

Developing topics

International initiative for harmonization of cerebrospinal fluid diagnostic comments in Alzheimer's disease

Constance Delaby¹ | Charlotte E Teunissen² | Daniel Alcolea³ |
 Elodie Bouaziz Amar⁴ | Anne Beaume⁵ | Aurélie Bedel⁶ | Edith Bigot-Corbel⁷ |
 Maria Bjerke⁸ | Marie-Céline Blanc⁹ | Olivier Bousiges¹⁰ | Miles D Chapman¹¹ |
 Mari L DeMarco¹² | Mara D'Onofrio¹³ | Diane Dufour-Rainfray¹⁴ |
 Sebastiaan Engelborghs¹⁵ | Hermann Esselmann¹⁶ | Anne Fogli¹⁷ |
 Elisabetta Galloni¹⁸ | Clémentine Gondolf¹⁹ | Frédérique Grandhomme¹⁹ |
 Oriol Grau-Rivera²⁰ | Melanie Hart²¹ | Andreas Jeromin²² | Ashvini Keshavan²³ |
 Michael Khalil²⁴ | Peter Koertvelyessy²⁵ | Agnieszka Kulczynska-Przybik²⁶ |
 Jean-Louis Laplanche²⁷ | Alberto Lleó³ | Catherine Malaplate²⁸ | Barbara Mroszko²⁹ |
 Léonor Nogueira³⁰ | Adelina Orellana³¹ | Markus Otto³² | Jean-Baptiste Oudart³³ |
 Claire Paquet³⁴ | Lucilla Parnetti³⁵ | Armand Perret-Liaudet³⁶ | Katell Poec²⁷ |
 Koen Poesen³⁷ | Albert Puig-Pi Joan³⁸ | Isabelle Quadrio³⁶ |
 Muriel Quillard-Muraine³⁹ | Benoit Rucheton⁴⁰ | Susanna Schraen⁴¹ |
 Marc Suárez-Calvet⁴² | Magda Tsolaki⁴³ | Hayrettin Tumani³² |
 Chinedu T Udeh-Momoh⁴⁴ | Lucie Vaudran⁴⁵ | Marcel M Verbeek⁴⁶ |
 Federico Verde⁴⁷ | Lisa Vermunt⁴⁸ | Jonathan Vogelgsang¹⁶ | Jens Wiltfang¹⁶ |
 Henrik Zetterberg⁴⁹ | Sylvain Lehmann¹

¹ IRMB, Univ Montpellier, INSERM, CHU Montpellier, (LBPC-PPC), Montpellier, France

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

³ Hospital de la Santa Creu i Sant Pau - Biomedical Research Institute Sant Pau - Universitat Autònoma de Barcelona, Barcelona, Spain

⁴ Lariboisiere Hospital, Paris, France

⁵ CHU Poitiers, Poitiers, France

⁶ CHU Bordeaux, Bordeaux, France

⁷ CHU Nantes, Nantes, France

⁸ Vrije Universiteit Brussel, UZ Brussel, UAntwerp, Brussel, Belgium

⁹ APHP Site Cochin, Paris, France

¹⁰ Hôpitaux Universitaire de Strasbourg, Laboratoire de Biochimie et Biologie Moléculaire, et CNRS, Laboratoire de Neurosciences Cognitives et Adaptatives (LNCA), Strasbourg, France

¹¹ Department of Neuroimmunology, National Hospital for Neurology and Neurosurgery, Queen Square, London, United Kingdom

¹² St. Paul's Hospital, Providence Health Care, Vancouver, BC, Canada

¹³ EBRI Rita Levi-Montalcini, Roma, Italy

¹⁴ CHU Tours, UMR 1253- iBrain, Tours, France

- ¹⁵ Institute Born-Bunge, Antwerp, Belgium
- ¹⁶ University Medical Center Goettingen (UMG), Goettingen, Germany
- ¹⁷ CHU Clermont-Ferrand, Clermont-Ferrand, France
- ¹⁸ Dipartimento di Neuroscienze Divisione di Neurologia, Vicenza, Italy
- ¹⁹ CHU Cote de Nacre Caen, Caen, France
- ²⁰ IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain
- ²¹ Neuroimmunology & CSF Laboratory 9th floor, UCL Queen Square Institute of Neurology Queen Square London, London, United Kingdom
- ²² Cohen Veterans Bioscience, Cambridge, MA, USA
- ²³ UCL Queen Square Institute of Neurology, London, United Kingdom
- ²⁴ Medical University of Graz, Graz, Austria
- ²⁵ German Center for Neurodegenerative Diseases, Magdeburg, Germany Dept. of Neurology, Charité Universitätsmedizin Berlin, Germany, Magdeburg, Germany
- ²⁶ Medical University of Białystok, Białystok, Poland
- ²⁷ APHP, Paris, France
- ²⁸ CHRU de Nancy/Université de Lorraine, Nancy, France
- ²⁹ Department of Neurodegeneration Diagnostics, Department of Biochemical Diagnostics, Medical University of Białystok, Białystok, Poland
- ³⁰ Laboratoire de Biologie Cellulaire et Cytologie, CHU-PURPAN, Toulouse, France
- ³¹ Research Center and Memory Clinic. Fundació ACE, Institut Català de Neurociències Aplicades, Barcelona, Spain
- ³² University of Ulm, Ulm, Germany
- ³³ Université de Reims Champagne-Ardenne, CNRS UMR 7369, CHU Reims, Reims, France
- ³⁴ INSERM UMR-S1144, Paris, France
- ³⁵ Lab of Clinical Neurochemistry, University of Perugia, Perugia, Italy
- ³⁶ Lyon University Hospital, Lyon Neuroscience Research Center BIORAN Team - CNRS UMR 5292, INSERM U1028, Université de Lyon, Lyon, France
- ³⁷ Laboratory for Molecular Neurobiomarker Research (LaMoN), Department of Neurosciences, Leuven Brain Institute, KU Leuven, Leuven, Belgium
- ³⁸ Servei de Neurologia, Hospital del Mar, Barcelona, Spain
- ³⁹ Normandie Univ, UNIROUEN, Inserm U1245 and Rouen University Hospital, Department of Biology, Rouen France, Rouen F 76000, France
- ⁴⁰ DMU BioGeM, AP-HP Sorbonne University, Paris, France
- ⁴¹ Inserm, UMR 837, Alzheimer & Tauopathies, Faculté de Médecine IILLE, France
- ⁴² Hospital del Mar, Barcelona, Spain
- ⁴³ Aristotle University of Thessaloniki, Thessaloniki, Greece
- ⁴⁴ Imperial College London, London, United Kingdom
- ⁴⁵ Univ. Lille, CHU Lille, Lille, France
- ⁴⁶ Radboud University Medical Center, Donders Institute for Brain, Cognition and Behaviour, Radboud Alzheimer Centre, Nijmegen, Netherlands
- ⁴⁷ Stroke Unit and Laboratory of Neuroscience, IRCCS Istituto Auxologico Italiano, Università degli Studi di Milano, Milan, Milan, Italy
- ⁴⁸ Amsterdam UMC, VU University, Amsterdam, Netherlands
- ⁴⁹ Institute of Neuroscience and Physiology, The Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

Correspondence

Constance Delaby, IRMB, Univ Montpellier, INSERM, CHU Montpellier, (LBPC-PPC), Montpellier, France.
Email: constance.delaby@inserm.fr

Abstract

Background: The quantification of cerebrospinal fluid (CSF) biomarkers (Aβ peptides [Aβ₁₋₄₀ and Aβ₁₋₄₂], tau protein and its phosphorylated form phospho-tau) is progressively implemented in laboratories as an aid for the multidisciplinary diagnosis of Alzheimer disease (AD), *DeKosky ST, Alz dementia, 2011, PMID: 21322828*. However, no consensus has been defined among the different laboratories involved to adapt the conclusions/comments to the level of quantified CSF biomarkers. As a result, although the analytical methods for such quantification may be similar across the laboratories involved in this clinical task, the conclusions transmitted to the physician in charge (neurologist or psychiatrist) may be quite different. Harmonization of this report is

thus necessary so patients' care and research stratification can be similar wherever the analysis is performed.

Method: A total of 34 laboratories (involved in CSF biomarkers measurement) across the world accepted to be part of our project of diagnostic's comments harmonization (represented countries: Austria, Belgium, Canada, France, Germany, Italy, Netherlands, Poland, Spain, Sweden, United Kingdom, USA). As a first step, we defined the 9 most typical biochemical profiles, according to the level of CSF biomarkers and their combination. For each profile, each laboratory was asked to provide us with the comments/conclusions given in routine clinical practice. We then collected and pooled all the comments in a common file, so that the laboratories could, as a second step, choose and order three of these comments (for each biochemical profile defined), according to their reliability in clinical practice.

Result: We are currently analysing the second step-answers of the laboratories, in order to define a consensual pattern of comments and conclusions that could be implemented in all the laboratories involved in the biochemical diagnosis of AD. Obtained data will be presented.

Conclusion: The discrepancies of the comments for AD biochemical diagnosis across laboratories worldwide can be confusing and it is of strong importance to harmonize them (according to the level of quantified biomarkers and other information likely available such as the age, APOE genotype...). Our initiative will likely provide such harmonized pattern of comments/conclusions, thus ensuring equal care of patients across the different diagnostic centres.