

## 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, Bucholtz 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.

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.

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- $\beta$  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 staging 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. Flortetapir PET analysis of amyloid- $\beta$  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 flortetapir ([<sup>18</sup>F] 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. [<sup>18</sup>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- $\beta$  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.

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.

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

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)1C]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.

157. Thawkar BS, Kaur G. Inhibitors of NF- $\kappa$ B 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 Neurosurg 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

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]

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  $\beta$  (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 A $\beta$ , tau, and  $\alpha$ -synuclein. *Science* 2015;349(6248):1255-555.
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, Vértés 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  $\alpha$ -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

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  $\beta$ -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  $\beta$ -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.

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 serotonergic 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.

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, Quattropiani 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, Szoeki 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