

BIOMARKERS

POSTER PRESENTATION

NEUROIMAGING

Association between gene expression and neurodegeneration in dementia with Lewy bodies

Annegret Habich¹ | Janna M. Baumann² | Christopher G. Schwarz³ |
Scott A. Przybelski⁴ | Matteo Pardini⁵ | Francesco Calizzano⁶ | Anna Inguanzo⁷ |
Ketil Oppedal⁸ | Frédéric Blanc⁹ | Afina Willemina Lemstra¹⁰ | Jakub Hort¹¹ |
Matthias Brendel¹² | Miguel A Ochoa-Figueroa¹³ | Valentina Garibotto¹⁴ |
Milica G. Kramberger¹⁵ | andrea pilotto¹⁶ | Brad F. Boeve¹⁷ | Dag Aarsland¹⁸ |
Eric Westman¹⁹ | Thomas Dierks²⁰ | Kejal Kantarci²¹ | Silvia Morbelli²² |
Laura E. Jonkman²³ | Daniel Ferreira¹⁹

¹Division of Clinical Geriatrics, Department of Neurobiology, Care Sciences and Society, Karolinska Institute, Stockholm, Sweden, Stockholm, Sweden

²Alzheimer Center Amsterdam, Department of Neurology, Amsterdam Neuroscience, Vrije Universiteit Amsterdam, Amsterdam UMC, Amsterdam, Netherlands

³Mayo Clinic, Radiology, Rochester, MN, USA

⁴Department of Quantitative Health Sciences, Mayo Clinic, Rochester, MN, USA

⁵Università degli studi di Genova, Genova, Liguria, Italy

⁶University of Genoa, Genoa, Liguria, Italy

⁷Division of Clinical Geriatrics, Centre for Alzheimer Research, Karolinska Institutet, Stockholm, Sweden

⁸University of Stavanger, Stavanger, Norway

⁹Day Hospital of Geriatrics, Memory Resource and Research Centre (CM2R) of Strasbourg, Hopitaux Universitaires de Strasbourg, Strasbourg, France

¹⁰Alzheimer Center Amsterdam, Neurology, Vrije Universiteit Amsterdam, Amsterdam UMC, Amsterdam, Netherlands

¹¹Memory Clinic, Department of Neurology, Charles University, Second Faculty of Medicine and Motol University Hospital, Prague, Czech Republic

Abstract

Background: Patterns of regional atrophy and hypometabolism have been observed in dementia with Lewy bodies (DLB). However, determinants of regional vulnerability to structural and functional neurodegeneration remain largely unexplored. First, we investigated the association between regional gene expression and grey matter volumes in probable DLB patients. Since hypometabolism presumably precedes overt brain atrophy, we additionally investigate the association between regional gene expression and hypometabolism in DLB.

Method: To investigate the association between gene expression and regional volumes, 165 DLB patients along with 165 age- and sex-matched healthy controls from three European centres and the Mayo Clinic (USA) were included. Regional volumes were quantified from MRI using SPM12 in 112 cortical, subcortical, and cerebellar brain regions, and compared between groups, using w-scores. Regional expression data of seven genes involved in the formation and degradation of pathological protein aggregates (APOE, APP, BIN1, GBA, MAPT, SNCA, TMEM175) was extracted from six healthy donors from the Allen Human Brain Atlas and correlated with regional volumetric w-scores. To assess the predictive value of regional gene expression on regional volumes we used Gaussian stepwise backwards linear regression including all seven genes as predictors. To investigate the association between gene expression and hypometabolism, we are currently applying the same analysis pipeline to FDG-PET data of 139 DLB patients from 8 European centres.

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¹²LMU University Hospital, Munich, Germany

¹³Linköping University, Linköping, Sweden

¹⁴Division of Nuclear Medicine and Molecular Imaging, Geneva University Hospitals, Geneva, Switzerland

¹⁵University Medical Centre Ljubljana, Medical Faculty, University of Ljubljana, Ljubljana, Ljubljana, Slovenia

¹⁶University of Brescia, Brescia, Italy, Italy

¹⁷Department of Neurology, Mayo Clinic, Rochester, MN, USA

¹⁸Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

¹⁹Division of Clinical Geriatrics, Center for Alzheimer Research, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden

²⁰University Hospital of Psychiatry and Psychotherapy Bern, Bern, Switzerland

²¹Department of Radiology, Mayo Clinic, Rochester, MN, USA

²²IRCCS Ospedale Policlinico San Martino, Genova, Liguria, Italy

²³Amsterdam UMC, location VUmc, Department of Anatomy and Neurosciences, Section Clinical Neuroanatomy and Biobanking, Amsterdam, Netherlands

Correspondence

Annegret Habich, Division of Clinical Geriatrics, Department of Neurobiology, Care Sciences and Society, Karolinska Institute, Stockholm, Sweden, Stockholm, Sweden.
Email: annegret.habich@ki.se

Result: Most brain regions showed lower volumes in DLB patients compared to healthy controls, with differences being most pronounced in occipital and parietal lobes. Regional expression of APOE correlated positively with regional volumes in DLB. Conversely, regional expression of MAPT correlated negatively with regional volumes. Both APOE and MAPT gene expression were significant predictors of regional volumes in the regression analysis. None of the other gene expression values was significantly associated with regional volumes in DLB.

Conclusion: Our findings show that regional expression of genes associated with the abnormal accumulation of amyloid and tau, common co-pathologies in DLB, partially account for the brain atrophy pattern observed in DLB patients. Analyses are ongoing for the hypometabolism pattern. Our finding emphasises the relevance of co-pathologies in predicting atrophy progression and identifying potential targets for future disease-modifying treatments.