alzheimer's association

Alzheimer's Association
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NEW STUDIES UNDERSCORE GLOBAL IMPORTANCE OF MILD COGNITIVE IMPAIRMENT IN ALZHEIMER'S DISEASE CONTINUUM

PARIS, July 19, 2011 – New research reported today in Paris at the Alzheimer's Association International Conference 2011 (AAIC 2011) offers insight on the global incidence and prevalence of mild cognitive impairment (MCI) – a condition involving problems with memory or another mental function severe enough to be noticeable to the affected person or to others but not serious enough to interfere with daily life. The research also identifies the conditions that most accurately predict progression from MCI to Alzheimer's disease.

This global perspective on MCI – offered for the first time at AAIC 2011 – includes data from six countries: the USA, Australia, Germany, the UK, Sweden and France.

MCI often - but not inevitably - leads to Alzheimer's disease. As a result of the growing global Alzheimer's epidemic, MCI is receiving increasing attention as the first clinical presentation of Alzheimer's and a potentially pivotal opportunity for intervention. Recently published National Institute on Aging/Alzheimer's Association diagnostic guidelines and criteria – which address pre-clinical Alzheimer's, MCI due to Alzheimer's and Alzheimer's disease dementia – recognize MCI as a critical stage in the Alzheimer's continuum.

"The earlier in the disease process that people at risk for developing Alzheimer's are identified, the sooner we can intervene," said William Thies, PhD, Chief Medical and Scientific Officer at the Alzheimer's Association. "Earlier detection will be our best opportunity to prevent continuing damage to the brain, once more effective therapies are developed."

"Understanding MCI is a key to this endeavor. It is has become increasingly important for us to understand how prevalent MCI is throughout the world and how it varies from country to country. These six new studies explore and examine the similarities and differences around the globe," Thies added.

Risk Factors for Progression from MCI to Alzheimer's

While some individuals with MCI do not progress to dementia, identification of factors that enable prediction of progression has emerged as an important Alzheimer's research priority.

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"Understanding the multiple causes of MCI, and both the cognitive and biological changes that occur in MCI patients who progress to Alzheimer's, provides a greater opportunity to determine treatment pathways and potentially identify a population for earlier interventions," said Henry Brodaty, MD, DSc, FRACP, FRANZCP, Professor of Ageing and Mental Health and Director of the Dementia Collaborative Research Centre at the University of New South Wales in Sydney, and Director, Aged Care Psychiatry and Head of the Memory Disorders Clinic at Prince of Wales Hospital.

Data from the six countries suggest that MCI is a surprisingly common condition, especially in industrialized nations, affecting between 15.4 and 42 percent of the studied populations. They also suggest that advanced brain imaging tests and other biomarkers, plus assessment of certain lifestyle-based risk factors, may improve the scientific community's ability to identify who will go on to develop Alzheimer's.

A number of common factors emerge from the studies as indicators of the likely progression from MCI to Alzheimer's, including: depression, apathy, anxiety, age, education, loss of ability in activities of daily living, cardiovascular factors (including stroke and diabetes), and low level of education.

- In the U.S. study, the risk of progression to dementia was elevated for people with stroke, depression and a high burden of other medical conditions.
- Similarly, in the U.K. and Swedish studies, depression, the presence of other diseases, and MCI affecting several cognitive functions (not just memory) hastened progression to dementia. In particular, in Sweden, diabetes accelerated the progression from MCI to dementia by three years.
- In the study from France, diabetes, stroke and depression were risk factors for progression. In both France and Germany, impairment in activities of daily living was significantly associated with a higher conversion rate and shorter time to onset of dementia.

"There are a variety of types of MCI, and only some forms have a high likelihood of progression to Alzheimer's," said Ronald Petersen, PhD, MD, Professor of Neurology, Cora Kanow Professor of Alzheimer's Disease Research, and Director of the Mayo Alzheimer's Disease Research Center, Mayo Clinic College of Medicine, Rochester, MN. "The research done to date has shown us that different study populations have different MCI prevalence and incidence rates, so more research needs to be conducted to explore additional similarities and differences between countries and among subpopulations."

"That said, these large data sets are from the major epidemiological studies from around the world. They range from 1,000 to as high as 12,000 subjects who have been followed for long periods of time. The increasing use of imaging techniques along with the new diagnostic guidelines for this group will help further strengthen scientific knowledge about the role of MCI and its impact on Alzheimer's risk," Petersen said.

Subjective Concerns Should Be Taken Seriously

"Another important finding from these multi-country studies is that subjective memory complaints in previously cognitively healthy individuals should be taken seriously as a possible pre-stage of MCI. Individuals who experience memory problems should immediately seek medical evaluation," Brodaty said.

According to experts, early detection allows for prompt evaluation and treatment of reversible or treatable causes of cognitive impairment. For example, if memory or thinking problems are due to depression or insomnia, then there are appropriate treatment interventions that can be applied. If the MCI is due to Alzheimer's, then there are other treatment options that could be explored.

"This is particularly significant as growing evidence suggests that vascular risk factors, such as high blood pressure, diabetes and high cholesterol contribute to cognitive decline. The identification and management of these risk factors at the MCI stage could be an important strategy for preventing and delaying progression to Alzheimer's," Petersen said.

About AAIC

The Alzheimer's Association International Conference (AAIC) is the world's largest conference of its kind, bringing together researchers from around the world to report and discuss groundbreaking research and information on the cause, diagnosis, treatment and prevention of Alzheimer's disease and related disorders. As a part of the Alzheimer's Association's research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.

About the Alzheimer's Association

The Alzheimer's Association is the leading voluntary health organization in Alzheimer care, support and research. Our mission is to eliminate Alzheimer's disease through the advancement of research, to provide and enhance care and support for all affected, and to reduce the risk of dementia through the promotion of brain health. Our vision is a world without Alzheimer's. Visit www.alz.org or call 800-272-3900.

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- Henry Brodaty, AO, MB, BS, MD, DSc, FRACP, FRANZCP, Ronald Petersen, PhD, MD, et al. Global comparison of MCI incidence, prevalence, and predictors of progression (AAIC 2011 Featured Research Session). (Funders: National Health and Medical Research Council (Australia), U.S. National Institute on Aging, Robert H. Smith and Abigail Van Buren Alzheimer's Disease Research Program)

AAICAD 2011, Feature Research Session F3-02
Tuesday, July 19, 2011, 10:30-12:30 pm
Proposal ID: 8878
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Global comparison of MCI incidence, prevalence and predictors of progression

Abstract Details

Topics

Topic:	Clinical Diagnosis and MCI
Clinical Diagnosis and MCI Subtopic:	Diagnosis and disease progression: mild cognitive impairment

Presenting Author 1 Information

Presenting Author 1: Henry Brodaty

Name:	Henry Brodaty, AO, MB, BS, MD, DSc, FRACP, FRANZCP
Institution/Organization:	Dementia Collaborative Research Centre
Title of Abstract:	Sydney Memory and Ageing Study
Backgrounds:	To determine the prevalence, incidence and predictors of MCI and of progression and reversion to normal in a population based sample of people aged 70-90 without dementia and living in the community
Methods:	A sample of 1037 older community dwellers derived from the Electoral Roll agreed to participate in a comprehensive clinical, neuropsychological, blood, genetic and (for over half) MRI assessment. They were followed up by telephone at 1 year, and fully reassessed at 2 years. Dementia was an exclusion at wave 1. MCI and dementia were diagnosed by a panel of clinicians using standard criteria.
Results:	At wave 1 36.7% of the sample had MCI and from wave 1 to wave 2, over two years, the incidence was 101.6 per 1000 person years. Predictors for incident MCI were male sex, high homocysteine, ApoE e4, and heart disease; better odor identification and visual acuity as well as greater mental activity decreased the risk . Over the 2 years 4.8% of the MCI participants progressed to dementia and 28.6% reverted to no cognitive impairment.; 66.5% remained as diagnosed with MCI. Those with multidomain MCI were more likely to progress to dementia.
Conclusions:	The prevalence of MCI was higher than reported in similar studies. Incidence and rates of reversion to no cognitive impairment were in the upper range of previous reports. In general risk factors support previous findings.

Presenting Author 2 Information	
Presenting Author 2: Rosebud Roberts	
Name:	Rosebud Roberts, M.B.Ch.B.
Institution/Organization:	Mayo Clinic
Title of Abstract:	MCI Incidence, Progression to Dementia, and Reversion to Normal in a Population-Based Cohort: The Mayo Clinic Study of Aging
Backgrounds:	To estimate mild cognitive impairment (MCI) incidence, progression to dementia, and identify predictors of progression in a population-based cohort.
Methods:	The Mayo Clinic Study of Aging is a prospective study of subjects aged 70-89 years on October 1, 2004, who were randomly selected from the Olmsted County, Minnesota, population. At baseline and during repeated follow-up, participants were clinically evaluated by a nurse, a neuropsychologist, and a physician; a diagnosis of normal cognition, MCI, or dementia was made using published criteria. At each 15-month follow-up, the evaluators were blinded to the previous diagnostic classification.
Results:	Among 1,640 subjects who were cognitively normal at baseline (1,450 had at least one follow-up), the incidence of MCI (per 1,000 person-years) was 63.6 over a median of 3.4 (range: 0.5 – 5.5). Predictors of MCI were stroke (hazard ratio [HR}, 1.53; 95% confidence interval [CI}, 1.11-2.12), less than12 years of education (HR, 1.61; 95% CI, 1.28-2.02), male sex (HR, 1.38; 95% CI, 1.10-1.73), type 2 diabetes (HR, 1.37; 95% CI, 1.05-1.80), and apolipoprotein (APOE) epsilon 4 allele (HR, 1.34; 95% CI, 1.01-1.77). Among 329 subjects with prevalent MCI and 284 with incident MCI, the rate of progression to dementia (per 1,000 person-years) was 99.1 over a median of 2.6 years of follow-up for the prevalent cases and 79.7 over a median 2.0 years for the combined group. The risk of progression to dementia was elevated for subjects with stroke, depression, and a high Charlson Comorbidity Index. The reversion rate (per 1,000 person-years) from MCI to normal cognition was 76.8 for the prevalent cases and 92.8 for the combined group.
Conclusions:	Our population-based estimates suggest that the incidence of MCI and its progression to dementia are both high. The low reversion rate from MCI to normal suggests that the diagnosis of MCI in this population-based setting is relatively stable.

Presenting Author 3 Information	
Presenting Author 3: Steffi Riedel-Heller	
Name:	Dr. med. Steffi Riedel-Heller, MPH
Institution/Organization:	University of Leipzig
Title of Abstract:	MCI in Germany - Results from the AgCoDe and the LEILA75+ Study
Backgrounds:	Mild Cognitive Impairment (MCI) is a condition of considerable clinical interest because it constitutes a pre-stage of dementia in many cases. Estimates of prevalence, age- and gender-specific incidence of MCI, risk factors for incident MCI in two samples (a population-based sample and a sample of GP patients) of cognitively healthy subjects aged 75 years and older. Furthermore data on progression to dementia are given and ways to improve prediction of dementia are searched.
Methods:	Data were derived from the primary-care-based German Study on Ageing, Cognition and Dementia in Primary Care Patients (AgeCoDe) with n= 3327 individuals 75+ at baseline and the population-based Leipzig Longitudinal Study of the Aged (LEILA75+) with n=1378 individuals 75+ at baseline. Study participants were assessed at 1.5year assessment intervals. Diagnoses were made using standardized criteria. Incidence rates were calculated according to the 'person-years-at-risk' method. Risk factors for MCI were analysed using multivariate logistic regression models and Cox proportional hazards models. The impact of MCI and IADL impairment on incident dementia was analysed using Receiver Operating Characteristic, Kaplan-Meier survival analyses and Cox proportional hazards models.
Results:	MCI is a common condition with 15.4% (95% CI: 14.1-16.6) in the AgeCoDe and 19.3% (95% CI: 16.8-21.8) in the LEILA75+ study. The overall incidence rates of MCI for subjects aged 75 years and older was 76.5 (95%-PCI = 64.7-90.4) (LEILA 75+) and 56.5 (95% CI = 50.7-62.7) (AgeCoDe) per 1,000 person-years. The incidence rates were highest in age group 85+ years. Older age, vascular diseases, the apoE Îµ4 allele, subjective memory complaints, impairment in instrumental activities of daily living, and lower cognitive performance were identified as significant risk factors for future MCI. Predicting progression to dementia can be improved by considering impairment in instrumental activities of daily living (IADL). MCI and IADL impairment were found to be significantly associated with higher conversion to, shorter time to, and better predictive power for future dementia.
Conclusions:	MCI is a common condition. Subjective memory complaints in previously cognitively healthy individuals should be taken seriously as a possible pre-stage of MCI. Especially vascular risk factors provide the opportunity of preventive approaches. The inclusion of restrictions in instrumental activities of daily living in the criteria of MCI particularly might be useful to improve the prediction of dementia.

Presenting Author 4 Information	
Presenting Author 4: Blossom Stephan	
Name:	Blossom Stephan, PhD
Institution/Organization:	Cambridge University
Title of Abstract:	Mild Cognitive Impairment from the perspective of the Medical Research Council Cognitive Function and Ageing Study
Backgrounds:	Mild cognitive impairment (MCI) defines an intermediate state between normal cognitive ageing and dementia intended to identify those individuals at increased risk of dementia progression. Three main subtypes have been defined including amnestic (A-MCI), non-amnestic (N-MCI) and multi-domain MCI (M-MCI). Prevalence and the annual conversion rate from MCI to dementia vary depending on definition. Further, not all individuals with MCI progresses to dementia and identification of risk factors that increase the accuracy of MCI criteria for the prediction of dementia has become a research priority. This presentation will give an overview of the topic of MCI and dementia risk prediction from a population-based perspective.
Methods:	Data were from The Medical Research Council Cognitive Function and Ageing Study (MRC CFAS). The CFAS is a large scale, multi-centre longitudinal study of ageing that began in 1991. The sample includes 13,004 individuals aged 65 years and older representative of the population of England and Wales. Two year follow-up provided measure of change.
Results:	Population prevalence estimates of MCI were variable (A-MCI: 2.5% [95%CI: 1.7-3.6%]; M-MCI: 2.6% [1.8-3.5%]; N-MCI: 5.3% [4.2-6.8%]), reflecting differences in the focus area and content in the defining criteria. MCI definitions varied in their ability to predict two-year incident dementia. Progression was highest in classifications where impairment was associated with memory or in multiple domains (M-MCI: 14.3%; A-MCI 13.4%). The lowest progression was observed in the non-amnestic subtype (N-MCI: 2.6%). Overall, however, a large proportion of MCI cases reverted to normal at two-years follow-up (Range: 20.1-44.8%). Co-morbid disease associated with anaemia and depression increased the risk of dementia progression from MCI.
Conclusions:	MCI criteria when applied in the population have different prevalence and dementia predictability compared to clinical samples. This may be reflecting differences in the operability of criteria (e.g., clinical judgement) or severity of impairment. Given the importance of early detection of dementia there is an urgent need to determine the best way to operationalise MCI to differentiate progressive and non-progressive sub-types in population-based samples.

Presenting Author 5 Information	
Presenting Author 5: Laura Fratiglioni	
Name:	Laura Fratiglioni, MD, PhD
Institution/Organization:	Karolinska Institute
Title of Abstract:	MCI: occurrence, risk factors, progression - Evidence from the Kungsholmen Project.
Backgrounds:	The Kungsholmen Project, with its community-based, 12 year-long, longitudinal design has been an optimal platform for the prospective study of mild cognitive impairment (MCI).
Methods:	The Kungsholmen Project is a community-based, 12 year-long, longitudinal design. Incidence rates of MCI and CIND, their risk factors and their progression were calculated correcting for attrition.
Results:	We have observed an incidence of 11.4 (8.6 to 15.1) per 1000 person-years for amnestic MCI (aMCI) and an incidence of 33.8 (28.7 to 39.8) per 1000 person-years for cognitive impairment no dementia (CIND). Incidence estimates of both aMCI and CIND increased after correction for attrition. We also studied different risk factors for MCI development and found that low mood was associated to a 5.8 (3.1-10.9) increased risk of aMCI and to a 2.2 (1.5-3.3) increased risk of CIND. Other factors associated to the development of MCI were: hip fracture (OR 2.9, 1.1-7.8), psychosis (OR 5.0, 1.1-23.6), polypharmacy (OR 3.1, 1.2-8.0) and APOE É›2É›4/É›3É›4 (HR 1.74, 1.21-2.52) Factors promoting the progression of MCI to Alzheimer's disease (AD) or dementia were: low mood (dementia: HR 5.3-fold, 1.2 to 23.3), anxiety symptoms (AD: HR 1.8, 1.2 to 2.7) diabetes (dementia: HR 2.87, 1.30-6.34) and prediabetes (dementia: HR 4.96, 2.27-10.84) ,and APOE É›2É›4/É›3É›4 (dementia: HR 4.35, 1.97- 9.63; AD: HR 5.65, 2.49-12.82).
Conclusions:	Based on these results, our current working hypothesis is that a multiplicity of causal pathways can lead to MCI. Due to the different mechanisms that can underlie the clinical manifestation of MCI, clinical outcomes can also differ. In some cases MCI could be caused by the neurodegenerative process that leads to AD and dementia, while in other instances MCI could result from other medical conditions or from psychosocial factors. Therefore, MCI does not necessarily progress to AD or dementia.

Presenting Author 6 Information	
Presenting Author 6: Karen Ritchie	
Name:	Karen Ritchie, PhD
Institution/Organization:	INSERM
Title of Abstract:	3 City Study - an epidemiological study from France
Backgrounds:	The characteristics of MCI subjects are described using data from the French multi-site study of dementia (3C Study) including 6892 participants over 65.
Methods:	Subjects without dementia were recruited from a population-based cohort in three French cities. Cognitive performance, clinical diagnosis of dementia, and clinical and environmental risk factors were evaluated at baseline and 2-year and 4-year follow-ups.
Results:	42% of the population were classified as having MCI at baseline. After adjustment for confounding with logistic regression models, men and women classified as having MCI were more likely to have depressive symptomatology and to be taking anticholinergic drugs. Men were also more likely to have a higher body mass index, diabetes and stroke, whereas women were more likely to have poor subjective health, to be disabled, to be socially isolated, and to suffer from insomnia. The principal adjusted risk factors for men for progression from MCI to dementia in descending order were ApoE4 allele (OR=3.2, 95% CI 1.7 to 5.7), stroke (OR=2.8, 95% CI 1.2 to 6.9), low level of education (OR=2.3, 95% CI 1.3 to 4.1), loss of Instrumental Activities of Daily Living (IADL) (OR=2.2, 95% CI 1.1 to 4.5) and age (OR=1.2, 95% CI 1.1 to 1.2). In women, progression is best predicted by IADL loss (OR=3.5, 95% CI 2.1 to 5.9), ApoE4 allele (OR=2.3, 95% CI 1.4 to 4.0), low level of education (OR=2.2, 95% CI 1.3 to 3.6), subclinical depression (OR=2.0, 95% CI 1.1 to 3.6), use of anticholinergic drugs (OR=1.8, 95% CI 1.0 to 3.0) and age (OR=1.1, 95% CI 1.1 to 1.2) Rates of evolution towards dementia were observed, however, to be very low so an alternative approach was taken to further examine these risk factors by working retrospectively from cases of dementia incidence.
Conclusions:	This approach validated initial risk factors and also introduced others which may improve specificity when included in MCI algorithms.

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