Cerebrospinal Fluid Lactate Levels along the Alzheimer’s Disease Continuum and Associations with Blood-Brain Barrier Integrity, Age, Cognition and Biomarkers

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Abstract

Background: Cerebrospinal fluid (CSF) lactate levels have been suggested to be associated with disease severity and progression in several neurological diseases as an indicator of impaired energy metabolism, neuronal death or microglial activation. A small number of studies have examined CSF lactate levels in dementia due to Alzheimer’s disease (AD) and found higher values in AD patients compared to healthy controls (HC). However, these studies were mostly small in size, the inclusion criteria were not always well defined, and the diagnostic value and pathophysiological significance of CSF lactate in AD remains unclear.

Methods: We examined CSF lactate levels and potentially associated factors in a large (n=312), biologically and clinically well-defined sample of patients with AD at the stage of mild cognitive impairment (MCI-AD) and dementia (ADD), HC, and patients with frontotemporal lobar degeneration (FTLD).

Results: Contrary to previous studies, patients with ADD and HC did not differ in CSF lactate levels. However, we found higher values for patients with MCI-AD compared to those with ADD and to HC in univariate analysis, as well as for MCI-AD compared to ADD when controlling for age and blood-brain barrier integrity. CSF lactate levels were associated with age and blood-brain barrier integrity but not with clinical severity or CSF biomarkers of AD.

Conclusion: CSF lactate does not indicate biological or clinical disease severity in AD, nor does it differentiate between patients with AD and healthy controls or patients with FTLD. However, higher CSF lactate levels were found in earlier stages of AD, which might be interpreted in the context of inflammatory processes.