

## CSF and PET biomarkers for noradrenergic dysfunction in neurodegenerative disease: a systematic review and meta-analysis

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### Abstract:

**Background and Objectives:** the noradrenergic system shows pathological modifications in aging and neurodegenerative diseases and is thought to be affected in the early stages of both Alzheimer and Parkinson's diseases.

**Methods:** We conducted a meta-analysis of noradrenergic differences in Alzheimer's disease type dementia (ADD) and Parkinson's disease (PD) using CSF and PET biomarkers. CSF noradrenaline (NA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) as well as NA transporter availability (PET MeNER) levels in controls, ADD and PD patients were summarized from 26 articles (1025 patients and 839 controls in total) using a random-effects model meta-analysis.

**Results:** Compared with controls, PD patients showed significantly decreased levels of CSF NA and MHPG, and PET MeNER binding in the hypothalamus. In ADD, MHPG levels were increased compared with controls while CSF NA showed no significant difference. Age correlated with CSF MHPG levels in ADD, but not in PD.

**Discussion:** Noradrenergic biomarkers are a promising tool in clinical setting. Validation through more studies confirming sample pathology is required to infer robust conclusions on their pathology-specific trajectories.