Risk factors for dementia
Lifestyle, hormones, neurochemistry, and genetics

Akademisk avhandling
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Abstract
Objective: The aim of this thesis was to expand the understanding about the effects of
lifestyle factors, indicators of endogenous estrogens, and genetic factors on the risk of
dementia and cerebrospinal fluid (CSF) markers for Alzheimer’s disease (AD).
Method: We used population-based samples from the Gothenburg H70 Birth Cohort
Studies (H70-studies), the Prospective Population Study of Women (PPSW), and the
Mayo Clinic Study of Aging (MCSA 70+ study). Information on exposures (marital
status [married vs not married], cognitive and physical activity [active vs inactive],
indicators of endogenous estrogen [age at menarche and menopause, reproductive
period, number of pregnancies, and months of breastfeeding], and genetic factors
[polygenic risk scores for AD (AD-PRSs), and APOE genotype]) was obtained
through interviews and examinations performed by experienced health personnel.
Dementia was diagnosed according to established criteria based on information from
the examinations. CSF levels of Aβ42, Aβ40, P-tau, and T-tau were measured with
immunochemical methods.
Results: In Project I (the H70-studies, n=913; the MCSA 70+ study, n=3,471), we
found that married men had a reduced risk of dementia compared to unmarried men,
while no association was observed in women. In Project II (PPSW and the H70-
studies, n=784), we found that midlife cognitive and physical activity were
independently associated with reduced risk of late-life dementia disorders. In Project
III (PPSW and the H70-studies, n=1,364), we found that longer reproductive period
and later age at menopause were associated with increased risk of dementia and AD.
In Project IV (PPSW and the H70-studies, n=75), we found that longer reproductive
period was associated with CSF biomarkers for AD (lower levels of Aβ42, lower ratio
of Aβ42/Aβ40, and higher levels of P-tau). In Project V (the H70-studies, n=2,052),
we found that AD-PRSs (including 39 and 57 genetic variants) and APOE genotype
were associated with risk of dementia up to very old ages.
Conclusion: The results from this thesis add knowledge about risk factors for
dementia, and add further knowledge on the protective effects of cognitive and
physical activity on risk of dementia disorders.
Keywords: Dementia, Alzheimer’s disease, marital status, leisure time activity,
menopause, polygenic risk scores, APOE genotype.