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Practice effects in genetic frontotemporal dementia and at-risk individuals: a GENFI study

Linn Öijerstedt
Karolinska Institutet

Christin Andersson
Karolinska Institutet

Vesna Jelic
Karolinska Institutet

John Cornelis van Swieten
Erasmus MC

Lize C. Jiskoot
Erasmus MC

See next page for additional authors

Authors

Linn Öijerstedt, Christin Andersson, Vesna Jelic, John Cornelis van Swieten, Lize C. Jiskoot, Harro Seelaar, Barbara Borroni, Raquel Sanchez-Valle, Fermin Moreno, Robert Laforce, Matthis Synofzik, Daniela Galimberti, James Benedict Rowe, Mario Masellis, Maria Carmela Tartaglia, Elizabeth Finger, Rik Vandenberghe, Alexandre de Mendonca, Fabrizio Tagliavini, Isabel Santana, Simon Ducharme, Christopher R. Butler, Alexander Gerhard, Johannes Levin, Adrian Danek, Markus Otto, Giovanni Frisoni, Roberta Ghidoni, Sandro Sorbi, and Jonathan Daniel Rohrer

Letters

Practice effects in genetic frontotemporal dementia and at-risk individuals: a GENFI study

INTRODUCTION

Frontotemporal dementia (FTD) is a heterogeneous group of neurodegenerative diseases with an onset usually before the age of 65 years even if it can appear also in older ages.[1]

On cognitive tests, patients with FTD show deficits in executive functions, social cognition and language, whereas the initial performances in memory and visuoconstruction tasks usually are preserved.[1] The general approach to detect cognitive decline in dementia is to repeat cognitive testing and observe changes over time. However, exposure to similar tasks could improve performance as the individual gets familiar with both the tasks themselves and the test setting (ie, practice effect or learning effect).[2 3]

Different attempts to adjust for practice effects in repeated testing have been proposed.[4] However, recent research suggests that the phenomenon of practice effects can provide useful information. Patients with neurological and psychiatric conditions show lower practice effects than healthy controls, and individuals with mild cognitive impairment (MCI) that do not show practice effects are more likely to develop Alzheimer disease (AD) within a year than individuals with MCI that have preserved practice effects.[3] In addition to the findings of lower practice effects in patients with dementia, Hassenstab *et al*[5] found that preclinical individuals who later progressed to AD had substantially reduced practice effects in episodic memory compared with cognitively stable individuals. Thus, absence of practice effects might serve as an early marker for cognitive decline.

To our knowledge, practice effects have never been investigated in FTD before. The aim of this study was to examine practice effects in the GENetic Frontotemporal dementia Initiative (GENFI) cohort. More specifically, we investigated whether there is a difference in practice effects between presymptomatic mutation carriers (PMC) and mutation non-carriers (NC).

MATERIALS AND METHODS

Participants

All participants (317 NC, 327 PMC and 159 affected mutation carriers (AMC)) were recruited through GENFI from January 2012 to March 2018 (online supplemental table 1). Of the 803 participants, 471 had two visits; 249 had three visits; and 108 had four visits. After the fourth visit, the number of participants rapidly decreased and only 12 had six test occasions (online supplemental figure 1).

Statistics

A global cognitive score was calculated including the mean z-scores of all tests in the standardised GENFI neuropsychological battery. Additionally, practice effects for different cognitive domains were explored. A linear mixed-effects model was applied to examine potential practice effects. Further details including neuropsychological tests, composite score calculation and model selection criteria are described in the online supplemental materials.

RESULTS

Practice effects

An increase in mean global cognitive test scores was seen in NC over the first five visits (online supplemental figure 2). When investigating different cognitive domains, practice effects were found across visits 1–3 in all domains except for visuoconstruction (online supplemental table 2). The largest practice effect was observed in memory and social cognition. After the third visit, there was a plateau, and the practice effects between visits 3 and 4 as well as visits 4 and 5 were not statistically significant. In contrast, a progressive decline in the mean global score was identified longitudinally in AMC, as could be expected (online supplemental figure 2). PMC carrying a *C9orf72* expansion and with less than 5 years to expected symptom onset (PMC-C9 in proximity to onset) showed no practice effect on their global test score and had the same mean performance at all three visits (figure 1A and online supplemental table 3). Furthermore, PMC-C9 with more than 5 years to expected onset had a lower practice effect between visits 1 and 2 than NC; however, the total practice effect (visits 1–3) was not significantly different from NC.

Similar to PMC-C9, there was a lower practice effect across visits 1–3 in PMC with a proganulin (*GRN*) mutation in proximity to onset compared with NC. However, PMC-GRN in proximity to onset appear to initially have a practice effect but subsequently do not improve their performance at the third visit (figure 1B).

PMC with a *MAPT* mutation (PMC-MAPT) had a similar trajectory in mean cognitive test score across visits 1–3 as NC (figure 1C).

DISCUSSION

In this study, we explored practice effects due to repeated cognitive assessments in

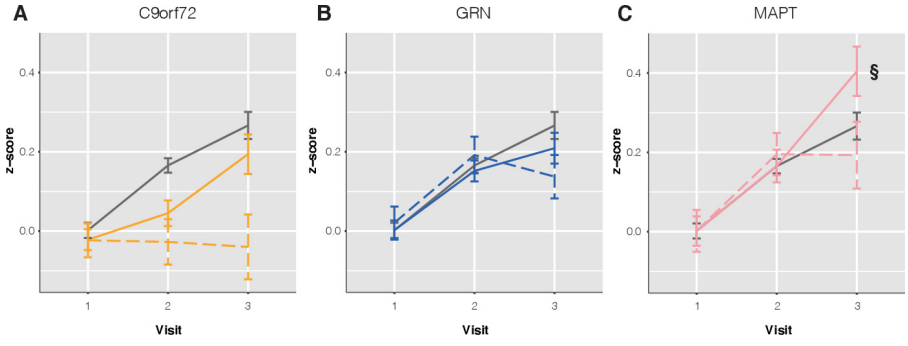

Figure 1 Trajectories of global cognitive test scores in NC and PMC by mutated gene.(A) PMC-C9 and NC (grey line, NC; yellow solid line, PMC-C9 with >5 years to expected symptom onset; yellow dashed line, PMC-C9 with <5 years to expected symptom onset). (B) PMC-GRN and NC (grey line, NC; blue solid line, PMC-GRN with >5 years to expected symptom onset; blue dashed line, PMC-GRN with <5 years to expected symptom onset). (C) PMC-MAPT and NC (grey line, NC; pink solid line, PMC-MAPT with >5 years to expected symptom onset; pink dashed line, PMC-MAPT with <5 years to expected symptom onset). All lines are fitted from the same linear mixed-effect model but plotted in A–C to simplify visualisation. Error bars represent the SEs of the means. §The difference between PMC-MAPT with >5 years to expected symptom onset and NC is no longer observed when PMC-MAPTs are compared with age-matched and family-matched controls. C9, chromosome 9 open reading frame 72; GRN, progranulin; MAPT, microtubule-associated protein tau; NC, non-carrier; PMC, presymptomatic mutation carrier.

a large cohort of individuals with genetic presymptomatic or symptomatic FTD as well as non-mutation carrier family members. Practice effects have been suggested to provide useful information of the progression of cognitive decline but have never been studied in the context of FTD before. Compared with their baseline test scores, NC improved in global cognition at each visit (visits 2 and 3). Presymptomatic individuals carrying the *C9orf72* expansion or a *GRN* mutation had significantly lower practice effects than NC, and this difference was most apparent in PMC-C9 within 5 years of expected symptom onset. However, it is not possible to know if the stable performance over time in PMC in proximity to onset is due to lower practice effects per se or an actual cognitive decline that is masked by practice effects. The question of genuine practice effects applies also to AMC, who showed a progressive decline in global cognitive test scores at each visit. The scores measured after repeated testing in AMC might include a 'hidden' practice effect, and therefore the true cognitive dysfunction would in fact be greater than what was captured in the test scores. Cognitive functions in FTD are expected to decline over the test interval used in this study (mean 1.3 years). Consequently, a potential absence of practice effects in clinical FTD, as reported in AD,[3] cannot be evaluated with the current setup but could be addressed if the retest is performed within days or weeks of the first assessment. Besides the PMC in proximity to onset, also PMC-C9 with more than 5 years to expected symptom onset had lower practice effects than NC which could not be explained by early conversion into a symptomatic stage. Progression of brain atrophy in *C9orf72* expansion carriers can be slow, and some patients have been described with a remarkably long disease duration.[1] Pathological changes in the brain of *C9orf72* expansion carriers are present already in early adulthood, and the potential neurodevelopmental effects could lead to a long prodromal phase in PMC-C9. Previous findings show that cognitive performance in PMC is not different from NC until very close to the disease onset,[1] which is in line with the results of the current study. Nevertheless, an inability to use acquired skills from previous tests might be a marker for very early disease development in PMC-C9. However, the diagnostic potential of practice effects and whether they can be used for differentiating PMC-C9 from NC are yet to be explored.

As the field of FTD research is greatly evolving and treatment opportunities are emerging, knowledge about different stages of the disease is highly required. As we are preparing for clinical trials, several initiatives have been searching for both fluid biomarkers as surrogate endpoints as well as clinical and neuropsychological tests used to evaluate a future treatment response. Practice effects can have implications for the interpretation of longitudinal changes in cognitive performance as it could impact estimations of treatment effects after an intervention, particularly early in the disease course. Furthermore, one could speculate that identifying individuals with lower-than-expected practice effects would be a cost-effective approach for inclusion into clinical trials.[3] The presence of practice effects should thus be considered in future clinical trials especially if neuropsychological measures are included as end points.

Linn Öijerstedt,[1,2] **Christin Andersson**,[3,4] **Vesna Jelic**,[1] **John Cornelis van Swieten**,[5] **Lize C Jiskoot**,[5] **Harro Seelaar**,[5] **Barbara Borroni**,[6] **Raquel Sanchez-Valle**,[7] **Fermin Moreno**,[8,9] **Robert Laforce Jr**,[10] **Matthis Synofzik**,[11,12] **Daniela Galimberti**,[13,14] **James Benedict Rowe**,[15] **Mario Masellis**,[16] **Maria Carmela Tartaglia**,[17] **Elizabeth Finger**,[18] **Rik Vandenberghe**,[19,20] **Alexandre de Mendonca**,[21] **Fabrizio Tagliavini**,[22] **Isabel Santana**,[23,24] **Simon Ducharme**,[25,26] **Christopher R Butler**,[27,28] **Alexander Gerhard**,[29,30] **Johannes Levin**,[31,32] **Adrian Danek**,[31] **Markus Otto**,[33] **Giovanni Frisoni**,[34] **Roberta Ghidoni**,[35] **Sandro Sorbi**,[36,37] **Jonathan Daniel Rohrer**,[38] **Caroline Graff**,[1,2] **Genetic Frontotemporal Dementia Initiative (GENFI)**

[1]Department of Neurobiology, Care Sciences and Society, Neurogeriatrics, Karolinska Institute, Stockholm, Sweden
[2]Unit for Hereditary Dementias, Theme Aging, Karolinska University Hospital, Stockholm, Sweden
[3]Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden
[4]Department of Medical Psychology, Karolinska University Hospital, Stockholm, Sweden
[5]Neurology, Erasmus MC, Rotterdam, Netherlands
[6]Centre for Ageing Brain and Neurodegenerative Disorders, Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[7]Alzheimer's Disease and Other Cognitive Disorders Unit, Neurology Service, Hospital Clinic de Barcelona, Barcelona, Spain
[8]Cognitive Disorders Unit, Department of Neurology, Donosti, Donostia San Sebastian, Spain
[9]Neuroscience Area, Biodonostia Health Research Institute, Donostia San Sebastian, Spain
[10]Clinique Interdisciplinaire de Mémoire, Département des Sciences Neurologiques, Faculté de Médecine, CHU de Quebec-Universite Laval, Montreal, Quebec, Canada
[11]Department of Neurodegenerative Diseases, Univeristy of Tübingen, Eberhard Karls University Tubingen Hertie Institute for Clinical Brain Research, Tubingen, Germany
[12]German Centre for Neurodegenerative Diseases, Tübingen, Germany
[13]Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milano, Italy
[14]Centro Dino Ferrari, University of Milan, Milano, Italy
[15]Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK
[16]Sunnybrook Research Insitute, University of Toronto, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
[17]Tanz Centre for Research in Neurodegenerative Disease, University of Toronto, Toronto, Ontario, Canada
[18]Clinical Neurological Sciences, University of Western Ontario, London, Ontario, Canada
[19]Laboratory for Cognitive Neurology, Department of Neurosciences, KU Leuven, Leuven, Belgium
[20]Neurology Service, KU Leuven University Hospitals Leuven, Leuven, Belgium
[21]Faculty of Medicine, University of Lisbon, Lisboa, Portugal
[22]Fondazione IRCCS, Istituto Nazionale Neurologico Carlo Besta, Milano, Italy
[23]Neurology Service, Faculty of Medicine, Hospital and University Centre of Coimbra, Coimbra, Portugal
[24]Center for Neuroscience and Cell Biology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal
[25]Department of Psychiatry, McGill University Health Centre, Montreal, Quebec, Canada
[26]McConnel Brain Imaging Centre, Montreal Neurological Institute and Hospital, Montreal, Quebec, Canada
[27]Nuffield Department of Clinical Neurosciences, Medical Sciences Division, University of Oxford, Oxford, UK
[28]Brain Sciences, Imperial College London, London, UK
[29]Division of Neuroscience and Experimental Psychology, The University of Manchester, Manchester, UK
[30]Geriatric Medicine and Nuclear Medicine, University of Duisburg-Essen, Duisburg, Germany
[31]Neurologische Klinik, Ludwig Maximilians University Munich, Munchen, Germany
[32]German Centre for Neurodegenerative Diseases, Münich, Germany
[33]Neurology, University of Ulm, Ulm, Germany
[34]IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy
[35]Molecular Markers Lab, IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy
[36]Neurofarba, University of Florence, Firenze, Italy
[37]IRCCS Firenze, Fondazione Don Carlo Gnocchi Onlus, Firenze, Italy
[38]Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, London, UK

Correspondence to Dr Linn Öijerstedt, Department of Neurobiology, Care Sciences and Society, Neurogeriatrics, Karolinska Institute, Stockholm, Sweden; linn.oijerstedt@ki.se

Correction notice This article has been corrected since it was first published online. The 'Results' heading has been added in the text.

Twitter Harro Seelaar @HarroSeelaar and Simon Ducharme @sducharme66

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Collaborators Genetic Frontotemporal Dementia Initiative (GENFI): Sónia Afonso (Instituto Ciencias Nucleares Aplicadas a Saude, Universidade de Coimbra, Coimbra, Portugal), Maria Rosario Almeida (Faculty of Medicine, University of Coimbra, Coimbra, Portugal), Sarah Anderl-Straub (Department of Neurology, University of Ulm, Ulm, Germany), Anna Antonell (Alzheimer's disease and Other Cognitive Disorders Unit, Neurology Service, Hospital Clínic, Barcelona, Spain), Silvana Archetti (Biotechnology Laboratory,

Department of Diagnostics, ASST Brescia Hospital, Brescia, Italy), Andrea Arighi (Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurodegenerative Diseases Unit, Milan, Italy; University of Milan, Centro Dino Ferrari, Milan, Italy), Mircea Balasa (Alzheimer's disease and Other Cognitive Disorders Unit, Neurology Service, Hospital Clínic, Barcelona, Spain), Myriam Barandiaran (Cognitive Disorders Unit, Department of Neurology, Donostia University Hospital, San Sebastian, Gipuzkoa, Spain; Neuroscience Area, Biodonostia Health Research Insitute, San Sebastian, Gipuzkoa, Spain), Nuria Bargalló (Imaging Diagnostic Center, Hospital Clínic, Barcelona, Spain), Robart Bartha (Department of Medical Biophysics, The University of Western Ontario, London, Ontario, Canada; Centre for Functional and Metabolic Mapping, Robarts Research Institute, The University of Western Ontario, London, Ontario, Canada), Benjamin Bender (Department of Diagnostic and Interventional Neuroradiology, University of Tübingen, Tübingen, Germany), Alberto Benussi (Centre for Neurodegenerative Disorders, Department of Clinical and Experimental Sciences, University of Brescia, Italy), Luisa Benussi (Istituto di Ricovero e Cura a Carattere Scientifico Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy), Valentina Bessi (Department of Neuroscience, Psychology, Drug Research and Child Health, University of Florence, Florence, Italy), Giuliano Binetti (Istituto di Ricovero e Cura a Carattere Scientifico Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy), Sandra Black (Sunnybrook Health Sciences Centre, Sunnybrook Research Institute, University of Toronto, Toronto, Canada), Martina Bocchetta (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Sergi Borrego-Ecija (Alzheimer's disease and Other Cognitive Disorders Unit, Neurology Service, Hospital Clínic, Barcelona, Spain), Jose Bras (Center for Neurodegenerative Science, Van Andel Institute, Grand Rapids, Michigan, MI 49503, USA), Rose Bruffaerts (Laboratory for Cognitive Neurology, Department of Neurosciences, KU Leuven, Leuven, Belgium), Marta Cañada (CITA Alzheimer, San Sebastian, Gipuzkoa, Spain), Valentina Cantoni (Centre for Neurodegenerative Disorders, Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy), Paola Caroppo (Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy), David Cash (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Miguel Castelo-Branco (Faculty of Medicine, University of Coimbra, Coimbra, Portugal), Rhian Convery (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Thomas Cope (Department of Clinical Neuroscience, University of Cambridge, Cambridge, UK), Giuseppe Di Fede (Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy), Alina Díez (Neuroscience Area, Biodonostia Health Research Insitute, San Sebastian, Gipuzkoa, Spain), Diana Duro Faculty of Medicine, University of Coimbra, Coimbra, Portugal), Chiara Fenoglio (Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurodegenerative Diseases Unit, Milan, Italy; University of Milan, Centro Dino Ferrari, Milan, Italy), Camilla Ferrari (Department of Neuroscience, Psychology, Drug Research and Child Health, University of Florence, Florence, Italy), Catarina B. Ferreira (Laboratory of Neurosciences, Institute of Molecular Medicine, Faculty of Medicine, University of Lisbon, Lisbon, Portugal), Nick Fox (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Morris Freedman (Baycrest Health Sciences, Rotman Research Institute, University of Toronto, Toronto, Canada), Giorgio Fumagalli (Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurodegenerative Diseases Unit, Milan, Italy; University of Milan, Centro Dino Ferrari, Milan, Italy), Alazne Gabilondo (Neuroscience Area, Biodonostia Health Research Insitute, San Sebastian, Gipuzkoa, Spain), Roberto Gasparotti (Neuroradiology Unit, University of Brescia, Brescia, Italy), Serge Gauthier (Alzheimer Disease Research Unit, McGill Centre for Studies in Aging, Department of Neurology & Neurosurgery, McGill University, Montreal, Québec, Canada), Stefano Gazzina (Neurology, ASST Brescia Hospital, Brescia, Italy), Giorgio Giaccone (Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy), Ana Gorostidi (Neuroscience Area, Biodonostia Health Research Insitute, San Sebastian, Gipuzkoa, Spain), Caroline Greaves (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Rita Guerreiro (Center for Neurodegenerative Science, Van Andel Institute, Grand Rapids, Michigan, MI 49503, USA), Carolin Heller (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Tobias Hoegen (Neurologische Klinik, Ludwig-Maximilians-Universität München, Munich, Germany), Begoña Indakoetxea (Cognitive Disorders Unit, Department of Neurology, Donostia University Hospital, San Sebastian, Gipuzkoa, Spain; Neuroscience Area, Biodonostia Health Research Insitute, San Sebastian, Gipuzkoa, Spain), Hans-Otto Karnath (Division of Neuropsychology, Hertie-Institute for Clinical Brain Research and Center of Neurology, University of Tübingen, Tübingen, Germany), Ron Keren (The University Health Network, Toronto Rehabilitation Institute, Toronto, Canada), Tobias Langheinrich (Division of Neuroscience and Experimental Psychology, Wolfson Molecular Imaging Centre, University of Manchester, Manchester, UK, Manchester Centre for Clinical Neurosciences, Department of Neurology, Salford Royal NHS Foundation Trust, Manchester, UK), Maria João Leitão (Centre of Neurosciences and Cell Biology, Universidade de Coimbra, Coimbra, Portugal), Albert Lladó (Alzheimer's disease and Other Cognitive Disorders Unit, Neurology Service, Hospital Clínic, Barcelona, Spain), Gemma Lombardi (Department of Neuroscience, Psychology, Drug Research and Child Health, University of Florence, Florence, Italy), Sandra Loosli (Neurologische Klinik, Ludwig-Maximilians-Universität München, Munich, Germany), Carolina Maruta (Laboratory of Language Research, Centro de Estudos Egas Moniz, Faculty of Medicine, University of Lisbon, Lisbon, Portugal), Simon Mead (MRC Prion Unit, Department of Neurodegenerative Disease, UCL Institute of Neurology, Queen Square, London, UK), Lieke Meeter (Department of Neurology, Erasmus Medical Center, Rotterdam, Netherlands), Gabriel Miltenberger (Faculty of Medicine, University of Lisbon, Lisbon, Portugal), Rick van Minkelen (Department of Clinical Genetics, Erasmus Medical Center, Rotterdam, Netherlands, Sara Mitchell (Sunnybrook Health Sciences Centre, Sunnybrook Research Institute, University of Toronto, Toronto, Canada), Katrina Moore (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Benedetta Nacmias (Department of Neuroscience, Psychology, Drug Research and Child Health, University of Florence, Florence, Italy), Jennifer Nicholas (Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, UK), Jaume Olives (Alzheimer's disease and Other Cognitive Disorders Unit, Neurology Service, Hospital Clínic, Barcelona, Spain), Sebastien Ourselin (School of Biomedical Engineering & Imaging Sciences, King's College London, London, UK), Alessandro Padovani (Centre for Neurodegenerative Disorders, Department of Clinical and Experimental Sciences, University of Brescia, Italy), Jessica Panman (Department of Neurology, Erasmus Medical Center, Rotterdam, Netherlands), Janne M. Papma (Department of Neurology, Erasmus Medical Center, Rotterdam, Netherlands), Georgia Peakman (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Michela Pievani (Istituto di Ricovero e Cura a Carattere Scientifico Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy), Yolande Pijnenburg (Amsterdam University Medical Centre, Amsterdam VUmc, Amsterdam, Netherlands), Cristina Polito (Department of Biomedical, Experimental and Clinical Sciences "Mario Serio", Nuclear Medicine Unit, University of Florence, Florence, Italy), Enrico Premi (Stroke Unit, ASST Brescia Hospital, Brescia, Italy), Sara Prioni (Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy), Catharina Prix (Neurologische Klinik, Ludwig-Maximilians-Universität München, Munich, Germany), Rosa Rademakers (Department of Neurosciences, Mayo Clinic, Jacksonville, Florida, USA), Veronica Redaelli (Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy), Tim Rittman (Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK), Ekaterina Rogaeva (Tanz Centre for Research in Neurodegenerative Diseases, University of Toronto, Toronto, Canada), Pedro Rosa-Neto (Translational Neuroimaging Laboratory, McGill Centre for Studies in Aging, McGill University, Montreal, Québec, Canada), Giacomina Rossi Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy), Martin Rosser (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Beatriz Santiago (Neurology Department, Centro Hospitalar e Universitario de Coimbra, Coimbra, Portugal), Elio Scarpini (Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurodegenerative Diseases Unit, Milan, Italy; University of Milan, Centro Dino Ferrari, Milan, Italy), Sonja Schönecker Neurologische Klinik, Ludwig-Maximilians-Universität München, Munich, Germany), Elisa Semler (Department of Neurology, University of Ulm, Ulm), Rachelle Shafei (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Christen Shoesmith (Department of Clinical Neurological Sciences, University of Western Ontario, London, Ontario, Canada), Miguel Tábuas-Pereira (Neurology Department, Centro Hospitalar e Universitario de Coimbra, Coimbra, Portugal), Mikel Tainta (Neuroscience Area, Biodonostia Health Research Insitute, San Sebastian, Gipuzkoa, Spain), Ricardo Taipa (Neuropathology Unit and Department of Neurology, Centro Hospitalar do Porto - Hospital de Santo António, Oporto, Portugal), David Tang-Wai (The University Health Network, Krembil Research Institute, Toronto, Canada), David L Thomas (Neuroimaging Analysis Centre, Department of Brain Repair and Rehabilitation, UCL Institute of Neurology, Queen Square, London, UK), Paul Thompson (Division of Neuroscience and Experimental Psychology, Wolfson Molecular Imaging Centre, University of Manchester, Manchester, UK), Håkan Thonberg (Center for Alzheimer Research, Division of Neurogeriatrics, Karolinska Institutet, Stockholm, Sweden), Carolyn Timberlake (Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK), Pietro Tiraboschi (Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy), Emily Todd (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Philip Van Damme (Neurology Service, University Hospitals Leuven, Belgium; Laboratory for Neurobiology, VIB-KU Leuven Centre for Brain Research, Leuven, Belgium), Mathieu Vandenbulcke (Geriatric Psychiatry Service, University Hospitals Leuven, Belgium; Neuropsychiatry, Department of Neurosciences, KU Leuven, Leuven, Belgium), Michele Veldsman (Nuffield Department of Clinical Neurosciences, Medical Sciences Division, University of Oxford, Oxford, UK), Ana Verdelho (Department of Neurosciences and Mental Health,

Centro Hospitalar Lisboa Norte - Hospital de Santa Maria & Faculty of Medicine, University of Lisbon, Lisbon, Portugal), Jorge Villanua (OSATEK, University of Donostia, San Sebastian, Gipuzkoa, Spain), Jason Warren (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Carlo Wilke Department of Neurodegenerative Diseases, Hertie-Institute for Clinical Brain Research and Center of Neurology, University of Tübingen, Tübingen, Germany; Center for Neurodegenerative Diseases (DZNE), Tübingen, Germany), Ione Woollacott (Department of Neurodegenerative Disease, Dementia Research Centre, UCL Institute of Neurology, Queen Square, London, UK), Elisabeth Wlasich (Neurologische Klinik, Ludwig-Maximilians-Universität München, Munich, Germany), Henrik Zetterberg (Dementia Research Institute, Department of Neurodegenerative Disease, UCL Institute of Neurology, Queen Square, London, UK), Miren Zulaica (Neuroscience Area, Biodonostia Health Research Insitute, San Sebastian, Gipuzkoa, Spain).

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ORCID iDs
Linn Öijerstedt http://orcid.org/0000-0003-0635-6377
John Cornelis van Swieten http://orcid.org/0000-0001-6278-6844
Lize C Jiskoot http://orcid.org/0000-0002-1120-1858
Harro Seelaar http://orcid.org/0000-0003-1989-7527
Barbara Borroni http://orcid.org/0000-0001-9340-9814
Daniela Galimberti http://orcid.org/0000-0002-9284-5953
James Benedict Rowe http://orcid.org/0000-0001-7216-8679
Elizabeth Finger http://orcid.org/0000-0003-4461-7427
Simon Ducharme http://orcid.org/0000-0002-7309-1113
Alexander Gerhard http://orcid.org/0000-0002-8071-6062
Adrian Danek http://orcid.org/0000-0001-8857-5383
Markus Otto http://orcid.org/0000-0002-6647-5944
Sandro Sorbi http://orcid.org/0000-0002-0380-6670
Jonathan Daniel Rohrer http://orcid.org/0000-0002-6155-8417

REFERENCES

1 Ghetti B, Buratti E, Boeve B. *Frontotemporal dementias*. 1st ed. Springer International Publishing, 2021: 320.
2 Calamia M, Markon K, Tranel D. Scoring higher the second time around: meta-analyses of practice effects in neuropsychological assessment. *Clin Neuropsychol* 2012;26:543–70.
3 Jutten RJ, Grandoit E, Foldi NS, *et al*. Lower practice effects as a marker of cognitive performance and dementia risk: a literature review. *Alzheimers Dement* 2020;12:e12055.
4 Duff K. Current topics in science and practice evidence-based indicators of neuropsychological change in the individual patient: relevant concepts and methods. *Arch Clin Neuropsychol* 2012.
5 Hassenstab J, Ruvolo D, Jasielec M, *et al*. Absence of practice effects in preclinical Alzheimer's disease. *Neuropsychology* 2015;29:940–8.