Tau pathology, CSF lactate levels and cerebral glucose hypometabolism are associated in Alzheimer's Disease: evidence from BA10 analysis.

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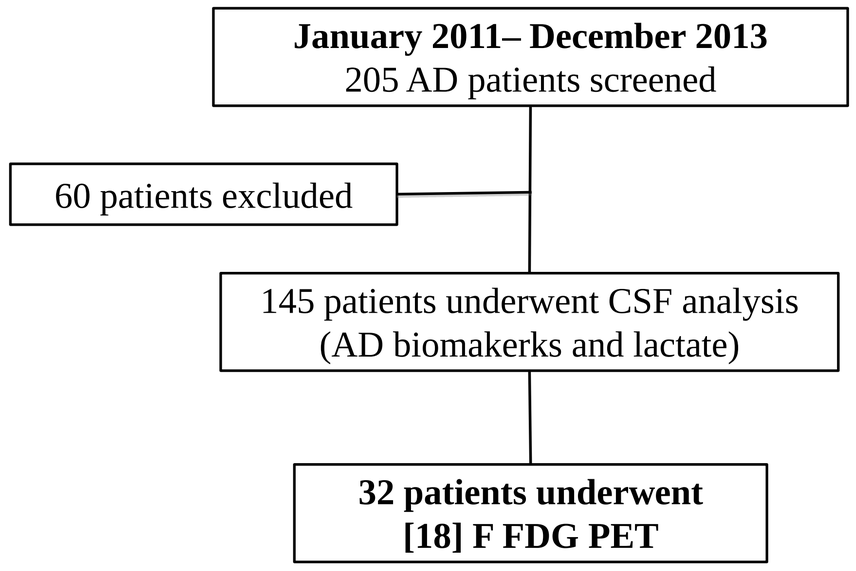
OBJECTIVE

Neurofibrillary tau pathology is one of the main hallmarks of Alzheimer's Disease (AD) neurodegeneration. Recent evidence suggests a possible causal role of tau pathology on cerebral glucose metabolism impairment and CSF lactate levels in AD (Kulic et al, NBA, 2011; Liguori C et al, JNNP, 2015).
On these basis, the aim of the present study is to investigate in AD patients possible interplays linking alteration of neuronal energy metabolism, measured via both CSF lactate concentrations and [18F]FDG PET assessments, to CSF total tau (t-tau) proteins levels.

METHODS

We measured CSF t-tau and lactate levels and performed [18F]FDG PET analysis in a population of AD patients. We compared AD patients to two populations of non-demented controls, the first who performed [18F]FDG PET evaluation (controls-1), and the second who underwent CSF biomarkers analysis (controls-2). Finally, we correlated CSF t-tau proteins levels to CSF lactate concentrations and cerebral glucose metabolism in the AD group.

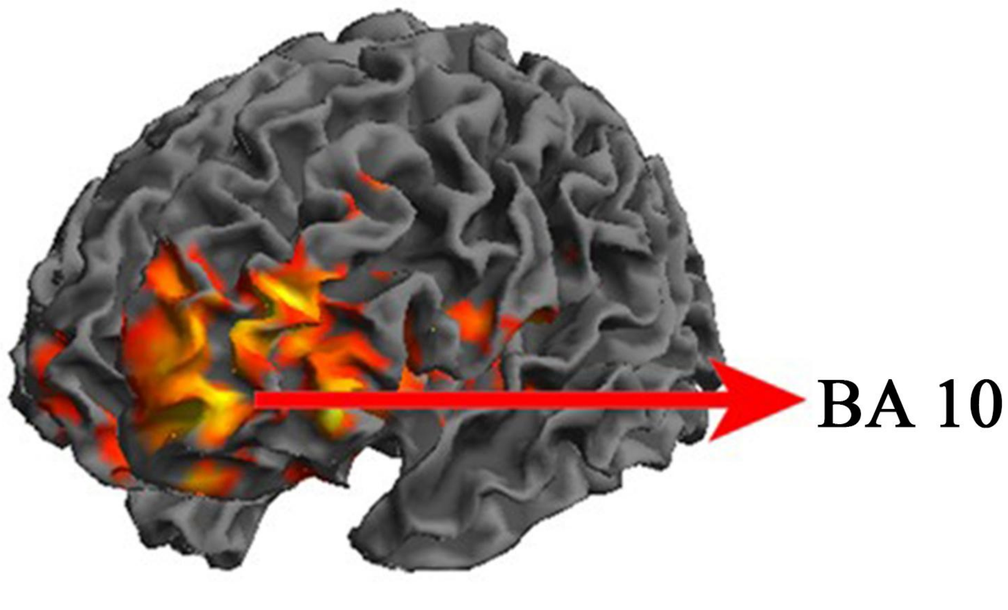


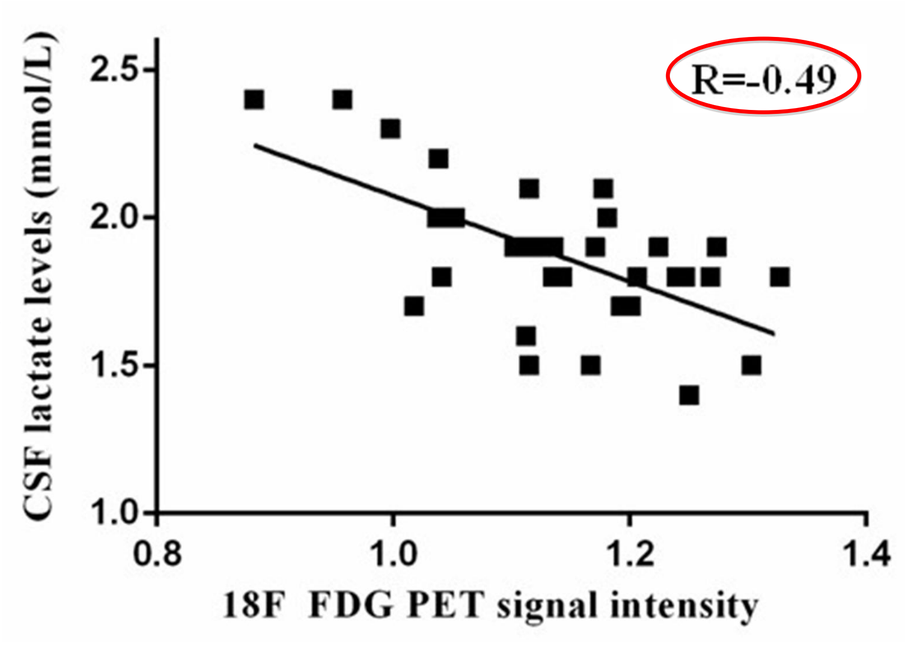
RESULTS

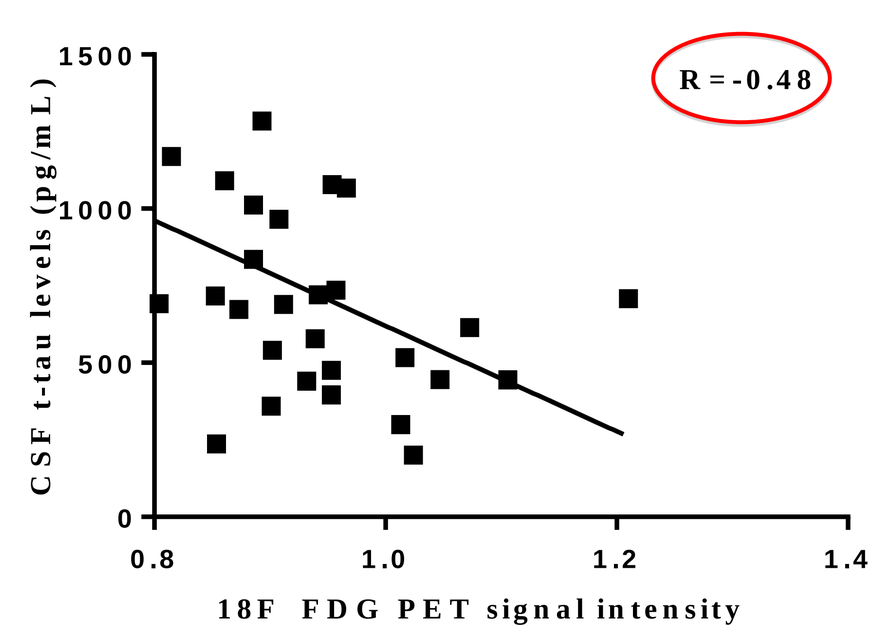
	AD patients (n=32) (mean±SD)
Age *(years)*	69.9±7.46
Sex	16F 16M
Disease Duration *(years)*	2.73±1.77
MMSE	18.81±5.72
Lactate *(mmol/L)*	**1.87±0.24**
T-tau *(pg/mL)*	**738.62±358.95**
P-tau *(pg/mL)*	96.37±47.98
Aβ$_{42}$ *(pg/mL)*	308.19±121.44

Analysis	Cluster level					Voxel level		
Negative correlation	cluster p(FWE-corr)	cluster p(FDR-corr)	Cluster extent	Cortical Region	Z score of maximum	Talairach coordinates	Cortical region	BA
	0.000	0.000	22045	L Frontal	3.49	-34,40,14	Middle Frontal Gyrus	10
				L Frontal	3.41	-4,32,-12	Medial frontal gyrus	11
				L Limbic	3.37	-28,-28,-20	Parahippocampal gyrus	35
Positive correlation	-	-	-	-	-	-	-	-

Analysis	Cluster level					Voxel level		
Negative correlation	cluster p(FWE-corr)	cluster p(FDR-corr)	Cluster extent	Cortical Region	Z score of maximum	Talairach coordinates	Cortical region	BA
	0.001	0.000	4960	R Temporal	4.66	50,10,-24	Superior temporal gyrus	38
				R Temporal	4.61	44,12,-32	Superior temporal gyrus	38
				L Frontal	3.42	40,14,-14	Inferior frontal gyrus	47
	0.001	0.000	5119	R Limbic	3.54	4, 42, 2	Anterior cingulate	32
				R limbic	3.49	16, 44, 4	Anterior cingulate	10
				L frontal	3.49	-34, 40, 14	Middle Frontal Gyrus	10







CONCLUSIONS

We verified the occurrence of high CSF t-tau and lactate levels in AD patients compared to controls. Significantly, CSF t-tau and lactate concentrations are not only linked in a mutual interplay, but also correlated to cerebral glucose hypometabolism. Significantly, CSF t-tau and lactate levels correlated with hypometabolism in BA10, which represents a key area in AD neurodegeneration.
We hypothesize that in AD neurodegeneration tau pathology may exert a detrimental effect on the neuronal energy metabolism, which could be evaluated by means of both CSF lactate levels and [18F]FDG PET assessments. This effect is more evident in BA10, a brain area significantly affected by AD pathology.