



**Karolinska
Institutet**

Institutionen för Neurobiologi, Vårdvetenskap och Samhälle

Cognitive Impairment in the Nondemented Elderly

Occurrence, risk factors, progression

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska
Institutet offentligen försvaras i Samuelssonsalen, Tomtebodavägen 6,
KI Campus, Solna

Tisdagen den 31 maj 2011, kl 10.00

av

Barbara Caracciolo

Huvudhandledare:

Professor Laura Fratiglioni
Karolinska Institutet
Institutionen för Neurobiologi, Vårdvetenskap
och Samhälle
Aging Research Center

Bihandledare:

Professor Bengt Winblad
Karolinska Institutet
Institutionen för Neurobiologi, Vårdvetenskap
och Samhälle
Aging Research Center

Fakultetsopponent:

Professor Howard Chertkow
McGill University, Montreal, Canada
Department of Neurology and Neurosurgery

Betygsnämnd:

Professor Maria Larsson
Stockholms Universitet
Psykologiska Institutionen

Professor Dag Aarsland
Karolinska Institutet
Institutionen för Neurobiologi, Vårdvetenskap
och Samhälle

Professor Matteo Bottai
Karolinska Institutet
Institutet för Miljömedicin

Stockholm 2011

ABSTRACT

This doctoral thesis investigated different issues related to cognitive impairment (CI) in the nondemented elderly, including occurrence of CI, risk factors leading to CI development, and progression of CI to dementia. Data were derived from the Kungsholmen Project, a community-based study of 75+ years old (Studies II and IV), and from the HARMONY Study (Studies I and III), a nation-wide, population-based study of twins in Sweden. The major findings are summarized below.

Study I. The prevalence of subjective cognitive impairment (SCI) and cognitive impairment no dementia (CIND) was estimated among nondemented elderly twins. Prevalence rates of SCI and CIND were 39 (38 to 39) and 25 (24 to 25) per cent. SCI was more prevalent among married people with higher education and occupational SES. A reverse pattern was observed in CIND. Both SCI and CIND were more prevalent among older compared to younger old. Probandwise concordance and tetrachoric correlations for SCI and CIND did not differ between monozygotic and dizygotic same-sex twins.

Study II. The incidence of amnesic mild cognitive impairment (aMCI), other cognitive impairment no dementia (oCIND), and dementia was estimated using 9-year follow-up data. Incidence rates per 1,000 person-years of aMCI, oCIND and dementia were 11.4 (8.6 to 15.1), 33.8 (28.7 to 39.8), and 70.4 (64.0 to 77.4). Both aMCI and oCIND incidence increased with advancing age in a nonlinear fashion. When correcting for attrition due to death, the increase with age appeared more linear and was similar to that observed for dementia.

Study III. The association of common chronic diseases with SCI and CIND was investigated, taking into account familial factors. In fully adjusted models, mental, musculoskeletal, respiratory, and urological diseases were associated with increased odds of both SCI and CIND. Gastrointestinal disorders were related to SCI, while endocrine diseases were associated with CIND. Multimorbidity was associated with 100% and 50% increased odds of SCI and CIND, respectively. In co-twin control analyses, the chronic diseases-SCI association remained significant, but the association with CIND was largely attenuated.

Study IV. Low mood was investigated in relation to aMCI and oCIND and their progression to dementia. People with low mood at baseline had a 2.7-fold (95% CI 1.9 to 3.7) increased risk of developing MCI at follow-up. The association was stronger for aMCI (HR 5.8; 95% CI 3.1 to 10.9) compared with oCIND (HR 2.2; 95% CI 1.5 to 3.3). Low mood at baseline was associated with a 5.3-fold (95% CI 1.2 to 23.3) increased risk of progression to dementia in aMCI.

Conclusions. Cognitive impairment is highly frequent in the elderly population. Rates increase with age, especially when detected longitudinally and corrected for attrition. Other sociodemographic factors can also affect the distribution of CI among the nondemented. Co-morbid chronic diseases and multimorbidity are associated to increased odds of subjective and objective CI, while low mood is a strong predictor of CI development and progression in the cognitively healthy elderly. Familial factors contribute to non-dementia CI in a complex fashion.

Key words: Attrition, chronic diseases, cognitive impairment no dementia, concordance, dementia, depressive symptoms, familial factors, incidence, low mood, mild cognitive impairment, multimorbidity, population-based, prevalence, prospective, sociodemographic factors, subjective cognitive impairment, twin study