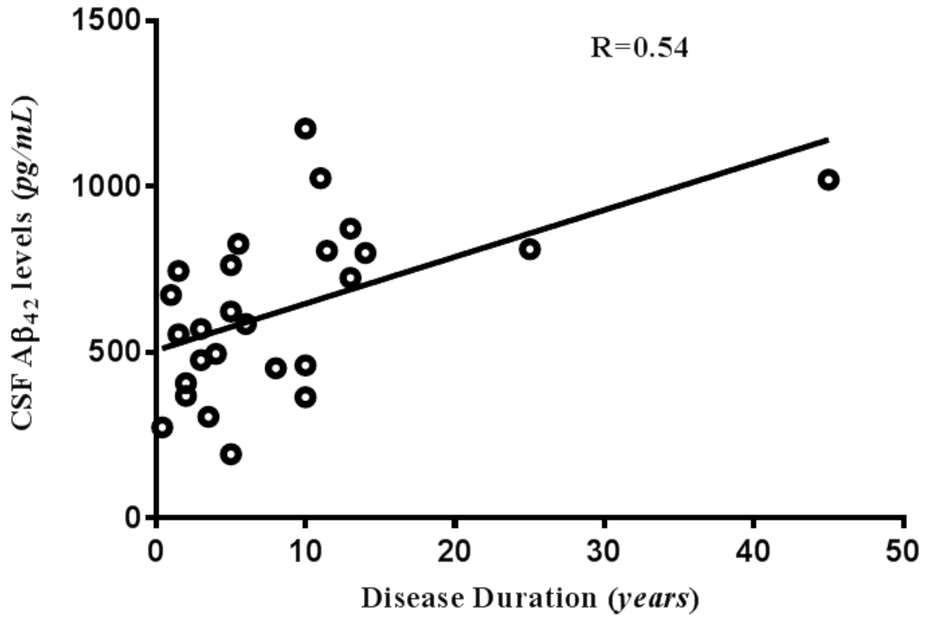
Demographic Data	Narcoleptic patients (n = 26) (mean value ± SD)	Controls (n = 17) (mean value ± SD)	P value
Age	33.72 ± 11.58	33.29 ± 8.39	NS
Sex	14M 12F	10M 7F	NS
Disease Duration (years)	8.29 ± 9.46	NA	NA
Cataplexy (%positive)	46%	NA	NA
Sleep Paralysis (%positive)	77%	NA	NA
Hypnagogic Hallucinations (%positive)	69%	NA	NA
MSLT Data	**Narcoleptic patients (n = 26)**	**Controls (n = 17)**	**P value**
Sleep Latency	3.99 ± 1.81	NA	NA
SOREMp	3.58 ± 1.06	NA	NA
CSF Data (expressed in pg/ml)	**Narcoleptic patients (n = 26)** (mean value ± SD)	**Controls (n = 17)** (mean value ± SD)	**P value**
Orexin A	79.12 ± 36.73	186.42 ± 22.29	***<0.001***
T-Tau	172.2 ± 69.68	212.41 ± 62.08	NS
P-Tau	28.52 ± 11.28	23.88 ± 2.95	NS
$A\beta_{42}$	623.24 ± 252.63	1039 ± 105.05	***<0.001***

Demographic Data	SdN (n = 13) (mean value ± SD)	LdN (n = 13) (mean value ± SD)	P value
Age	29.15 ± 10.24	38.67 ± 11.28	NS
Sex	8M 5F	6M 7F	NS
Disease Duration (years)	2.84 ± 1.58	14.21 ± 10.92	***<0.001***
Cataplexy (%positive)	53%	38%	NS
Sleep Paralysis (%positive)	84%	69%	NS
Hypnagogic Hallucinations (%positive)	77%	61%	NS
MSLT Data	**SdN (n = 13)** (mean value ± SD)	**LdN (n = 13)** (mean value ± SD)	**P value**
Sleep Latency	3.93 ± 1.85	4.06 ± 1.84	NS
SOREMp	3.77 ± 1.01	3.38 ± 1.12	NS
CSF Data (expressed in pg/ml)	**SdN (n = 13)** (mean value ± SD)	**LdN (n = 13)** (mean value ± SD)	**P value**
Orexin A	64.69 ± 36.88	92.19 ± 33.84	NS
T-Tau	168.84 ± 76.03	175.83 ± 65.28	NS
P-Tau	22.69 ± 8.58	30.67 ± 5.09	***<0.01***
$A\beta_{42}$	496.54 ± 180.91	760.5 ± 253.02	***<0.001***

Demographic Data	N1 (n = 12) (mean value ± SD)	N2 (n = 14) (mean value ± SD)	P value
Age	27.45 ± 9.47	38.64 ± 10.93	NS
Sex	7M 5F	7M 7F	NS
Disease Duration (years)	4.63 ± 4.37	11.18 ± 11.41	***<0.001***
Disease Duration (years)	8.29 ± 9.46	NA	NA
Cataplexy (%positive)	100%	0%	***<0.0001***
Sleep Paralysis (%positive)	92%	64%	NS
ypnagogic Hallucinations (%positive)	75%	64%	NS
MSLT Data	**N1 (n = 12)** (mean value ± SD)	**N2 (n = 14)** (mean value ± SD)	**P value**
Sleep Latency	3.91 ± 1.89	4.06 ± 1.82	NS
SOREMp	3.75 ± 1.05	3.43 ± 1.09	NS
CSF Data (expressed in pg/ml)	**N1 (n = 12)** (mean value ± SD)	**N2 (n = 14)** (mean value ± SD)	**P value**
Orexin A	45.53 ± 13.11	105.53 ± 25.56	***<0.001***
T-Tau	177 ± 58.79	168.43 ± 79.19	NS
P-Tau	25.64 ± 7.66	30.78 ± 13.31	NS
$A\beta_{42}$	574.82 ± 195.06	661.28 ± 291.57	NS







CONCLUSIONS

We hypothesize that beta-amyloid metabolism and cascade may be impaired in narcolepsy not only at the onset, but also along with the disease course, although they show a compensatory profile over time. Concurrently, also CSF biomarkers of neuron morphology and structure impairment (p–tau) appear to be altered in narcolepsy patients featured by a long disease duration. However, the mechanism underlying beta-amyloid and tau metabolisms impairment during narcolepsy remains still unclear and deserves to be better elucidated.