CSF lactate levels and brain 18F FDG-PET hypometabolism within the Default Mode Network in Alzheimer's Disease.

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OBJECTIVE

It has been increasingly suggested that neuronal energy metabolism may be involved in Alzheimer's Disease (AD) pathology. In this view, the finding of increased cerebrospinal-fluid (CSF) lactate levels in AD patients has been considered as result of the mitochondrial dysfunction occurring in these patients. In this study, we investigated the possible relationship between the mitochondrial neuronal energy metabolism, as measured via CSF lactate levels and specific patterns of glucose hypometabolism, as stated at the 2-deoxy-2-(18F)fluoro-D-glucose positron emission tomography (18F FDG PET) in a group of AD patients.

METHODS

We measured brain glucose metabolism at 18F FDG PET within Deafault Mode Network (DMN) brain areas in drug-naïve AD patients studied at rest and compared to a population of controls not affected by neurological disorders. Moreover, we correlated in the AD group the CSF lactate concentrations with the obtained 18F FDG PET data in DMN nodes, using sex, age, disease duration, Mini Mental State Examination (MMSE) and CSF levels of tau proteins and beta-amyloid as covariates.

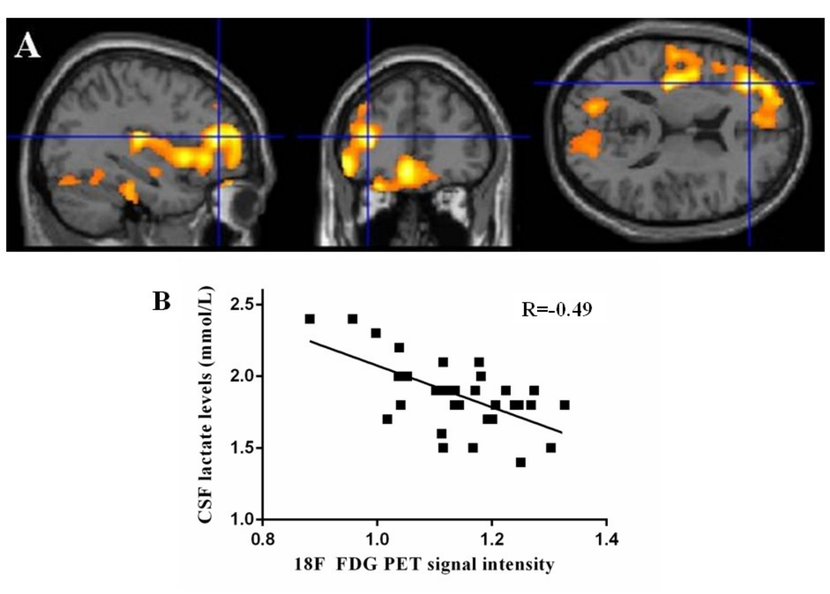
RESULTS

Thirty-two AD patients showed a significant reduction in the Broadmann Areas 10, 11 and 35, corresponding to the left medial prefrontal cortex (mPFC, $p<0.001$), left orbitofrontal cortex (OFC, $p<0.05$) and left parahippocampal gyrus (PHG, 0.01) compared to controls. Moreover, AD patients showed a significant correlation between the reduced 18F FDG uptake in DMN areas and the increased CSF lactate concentrations, with a selective correlation linking high CSF lactate levels to the reduced brain glucose consumption in the Broadmann Areas 10, 11 and 35, corresponding to the left medial prefrontal cortex (mPFC, $R=-0.49$, $p<0.01$), left orbitofrontal cortex (OFC, $R=-0.69$, $p=0.001$) and left parahippocampal gyrus (PHG, $R=-0.53$, $p<0.0001$).

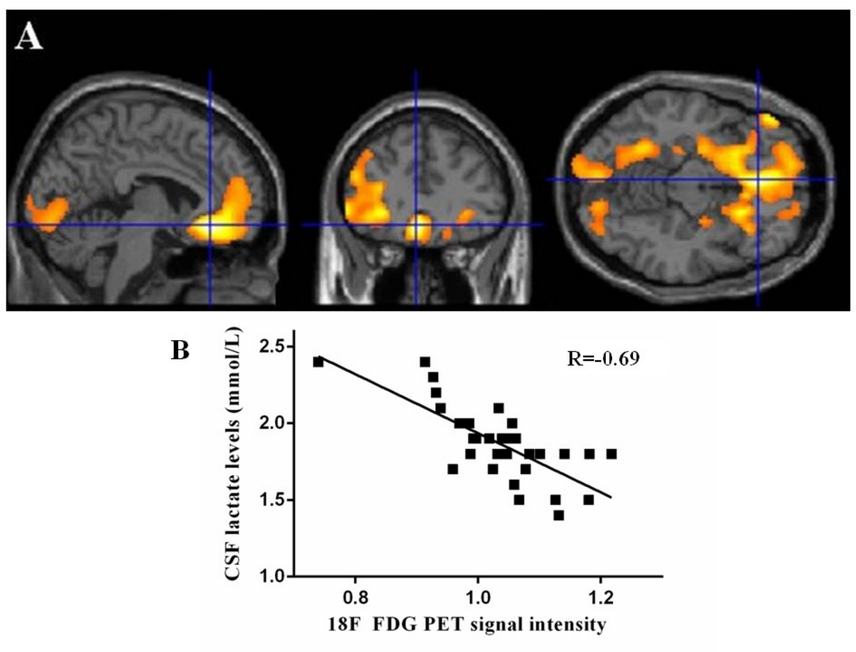
	Age *(years)*	***Sex***	***Disease Duration*** *(years)*	***MMSE***	***Lactate*** *(mmol/L)*	***T-tau*** *(pg/mL)*	***P-tau*** *(pg/mL)*	***Aβ42*** *(pg/mL)*
AD patients (n=32)	69.9±7.46	16F 16M	2.73±1.77	18.81±5.72	1.87±0.24	738.62±358.95	96.37±47.98	308.19±121.44
Controls (n=30)	68.8±2.91	15F 15M	*NA*	29.17±0.89	*NA*	*NA*	*NA*	*NA*

F, female; M, male; MMSE; Mini Mental State Examination; T-tau, total tau proteins; P-tau, phosphorylated tau proteins; Aβ42, beta amyloid1-42.

	Left BA10 **mPFC**	***Left BA11*** **OFC**	***Left BA35*** **PHG**
AD patients (n=32)	0.93±0.09	1.03±0.10	0.89±0.05
Controls (n=30)	0.99±0.05	1.07±0.06	0.93±0.05
	p<0.001	p<0.05	p<0.01



A: Superimposition of MRI T1 sequences on left medial prefrontal cortex (BA 10: sagittal, coronal and axial views] correlating with high CSF lactate concentrations. B: Scatter plot showing the correlation between 18F FDG PET signal intensity and CSF lactate levels.



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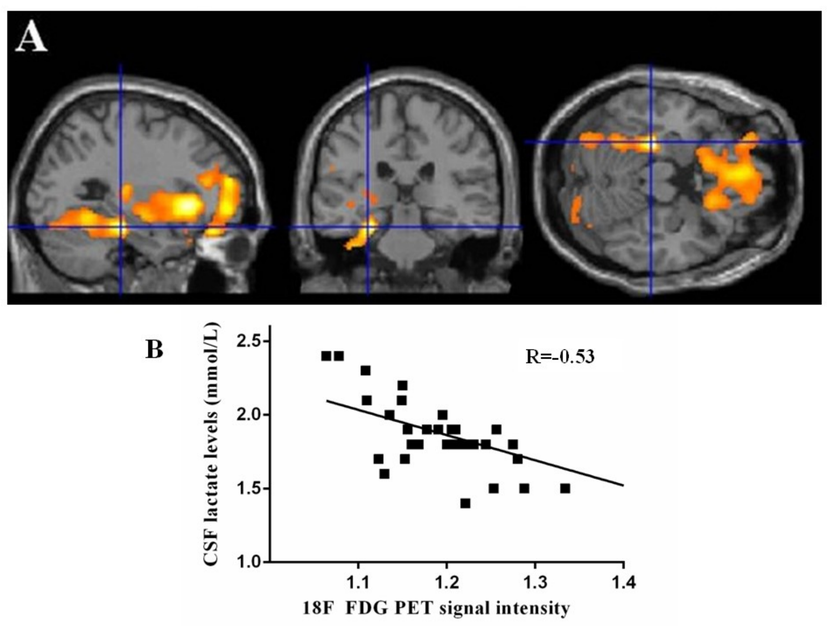

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CONCLUSIONS

We found that high CSF levels of lactate were coupled with a selective hypometabolism in the left mPFC, OFC and PHG. Taking into account that increased CSF concentrations of lactate suggest a mitochondrial dysfunction, we suggest that mitochondrial breakage could take part in affecting the DMN efficiency in AD. Therefore, this report not only confirms DMN inefficiency in AD patients, but also proposes the possible role of the damaged brain energetic machine in impairing DMN activity.