Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

Supplementary references

61. Jack Jr CR, Knopman DS, Jagust WJ, et al. Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. The Lancet Neurology 2010;9(1):119-28.

62. Stamer K, Vogel R, Thies E, et al. Tau blocks traffic of organelles, neurofilaments, and APP vesicles in neurons and enhances oxidative stress. The Journal of cell biology 2002;156(6):1051-63.

63. Spires-Jones TL, Hyman BT. The intersection of amyloid beta and tau at synapses in Alzheimer's disease. Neuron 2014;82(4):756-71.

64. Ding X, Bucholc M, Wang H, et al. A hybrid computational approach for efficient Alzheimer's disease classification based on heterogeneous data. Sci Rep 2018;8(1):1-10.

65. Ingram RU, Halai AD, Pobric G, et al. Graded, multi dimensional intragroup and intergroup variations in primary progressive aphasia and post stroke aphasia. bioRxiv 2019

66. Boxer AL, Yu J-T, Golbe LI, et al. Advances in progressive supranuclear palsy: new diagnostic criteria, biomarkers, and therapeutic approaches. The Lancet Neurology 2017;16(7):552-63.

67. Crutch SJ, Schott JM, Rabinovici GD, et al. Consensus classification of posterior cortical atrophy. Alzheimer's & Dementia 2017;13(8):870-84.

68. Park HK, Park KH, Yoon B, et al. Clinical characteristics of parkinsonism in frontotemporal dementia according to subtypes. J Neurol Sci 2017;372:51-56.

69. Lillo P, Hodges JR. Frontotemporal dementia and motor neurone disease: overlapping clinic-pathological disorders. J Clin Neurosci 2009;16(9):1131-35.

70. Armstrong MJ, Litvan I, Lang AE, et al. Criteria for the diagnosis of corticobasal degeneration. Neurology 2013;80(5):496-503. doi: 10.1212/WNL.0b013e31827f0fd1 [published Online First: 2013/01/30]

71. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's & dementia 2011;7(3):263-69.

72. Mills SM, Mallmann J, Santacruz AM, et al. Preclinical trials in autosomal dominant AD: implementation of the DIAN-TU trial. Rev Neurol (Paris) 2013;169(10):737-43.

73. Tabrizi SJ, Langbehn DR, Leavitt BR, et al. Biological and clinical manifestations of Huntington's disease in the longitudinal TRACK-HD study: cross-sectional analysis of baseline data. The Lancet Neurology 2009;8(9):791-801.

74. Klöppel S, Gregory S, Scheller E, et al. Compensation in preclinical Huntington's disease: evidence from the track-on HD study. EBioMedicine 2015;2(10):1420-29.

75. Vemuri P, Simon G, Kantarci K, et al. Antemortem differential diagnosis of dementia pathology using structural MRI: Differential-STAND. Neuroimage 2011;55(2):522-31.

76. Koikkalainen J, Rhodius-Meester H, Tolonen A, et al. Differential diagnosis of neurodegenerative diseases using structural MRI data. NeuroImage: Clinical 2016;11:435-49.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

77. Hentschel F, Kreis M, Damian M, et al. The clinical utility of structural neuroimaging with MRI for diagnosis and differential diagnosis of dementia: a memory clinic study. International Journal of Geriatric Psychiatry: A journal of the psychiatry of late life and allied sciences 2005;20(7):645-50.

78. Sørensen L, Igel C, Pai A, et al. Differential diagnosis of mild cognitive impairment and Alzheimer's disease using structural MRI cortical thickness, hippocampal shape, hippocampal texture, and volumetry. NeuroImage: Clinical 2017;13:470-82.

79. Bocchetta M, Espinosa MdMI, Lashley T, et al. In vivo staging of frontotemporal lobar degeneration TDP-43 type C pathology. Alzheimers Res Ther 2020;12(1):1-8.

80. Ashburner J, Csernansk JG, Davatzikos C, et al. Computer-assisted imaging to assess brain structure in healthy and diseased brains. The Lancet Neurology 2003;2(2):79-88.

81. Apostolova LG, Thompson PM, Green AE, et al. 3D comparison of low, intermediate, and advanced hippocampal atrophy in MCI. Hum Brain Mapp 2010;31(5):786-97.

82. Thompson PM, Hayashi KM, De Zubicaray G, et al. Dynamics of gray matter loss in Alzheimer's disease. J Neurosci 2003;23(3):994-1005.

83. Thompson PM, Hayashi KM, Dutton RA, et al. Tracking Alzheimer's disease. Ann N Y Acad Sci 2007;1097:183.

84. Frisoni GB, Fox NC, Jack CR, et al. The clinical use of structural MRI in Alzheimer disease. Nature Reviews Neurology 2010;6(2):67-77.

85. Foster NL, Heidebrink JL, Clark CM, et al. FDG-PET improves accuracy in distinguishing frontotemporal dementia and Alzheimer's disease. Brain 2007;130(10):2616-35.

86. Herholz K. FDG PET and differential diagnosis of dementia. Alzheimer Dis Assoc Disord 1995

87. Martin WH, Delbeke D, Patton JA, et al. FDG-SPECT: correlation with FDG-PET. Journal of nuclear medicine: official publication, Society of Nuclear Medicine 1995;36(6):988-95.

88. Mielke R, Pietrzyk U, Jacobs A, et al. HMPAO SPET and FDG PET in Alzheimer's disease and vascular dementia: comparison of perfusion and metabolic pattern. Eur J Nucl Med 1994;21(10):1052-60.

89. Messa C, Perani D, Lucignani G, et al. High-resolution technetium-99m-HMPAO SPECT in patients with probable Alzheimer's disease: comparison with fluorine-18-FDG PET. 1994

90. Van Dyck CH, Nygaard HB, Chen K, et al. Effect of AZD0530 on cerebral metabolic decline in alzheimer disease: a randomized clinical trial. JAMA neurology 2019;76(10):1219-29.

91. Johnson KA, Minoshima S, Bohnen NI, et al. Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. J Nucl Med 2013;54(3):476-90.

92. Ossenkoppele R, Jansen WJ, Rabinovici GD, et al. Prevalence of amyloid PET positivity in dementia syndromes: a meta-analysis. JAMA 2015;313(19):1939-50.

93. Sevigny J, Suhy J, Chiao P, et al. Amyloid PET screening for enrichment of early-stage Alzheimer disease clinical trials. Alzheimer Dis Assoc Disord 2016;30(1):1-7.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance
placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

94. Mattsson N, Carrillo MC, Dean RA, et al. Revolutionizing Alzheimer's disease and clinical trials through biomarkers. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring 2015;1(4):412-19.

95. Hansson O, Seibyl J, Stomrud E, et al. CSF biomarkers of Alzheimer's disease concord with amyloid-β PET and predict clinical progression: A study of fully automated immunoassays in BioFINDER and ADNI cohorts. Alzheimer's & Dementia 2018;14(11):1470-81.

96. Thijssen EH, La Joie R, Wolf A, et al. Diagnostic value of plasma phosphorylated tau181 in Alzheimer's disease and frontotemporal lobar degeneration. Nat Med 2020;26(3):387-97. doi: 10.1038/s41591-020-0762-2

97. Mielke MM, Hagen CE, Xu J, et al. Plasma phospho-tau181 increases with Alzheimer's disease clinical severity and is associated with tau-and amyloid-positron emission tomography. Alzheimer's & Dementia 2018;14(8):989-97.

98. Braak H, Braak E. Neuropathological stageing of Alzheimer-related changes. Acta Neuropathol 1991;82(4):239-59.

99. Braak H, Braak E. Staging of Alzheimer's disease-related neurofibrillary changes. Neurobiol Aging 1995;16(3):271-78.

100. Braak H, Del Tredici K. The preclinical phase of the pathological process underlying sporadic Alzheimer's disease. Brain 2015;138(10):2814-33.

101. Fleisher AS, Chen K, Quiroz YT, et al. Florbetapir PET analysis of amyloid-β deposition in the presenilin 1 E280A autosomal dominant Alzheimer's disease kindred: a cross-sectional study. The Lancet Neurology 2012;11(12):1057-65.

102. Utianski RL, Botha H, Whitwell JL, et al. Longitudinal flortaucipir ([18F] AV-1451) PET uptake in Semantic Dementia. Neurobiol Aging 2020

103. Tagai K, Ono M, Kubota M, et al. High-Contrast In Vivo Imaging of Tau Pathologies in Alzheimer's and Non-Alzheimer's Disease Tauopathies. Neuron 2020 doi: 10.1016/j.neuron.2020.09.042 [published Online First: 2020/10/31]

104. Chiotis K, Savitcheva I, Poulakis K, et al. [18 F] THK5317 imaging as a tool for predicting prospective cognitive decline in Alzheimer's disease. Mol Psychiatry 2020:1-13.

105. Goedert M, Wischik C, Crowther R, et al. Cloning and sequencing of the cDNA encoding a core protein of the paired helical filament of Alzheimer disease: identification as the microtubule-associated protein tau. Proceedings of the National Academy of Sciences 1988;85(11):4051-55.

106. Ballatore C, Lee VM-Y, Trojanowski JQ. Tau-mediated neurodegeneration in Alzheimer's disease and related disorders. Nature reviews Neuroscience 2007;8(9):663.

107. de Calignon A, Polydoro M, Suárez-Calvet M, et al. Propagation of tau pathology in a model of early Alzheimer's disease. Neuron 2012;73(4):685-97.

108. Bloom GS. Amyloid-β and tau: the trigger and bullet in Alzheimer disease pathogenesis. JAMA neurology 2014;71(4):505-08.

109. Maruyama M, Shimada H, Suhara T, et al. Imaging of tau pathology in a tauopathy mouse model and in Alzheimer patients compared to normal controls. Neuron 2013;79(6):1094-108.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance
placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

110. Okamura N, Furumoto S, Fodero-Tavoletti MT, et al. Non-invasive assessment of Alzheimer's disease neurofibrillary pathology using 18F-THK5105 PET. Brain 2014;137(6):1762-71.

111. Chien DT, Bahri S, Szardenings AK, et al. Early clinical PET imaging results with the novel PHF-tau radioligand [F-18]-T807. Journal of Alzheimer's Disease 2013;34(2):457-68.

112. Xia C-F, Arteaga J, Chen G, et al. [18 F] T807, a novel tau positron emission tomography imaging agent for Alzheimer's disease. Alzheimer's & Dementia 2013;9(6):666-76.

113. Marquié M, Normandin MD, Vanderburg CR, et al. Validating novel tau positron emission tomography tracer [F-18]-AV-1451 (T807) on postmortem brain tissue. Ann Neurol 2015;78:787-800. doi: 10.1002/ana.24517

114. Schöll M, Lockhart SN, Schonhaut DR, et al. PET imaging of tau deposition in the aging human brain. Neuron 2016;89(5):971-82.

115. Schöll M, Ossenkoppele R, Strandberg O, et al. Distinct 18F-AV-1451 tau PET retention patterns in early-and late-onset Alzheimer's disease. Brain 2017

116. Schwarz AJ, Yu P, Miller BB, et al. Regional profiles of the candidate tau PET ligand 18F-AV-1451 recapitulate key features of Braak histopathological stages. Brain 2016;139(5):1539-50.

117. Ossenkoppele R, Schonhaut DR, Schöll M, et al. Tau PET patterns mirror clinical and neuroanatomical variability in Alzheimer's disease. Brain 2016:aww027.

118. Dickson DW, Ahmed Z, Algom AA, et al. Neuropathology of variants of progressive supranuclear palsy. Curr Opin Neurol 2010;23(4):394-400. doi: 10.1097/WCO.0b013e32833be924 [published Online First: 2010/07/09]

119. Buée L, Delacourte A. Comparative biochemistry of tau in progressive supranuclear palsy, corticobasal degeneration, FTDP-17 and Pick's disease. Brain Pathol 1999;9(4):681-93.

120. Hodges JR, Davies RR, Xuereb JH, et al. Clinicopathological correlates in frontotemporal dementia. Ann Neurol 2004;56(3):399-406.

121. Dickson DW, Kouri N, Murray ME, et al. Neuropathology of frontotemporal lobar degeneration-tau (FTLD-tau). J Mol Neurosci 2011;45(3):384-89.

122. Compta Y, Parkkinen L, O'Sullivan SS, et al. Lewy-and Alzheimer-type pathologies in Parkinson's disease dementia: which is more important? Brain 2011;134(5):1493-505.

123. Mak E, Nicastro N, Malpetti M, et al. Imaging tau burden in dementia with Lewy bodies using [18F]-AV1451 positron emission tomography. Neurobiol Aging in press

124. Arai T, Ikeda K, Akiyama H, et al. Distinct isoforms of tau aggregated in neurons and glial cells in brains of patients with Pick's disease, corticobasal degeneration and progressive supranuclear palsy. Acta Neuropathol 2001;101(2):167-73.

125. Fitzpatrick AW, Falcon B, He S, et al. Cryo-EM structures of tau filaments from Alzheimer's disease. Nature 2017;547(7662):185-90.

126. Falcon B, Zhang W, Murzin AG, et al. Structures of filaments from Pick's disease reveal a novel tau protein fold. Nature 2018;561(7721):137-40.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

127. Jones DT, Knopman DS, Graff-Radford J, et al. In vivo F-AV-1451 tau-PET signal in MAPT mutation carriers varies by expected tau isoforms. Neurology 2018 doi: 10.1212/WNL.0000000000005117

128. Smith R, Scholl M, Widner H, et al. In vivo retention of 18 F-AV-1451 in corticobasal syndrome. Neurology 2017:1-10.

129. Bevan-Jones WR, Cope TE, Passamonti L, et al. [18F]AV-1451 PET in behavioral variant frontotemporal dementia due to MAPT mutation. Annals of Clinical and Translational Neurology 2016;3(12):940-47. doi: 10.1002/acn3.366

130. Smith R, Puschmann A, Schöll M, et al. 18F-AV-1451 tau PET imaging correlates strongly with tau neuropathology in MAPT mutation carriers. Brain 2016:aww163.

131. Hodges JR, Mitchell J, Dawson K, et al. Semantic dementia: demography, familial factors and survival in a consecutive series of 100 cases. Brain 2010;133(1):300-06.

132. Spinelli EG, Mandelli ML, Miller ZA, et al. Typical and atypical pathology in primary progressive aphasia variants. Ann Neurol 2017;81(3):430-43.

133. Broce I, Karch CM, Wen N, et al. Immune-related genetic enrichment in frontotemporal dementia : An analysis of genome-wide association studies. PLoS Med 2018:1-20.

134. Guerreiro RJ, Lohmann E, Bras JM, et al. Using Exome Sequencing to Reveal Mutations in TREM2 Presenting as a Frontotemporal Dementia-like Syndrome Without Bone Involvement. JAMA Neurology 2013;70:78-84. doi: 10.1001/jamaneurol.2013.579

135. Rayaprolu S, Mullen B, Baker M, et al. TREM2 in neurodegeneration : evidence for association of the p . R47H variant with frontotemporal dementia and Parkinson ' s disease. Mol Neurodegener 2013;8:1-5.

136. Miller ZA, Rankin KP, Graff-radford NR, et al. TDP-43 frontotemporal lobar degeneration and autoimmune disease. Jornal of neurology, neurosurgery and psychiatry 2013;84:956-62. doi: 10.1136/jnnp-2012-304644

137. Miller ZA, Sturm VE, Camsari GB, et al. Increased prevalence of autoimmune disease within C9 and FTD/MND cohorts Completing the picture. Neurology: Neuroimmunology and NeuroInflammation 2016;3:1-9. doi: 10.1212/NXI.0000000000000301

138. Lant SB, Robinson AC, Thompson JC, et al. Patterns of microglial cell activation in frontotemporal lobar degeneration. Neuropathol Appl Neurobiol 2014;40(6):686-96. doi: 10.1111/nan.12092

139. Venneti S, Wang G, Nguyen J, et al. The Positron Emission Tomography Ligand DAA1106 Binds With High Affinity to Activated Microglia in Human Neurological Disorders. J Neuropathol Exp Neurol 2008;67:1001-10.

140. Sjogren M, Folkesson S, Blennow K, et al. Increased intrathecal inflammatory activity in frontotemporal dementia: pathophysiological implications. J Neurol Neurosur Ps 2004;75:1107-11. doi: 10.1136/jnnp.2003.019422

141. Woollacott IOC, Nicholas JM, Heslegrave A, et al. Cerebrospinal fluid soluble TREM2 levels in frontotemporal dementia differ by genetic and pathological subgroup. Alzheimer's Research and Therapy 2018;10:1-14. doi: 10.1186/s13195-018-0405-8

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

142. Bhaskar K, Konerth M, Kokiko-cochran ON, et al. Regulation of Tau Pathology by the Microglial Fractalkine Receptor. Neuron 2010;68:19-31. doi: 10.1016/j.neuron.2010.08.023

143. Yin F, Banerjee R, Thomas B, et al. Exaggerated inflammation , impaired host defense , and neuropathology in progranulin-deficient mice. The journal of experimental medicine 2010;207:117-28. doi: 10.1084/jem.20091568

144. Yoshiyama Y, Higuchi M, Zhang B, et al. Synapse Loss and Microglial Activation Precede Tangles in a P301S Tauopathy Mouse Model. Neuron 2007;53:337-51. doi: 10.1016/j.neuron.2007.01.010

145. Gerhard A, Trender-Gerhard I, Turkheimer F, et al. In vivo imaging of microglial activation with [11C](R)-PK11195 PET in progressive supranuclear palsy. Mov Disord 2006;21(1):89-93. doi: 10.1002/mds.20668

146. Cagnin A, Brooks DJ, Kennedy AM, et al. In-vivo measurement of activated microglia in dementia. Lancet 2001;358(9280):461-7. doi: 10.1016/S0140-6736(01)05625-2

147. Gerhard A, Pavese N, Hotton G, et al. In vivo imaging of microglial activation with [11C](R)-PK11195 PET in idiopathic Parkinson's disease. Neurobiol Dis 2006;21(2):404-12. doi: 10.1016/j.nbd.2005.08.002

148. Schuitemaker A, Kropholler MA, Boellaard R, et al. Microglial activation in Alzheimer's disease: an (R)-[(1)(1)C]PK11195 positron emission tomography study. Neurobiol Aging 2013;34(1):128-36. doi: 10.1016/j.neurobiolaging.2012.04.021

149. Haarman BC, Riemersma-Van der Lek RF, de Groot JC, et al. Neuroinflammation in bipolar disorder - A [(11)C]-(R)-PK11195 positron emission tomography study. Brain Behav Immun 2014;40:219-25. doi: 10.1016/j.bbi.2014.03.016

150. Cagnin A, Rossor M, Sampson EL, et al. In Vivo Detection of Microglial Activation in Frontotemporal Dementia. Ann Neurol 2004;56:894-97. doi: 10.1002/ana.20332

151. Passamonti L, Vazquez Rodriguez P, Hong YT, et al. [11C] PK11195 binding in Alzheimer's disease and progressive supranuclear palsy. Neurology 2017:1-20.

152. Edison P, Archer HA, Gerhard A, et al. Microglia, amyloid, and cognition in Alzheimer's disease: An [11C](R)PK11195-PET and [11C]PIB-PET study. Neurobiol Dis 2008;32(3):412-9. doi: 10.1016/j.nbd.2008.08.001

153. Malpetti M, Passamonti L, Jones PS, et al. Neuroinflammation predicts disease progression in progressive supranuclear palsy. medRxiv 2020

154. Bevan-Jones WR, Cope TE, Jones PS, et al. In vivo evidence for pre-symptomatic neuroinflammation in a MAPT mutation carrier. Annals of clinical and translational neurology 2019;6(2):373-78.

155. Owen DR, Yeo AJ, Gunn RN, et al. An 18-kDa translocator protein (TSPO) polymorphism explains differences in binding affinity of the PET radioligand PBR28. J Cereb Blood Flow Metab 2012;32(1):1-5.

156. Koole M, Schmidt ME, Hijzen A, et al. 18F-JNJ-64413739, a novel PET ligand for the p2x7 ion channel: radiation dosimetry, kinetic modeling, test-retest variability, and occupancy of the p2x7 antagonist JNJ-54175446. J Nucl Med 2019;60(5):683-90.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance
placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

157. Thawkar BS, Kaur G. Inhibitors of NF-κB and P2X7/NLRP3/Caspase 1 pathway in microglia: Novel therapeutic opportunities in neuroinflammation induced early-stage Alzheimer's disease. J Neuroimmunol 2019;326:62-74.

158. Cai Z, Li S, Matuskey D, et al. PET imaging of synaptic density: A new tool for investigation of neuropsychiatric diseases. Neurosci Lett 2019;691:44-50. doi: 10.1016/j.neulet.2018.07.038

159. Tomita S, Fukata M, Nicoll RA, et al. Dynamic interaction of stargazin-like TARPs with cycling AMPA receptors at synapses. Science 2004;303(5663):1508-11.

160. Hughes D, Mallucci GR. The unfolded protein response in neurodegenerative disorders - therapeutic modulation of the PERK pathway. Febs J 2019;286(2):342-55. doi: 10.1111/febs.14422

161. NCT03270579. A Study to Investigate the Regional Brain Kinetics of the Positron Emission Tomography Ligand 18F JNJ-64511070: https://ClinicalTrials.gov/show/NCT03270579.

162. Hawkins RA, Huang S-C, Barrio JR, et al. Estimation of local cerebral protein synthesis rates with L-[1-11C] leucine and PET: methods, model, and results in animals and humans. J Cereb Blood Flow Metab 1989;9(4):446-60.

163. Veronese M, Bertoldo A, Bishu S, et al. A spectral analysis approach for determination of regional rates of cerebral protein synthesis with the L-[1-11C] leucine PET method. J Cereb Blood Flow Metab 2010;30(8):1460-76.

164. Shandal V, Sundaram SK, Chugani DC, et al. Abnormal brain protein synthesis in language areas of children with pervasive developmental disorder: a L-[1-11C]-leucine PET study. J Child Neurol 2011;26(11):1347-54.

165. Schmidt KC, Loutaev I, Quezado Z, et al. Regional rates of brain protein synthesis are unaltered in dexmedetomidine sedated young men with fragile X syndrome: A L-[1-11C] leucine PET study. Neurobiol Dis 2020:104978.

166. Bevan-Jones RW, Cope TE, Jones SP, et al. [18F]AV-1451 binding is increased in frontotemporal dementia due to C9orf72 expansion. Annals of Clinical and Translational Neurology 2018:11-13. doi: 10.1002/acn3.631

167. Spatiotemporal searchlight representational similarity analysis in EMEG source space. 2012 Second International Workshop on Pattern Recognition in NeuroImaging; 2012. IEEE.

168. Acosta-Cabronero J, Milovic C, Mattern H, et al. A robust multi-scale approach to quantitative susceptibility mapping. Neuroimage 2018;183:7-24. doi: 10.1016/j.neuroimage.2018.07.065

169. Rua C, Clarke WT, Driver ID, et al. Multi-centre, multi-vendor reproducibility of 7T QSM and R2* in the human brain: results from the UK7T study. bioRxiv 2020

170. Thomas GEC, Leyland LA, Schrag AE, et al. Brain iron deposition is linked with cognitive severity in Parkinson's disease. J Neurol Neurosur Ps 2020;91(4):418-25. doi: 10.1136/jnnp-2019-322042

171. Brundel M, Heringa SM, de Bresser J, et al. High prevalence of cerebral microbleeds at 7Tesla MRI in patients with early Alzheimer's disease. Journal of Alzheimer's Disease 2012;31(2):259-63.

172. Spallazzi M, Dobisch L, Becke A, et al. Hippocampal vascularization patterns: A high-resolution 7 Tesla time-of-flight magnetic resonance angiography study. Neuroimage Clin 2019;21:101609. doi: 10.1016/j.nicl.2018.11.019

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance
placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

173. Jochems ACC, Blair GW, Stringer MS, et al. Relationship Between Venules and Perivascular Spaces in Sporadic Small Vessel Diseases. Stroke 2020;51(5):1503-06. doi: 10.1161/STROKEAHA.120.029163 [published Online First: 2020/04/09]

174. Wardlaw JM, Benveniste H, Nedergaard M, et al. Perivascular spaces in the brain: anatomy, physiology and pathology. Nat Rev Neurol 2020;16(3):137-53. doi: 10.1038/s41582-020-0312-z [published Online First: 2020/02/26]

175. Valdes Hernandez MDC, Ballerini L, Glatz A, et al. Perivascular spaces in the centrum semiovale at the beginning of the 8th decade of life: effect on cognition and associations with mineral deposition. Brain Imaging Behav 2019 doi: 10.1007/s11682-019-00128-1 [published Online First: 2019/06/30]

176. Francis F, Ballerini L, Wardlaw JM. Perivascular spaces and their associations with risk factors, clinical disorders and neuroimaging features: A systematic review and meta-analysis. Int J Stroke 2019;14(4):359-71. doi: 10.1177/1747493019830321 [published Online First: 2019/02/15]

177. Wiley CA, Lopresti BJ, Venneti S, et al. Carbon 11-labeled Pittsburgh Compound B and carbon 11-labeled (R)-PK11195 positron emission tomographic imaging in Alzheimer disease. Arch Neurol 2009;66(1):60-7. doi: 10.1001/archneurol.2008.511

178. Femminella GD, Ninan S, Atkinson R, et al. Does Microglial Activation Influence Hippocampal Volume and Neuronal Function in Alzheimer's Disease and Parkinson's Disease Dementia? J Alzheimers Dis 2016;51(4):1275-89. doi: 10.3233/JAD-150827

179. Fan Z, Aman Y, Ahmed I, et al. Influence of microglial activation on neuronal function in Alzheimer's and Parkinson's disease dementia. Alzheimers Dement 2015;11(6):608-21 e7. doi: 10.1016/j.jalz.2014.06.016

180. Edison P, Ahmed I, Fan Z, et al. Microglia, amyloid, and glucose metabolism in Parkinson's disease with and without dementia. Neuropsychopharmacology 2013;38:938-49. doi: 10.1038/npp.2012.255

181. Malpetti M, Passamonti L, Rittman T, et al. PET markers of tau and neuroinflammation are co-localized in progressive supranuclear palsy. medRxiv 2019:19010702.

182. Bastos AM, Usrey WM, Adams RA, et al. Canonical microcircuits for predictive coding. Neuron 2012;76(4):695-711. doi: 10.1016/j.neuron.2012.10.038 [published Online First: 2012/11/28]

183. Crossley NA, Mechelli A, Vértes PE, et al. Cognitive relevance of the community structure of the human brain functional coactivation network. Proceedings of the National Academy of Sciences 2013;110(28):11583-88.

184. Smith SM, Fox PT, Miller KL, et al. Correspondence of the brain's functional architecture during activation and rest. Proc Natl Acad Sci U S A 2009;106(31):13040-5. doi: 10.1073/pnas.0905267106

185. Mallucci GR. Prion neurodegeneration: starts and stops at the synapse. Prion 2009;3(4):195-201.

186. Berron D, van Westen D, Ossenkoppele R, et al. Medial temporal lobe connectivity and its associations with cognition in early Alzheimer's disease. Brain 2020;143(4):1233-48. doi: 10.1093/brain/awaa068 [published Online First: 2020/04/07]

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

187. de Rover M, Pironti VA, McCabe JA, et al. Hippocampal dysfunction in patients with mild cognitive impairment: a functional neuroimaging study of a visuospatial paired associates learning task. Neuropsychologia 2011;49(7):2060-70.

188. Dai Z, Yan C, Li K, et al. Identifying and mapping connectivity patterns of brain network hubs in Alzheimer's disease. Cereb Cortex 2014:bhu246.

189. Buckner RL, Sepulcre J, Talukdar T, et al. Cortical hubs revealed by intrinsic functional connectivity: mapping, assessment of stability, and relation to Alzheimer's disease. J Neurosci 2009;29(6):1860-73.

190. Bullmore E, Sporns O. Complex brain networks: graph theoretical analysis of structural and functional systems. Nature Reviews Neuroscience 2009;10(3):186-98.

191. Bullmore E, Horwitz B, Honey G, et al. How good is good enough in path analysis of fMRI data? Neuroimage 2000;11(4):289-301.

192. McColgan P, Seunarine KK, Gregory S, et al. Topological length of white matter connections predicts their rate of atrophy in premanifest Huntington's disease. JCI insight 2017;2(8)

193. Prusiner SB. Some speculations about prions, amyloid, and Alzheimer's disease: Mass Medical Soc, 1984.

194. Baker H, Ridley R, Duchen L, et al. Induction of β (A4)-amyloid in primates by injection of Alzheimer's disease brain homogenate. Mol Neurobiol 1994;8(1):25-39.

195. Goedert M. Alzheimer's and Parkinson's diseases: The prion concept in relation to assembled Aβ, tau, and α-synuclein. Science 2015;349(6248):1255555.

196. Abdelnour F, Voss HU, Raj A. Network diffusion accurately models the relationship between structural and functional brain connectivity networks. Neuroimage 2014;90:335-47.

197. McColgan P, Seunarine KK, Razi A, et al. Selective vulnerability of Rich Club brain regions is an organizational principle of structural connectivity loss in Huntington's disease. Brain 2015;138(11):3327-44.

198. Franzmeier N, Neitzel J, Rubinski A, et al. Functional brain architecture is associated with the rate of tau accumulation in Alzheimer's disease. Nature Communications 2020;11(1):1-17.

199. Franzmeier N, Rubinski A, Neitzel J, et al. Functional connectivity associated with tau levels in ageing, Alzheimer's, and small vessel disease. Brain 2019;142(4):1093-107.

200. Kocagoncu E, Quinn A, Firouzian A, et al. Tau pathology in early Alzheimer's disease is linked to selective disruptions in neurophysiological networks dynamics. Neurobiol Aging 2020

201. Pascual B, Funk Q, Zanotti-Fregonara P, et al. Multimodal 18F-AV-1451 and MRI Findings in Nonfluent Variant of Primary Progressive Aphasia: Possible Insights on Nodal Propagation of Tau Protein Across the Syntactic Network. J Nucl Med 2020;61(2):263-69.

202. Rittman T, Rubinov M, Vértes PE, et al. Regional expression of the MAPT gene is associated with loss of hubs in brain networks and cognitive impairment in Parkinson disease and progressive supranuclear palsy. Neurobiol Aging 2016;48:153-60.

203. Appel SH. A unifying hypothesis for the cause of amyotrophic lateral sclerosis, parkinsonism, and Alzheimer disease. Ann Neurol 1981;10(6):499-505.

204. Schweighauser M, Shi Y, Tarutani A, et al. Structures of α-synuclein filaments from multiple system atrophy. Nature 2020:1-6.

205. Friston KJ, Harrison L, Penny W. Dynamic causal modelling. Neuroimage 2003;19(4):1273-302.

206. Brovelli A, Ding M, Ledberg A, et al. Beta oscillations in a large-scale sensorimotor cortical network: directional influences revealed by Granger causality. Proceedings of the National Academy of Sciences 2004;101(26):9849-54.

207. Huntenburg JM, Bazin P-L, Margulies DS. Large-scale gradients in human cortical organization. Trends in cognitive sciences 2018;22(1):21-31.

208. Hermundstad AM, Bassett DS, Brown KS, et al. Structural foundations of resting-state and task-based functional connectivity in the human brain. Proc Natl Acad Sci U S A 2013;110(15):6169-74. doi: 10.1073/pnas.1219562110

209. Maass A, Berron D, Libby LA, et al. Functional subregions of the human entorhinal cortex. Elife 2015;4 doi: 10.7554/eLife.06426 [published Online First: 2015/06/09]

210. Ranasinghe KG, Hinkley LB, Beagle AJ, et al. Distinct spatiotemporal patterns of neuronal functional connectivity in primary progressive aphasia variants. Brain 2017

211. Hughes LE, Ghosh BC, Rowe JB. Reorganisation of brain networks in frontotemporal dementia and progressive supranuclear palsy. Neuroimage Clin 2013;2:459-68. doi: 10.1016/j.nicl.2013.03.009 [published Online First: 2013/07/16]

212. Zarkali A, McColgan P, Leyland L, et al. Organisational and neuromodulatory underpinnings of structural-functional connectivity decoupling in Parkinson's disease. Communications Biology in press

213. Cannon TD, Keller MC. Endophenotypes in the genetic analyses of mental disorders. Annu Rev Clin Psychol 2006;2:267-90.

214. Ronan L, Alexander-Bloch AF, Wagstyl K, et al. Obesity associated with increased brain age from midlife. Neurobiol Aging 2016;47:63-70.

215. Shafto MA, Tyler LK, Dixon M, et al. The Cambridge Centre for Ageing and Neuroscience (Cam-CAN) study protocol: a cross-sectional, lifespan, multidisciplinary examination of healthy cognitive ageing. BMC Neurol 2014;14:204. doi: 10.1186/s12883-014-0204-1

216. Tsvetanov KA, Henson RN, Tyler LK, et al. Extrinsic and Intrinsic Brain Network Connectivity Maintains Cognition across the Lifespan Despite Accelerated Decay of Regional Brain Activation. J Neurosci 2016;36(11):3115-26. doi: 10.1523/JNEUROSCI.2733-15.2016

217. Tsvetanov KA, Ye Z, Hughes L, et al. Activity and Connectivity Differences Underlying Inhibitory Control Across the Adult Life Span. J Neurosci 2018;38(36):7887-900. doi: 10.1523/JNEUROSCI.2919-17.2018

218. Dickerson BC, Sperling RA. Functional abnormalities of the medial temporal lobe memory system in mild cognitive impairment and Alzheimer's disease: insights from functional MRI studies. Neuropsychologia 2008;46(6):1624-35. doi: 10.1016/j.neuropsychologia.2007.11.030

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

219. Maestú F, Peña J-M, Garcés P, et al. A multicenter study of the early detection of synaptic dysfunction in Mild Cognitive Impairment using Magnetoencephalography-derived functional connectivity. NeuroImage: Clinical 2015;9:103-09.

220. Conijn M, Geerlings M, Biessels G-J, et al. Cerebral microbleeds on MR imaging: comparison between 1.5 and 7T. Am J Neuroradiol 2011;32(6):1043-49.

221. van Veluw SJ, Biessels GJ, Klijn CJ, et al. Heterogeneous histopathology of cortical microbleeds in cerebral amyloid angiopathy. Neurology 2016;86(9):867-71.

222. Huber L, Handwerker DA, Jangraw DC, et al. High-resolution CBV-fMRI allows mapping of laminar activity and connectivity of cortical input and output in human M1. Neuron 2017;96(6):1253-63. e7.

223. Koster R, Chadwick MJ, Chen Y, et al. Big-loop recurrence within the hippocampal system supports integration of information across episodes. Neuron 2018;99(6):1342-54. e6.

224. Maass A, Schutze H, Speck O, et al. Laminar activity in the hippocampus and entorhinal cortex related to novelty and episodic encoding. Nat Commun 2014;5:5547. doi: 10.1038/ncomms6547 [published Online First: 2014/11/27]

225. Terry RD, Masliah E, Salmon DP, et al. Physical basis of cognitive alterations in Alzheimer's disease: synapse loss is the major correlate of cognitive impairment. Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society 1991;30(4):572-80.

226. Zhou L, McInnes J, Wierda K, et al. Tau association with synaptic vesicles causes presynaptic dysfunction. Nature communications 2017;8(1):1-13.

227. Menkes-Caspi N, Yamin HG, Kellner V, et al. Pathological tau disrupts ongoing network activity. Neuron 2015;85(5):959-66.

228. Selkoe DJ, Triller A. Synaptic plasticity and the mechanism of Alzheimer's disease: Springer Science & Business Media 2008.

229. Mucke L, Selkoe DJ. Neurotoxicity of amyloid β-protein: synaptic and network dysfunction. Cold Spring Harb Perspect Med 2012;2(7):a006338.

230. Palmqvist S, Schöll M, Strandberg O, et al. Earliest accumulation of β-amyloid occurs within the default-mode network and concurrently affects brain connectivity. Nature communications 2017;8(1):1-13.

231. Passamonti L, Tsvetanov K, Jones P, et al. Neuroinflammation and functional connectivity in Alzheimer's disease: interactive influences on cognitive performance. J Neurosci 2019;39(36):7218-26.

232. Šišková Z, Justus D, Kaneko H, et al. Dendritic structural degeneration is functionally linked to cellular hyperexcitability in a mouse model of Alzheimer's disease. Neuron 2014;84(5):1023-33.

233. Palop JJ, Mucke L. Network abnormalities and interneuron dysfunction in Alzheimer disease. Nature Reviews Neuroscience 2016;17(12):777-92.

234. Hughes LE, Rittman T, Robbins TW, et al. Reorganization of cortical oscillatory dynamics underlying disinhibition in frontotemporal dementia. Brain 2018;141(8):2486-99.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

235. Stephan KE, Penny WD, Moran RJ, et al. Ten simple rules for dynamic causal modeling. Neuroimage 2010;49(4):3099-109.

236. David O, Kiebel SJ, Harrison LM, et al. Dynamic causal modeling of evoked responses in EEG and MEG. Neuroimage 2006;30(4):1255-72. doi: 10.1016/j.neuroimage.2005.10.045 [published Online First: 2006/02/14]

237. Shaw AD, Hughes LE, Moran R, et al. In Vivo Assay of Cortical Microcircuitry in Frontotemporal Dementia: A Platform for Experimental Medicine Studies. Cereb Cortex 2019 doi: 10.1093/cercor/bhz024

238. Okello A, Koivunen J, Edison P, et al. Conversion of amyloid positive and negative MCI to AD over 3 years An 11C-PIB PET study. Neurology 2009;73(10):754-60.

239. Nordberg A, Carter SF, Rinne J, et al. A European multicentre PET study of fibrillar amyloid in Alzheimer's disease. European journal of nuclear medicine and molecular imaging 2013;40(1):104-14.

240. Vlassenko AG, Mintun MA, Xiong C, et al. Amyloid-beta plaque growth in cognitively normal adults: Longitudinal [11C] Pittsburgh compound B data. Ann Neurol 2011;70(5):857-61.

241. Doraiswamy PM, Sperling R, Johnson K, et al. Florbetapir F 18 amyloid PET and 36-month cognitive decline: a prospective multicenter study. Mol Psychiatry 2014;19(9):1044-51.

242. Chételat G, La Joie R, Villain N, et al. Amyloid imaging in cognitively normal individuals, at-risk populations and preclinical Alzheimer's disease. NeuroImage: Clinical 2013;2:356-65.

243. van Eimeren T, Antonini A, Berg D, et al. Neuroimaging biomarkers for clinical trials in atypical parkinsonian disorders: Proposal for a Neuroimaging Biomarker Utility System. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring 2019;11(1):301-09.

244. Risacher SL, Shen L, West JD, et al. Longitudinal MRI atrophy biomarkers: relationship to conversion in the ADNI cohort. Neurobiol Aging 2010;31(8):1401-18.

245. Staffaroni AM, Cobigo Y, Goh SYM, et al. Individualized atrophy scores predict dementia onset in familial frontotemporal lobar degeneration. Alzheimer's & Dementia 2020;16(1):37-48.

246. Düzel E, Acosta-Cabronero J, Berron D, et al. European Ultrahigh-Field Imaging Network for Neurodegenerative Diseases (EUFIND). Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring 2019;11(1):538-49.

247. Li X, Li D, Li Q, et al. Hippocampal subfield volumetry in patients with subcortical vascular mild cognitive impairment. Sci Rep 2016;6:20873. doi: 10.1038/srep20873

248. Koychev I, Lawson J, Chessell T, et al. Deep and Frequent Phenotyping study protocol: an observational study in prodromal Alzheimer's disease. BMJ open 2019;9(3):e024498.

249. Yang Y, Schmitt HP. Frontotemporal dementia: evidence for impairment of ascending serotoninergic but not noradrenergic innervation. Acta Neuropathol 2001;101(3):256-70.

250. Ye Z, Altena E, Nombela C, et al. Selective serotonin reuptake inhibition modulates response inhibition in Parkinson's disease. Brain 2014;137(4):1145-55.

251. Ye Z, Altena E, Nombela C, et al. Improving response inhibition in Parkinson's disease with atomoxetine. Biol Psychiatry 2015;77(8):740-48.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

J Neurol Neurosurg Psychiatry

252. Borchert RJ, Rittman T, Passamonti L, et al. Atomoxetine enhances connectivity of prefrontal networks in Parkinson's disease. Neuropsychopharmacology 2016;41(8):2171-77.

253. Rae CL, Nombela C, Rodríguez PV, et al. Atomoxetine restores the response inhibition network in Parkinson's disease. Brain 2016;139(8):2235-48.

254. Yuzwa SA, Macauley MS, Heinonen JE, et al. A potent mechanism-inspired O-GlcNAcase inhibitor that blocks phosphorylation of tau in vivo. Nat Chem Biol 2008;4(8):483-90.

255. Ryan JM, Quattropani A, Abd-Elaziz K, et al. O1-12-05: PHASE 1 STUDY IN HEALTHY VOLUNTEERS OF THE O-GLCNACASE INHIBITOR ASN120290 AS A NOVEL THERAPY FOR PROGRESSIVE SUPRANUCLEAR PALSY AND RELATED TAUOPATHIES. Alzheimer's & Dementia 2018;14(7S_Part_4):P251-P51.

256. Sayas CL. Tau-based therapies for Alzheimer's disease: Promising novel neuroprotective approaches. Neuroprotection in Autism, Schizophrenia and Alzheimer's Disease: Elsevier 2020:245-72.

257. van den Oord EJ, Sullivan PF. False discoveries and models for gene discovery. Trends Genet 2003;19(10):537-42.

258. Khalilzadeh J, Tasci AD. Large sample size, significance level, and the effect size: Solutions to perils of using big data for academic research. Tourism Management 2017;62:89-96.

259. Haufe S, Meinecke F, Görgen K, et al. On the interpretation of weight vectors of linear models in multivariate neuroimaging. Neuroimage 2014;87:96-110.

260. Van Essen DC, Smith SM, Barch DM, et al. The WU-Minn human connectome project: an overview. Neuroimage 2013;80:62-79.

261. Harms MP, Somerville LH, Ances BM, et al. Extending the Human Connectome Project across ages: Imaging protocols for the Lifespan Development and Aging projects. Neuroimage 2018;183:972-84.

262. Bauermeister S, Orton C, Thompson S, et al. The dementias platform UK (DPUK) data portal. Eur J Epidemiol 2020;35(6):601-11.

263. Gorgolewski KJ, Auer T, Calhoun VD, et al. The brain imaging data structure, a format for organizing and describing outputs of neuroimaging experiments. Scientific data 2016;3(1):1-9.

264. Niso G, Gorgolewski KJ, Bock E, et al. MEG-BIDS, the brain imaging data structure extended to magnetoencephalography. Scientific data 2018;5(1):1-5.

265. Adhikari BM, Jahanshad N, Shukla D, et al. A resting state fMRI analysis pipeline for pooling inference across diverse cohorts: an ENIGMA rs-fMRI protocol. Brain imaging and behavior 2019;13(5):1453-67.

266. Donovan NJ, Amariglio RE, Zoller AS, et al. Subjective cognitive concerns and neuropsychiatric predictors of progression to the early clinical stages of Alzheimer disease. The American Journal of Geriatric Psychiatry 2014;22(12):1642-51.

267. Dukart J, Mueller K, Barthel H, et al. Meta-analysis based SVM classification enables accurate detection of Alzheimer's disease across different clinical centers using FDG-PET and MRI. Psychiatry Research: Neuroimaging 2013;212(3):230-36.

268. Jo T, Nho K, Saykin AJ. Deep learning in Alzheimer's disease: diagnostic classification and prognostic prediction using neuroimaging data. Front Aging Neurosci 2019;11:220.

269. Mittelstadt BD, Floridi L. The ethics of big data: current and foreseeable issues in biomedical contexts. Science and engineering ethics 2016;22(2):303-41.

270. Knoppers BM, Thorogood AM. Ethics and big data in health. Current Opinion in Systems Biology 2017;4:53-57.

271. Boeve B, Boxer A, Rosen H, et al. The ARTFL LEFFTDS Frontotemporal Lobar Degeneration (ALLFTD) Protocol: Preliminary Data and Future Plans (2081): AAN Enterprises, 2020.

272. Ellis KA, Szoeke C, Bush AI, et al. Rates of diagnostic transition and cognitive change at 18-month follow-up among 1,112 participants in the Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing (AIBL). Int Psychogeriatr 2014;26(4):543-54.

273. Apostolova LG. Longitudinal Early-onset Alzheimer's Disease Study Protocol: https://ClinicalTrials.gov/show/NCT03507257, 2018.

274. Lang AE, Stebbins GT, Wang P, et al. The Cortical Basal ganglia Functional Scale (CBFS): Development and preliminary validation. Parkinsonism Relat Disord 2020

275. Jabbari E, Holland N, Chelban V, et al. Diagnosis across the spectrum of progressive supranuclear palsy and corticobasal syndrome. JAMA neurology 2020;77(3):377-87.

276. Tabrizi SJ, Leavitt BR, Landwehrmeyer GB, et al. Targeting huntingtin expression in patients with Huntington's disease. New England Journal of Medicine 2019;380(24):2307-16.

277. Leyland L-A, Bremner FD, Mahmood R, et al. Visual tests predict dementia risk in Parkinson disease. Neurology: Clinical Practice 2020;10(1):29-39.

278. Zarkali A, McColgan P, Leyland L-A, et al. Fiber-specific white matter reductions in Parkinson hallucinations and visual dysfunction. Neurology 2020;94(14):e1525-e38.

279. Greenland JC, Cutting E, Kadyan S, et al. Azathioprine immunosuppression and disease modification in Parkinson's disease (AZA-PD): a randomised double-blind placebo-controlled phase II trial protocol. BMJ Open 2020