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Title:
Untangling tau imaging

Date:
2016-01-01

Citation:
Villemagne, V. L., Okamura, N. & Rowe, C. C. (2016). Untangling tau imaging. Alzheimer S and Dementia Diagnosis Assessment and Disease Monitoring, 4 (1), pp.39-42. https://doi.org/10.1016/j.dadm.2016.05.001.

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Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring 4 (2016) 39-42

Neuroimaging

Untangling tau imaging

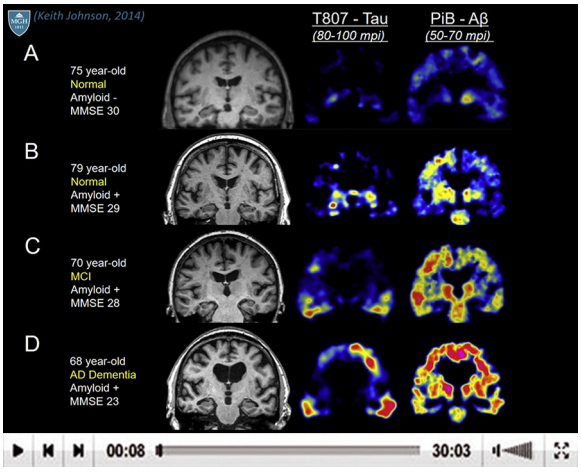
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Abstract In vivo imaging of tau deposits is providing a better understanding of the temporal and spatial tau deposition in the brain, allowing a more comprehensive insight into the causes, diagnoses, and potentially treatment of tauopathies such as Alzheimer's disease, progressive supranuclear palsy, corticobasal syndrome, chronic traumatic encephalopathy, and some variants of frontotemporal lobar degeneration. The assessment of tau deposition in the brain over time will allow a deeper understanding of the relationship between tau and other variables such as cognition, genotype, and neurodegeneration, as well as assessing the role tau plays in ageing. Preliminary human studies suggest that tau imaging could also be used as a diagnostic, prognostic, and theranostic biomarker, as well as a surrogate marker for target engagement, patient recruitment, and efficacy monitoring for disease-specific therapeutic trials.

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Keywords: PET; Tau imaging; Alzheimer's disease; Positron emission tomography; Tauopathies; Dementia



Acknowledgments

We thank Professors Yukitsuda Kudo, Colin Masters, Kazuhiko Yanai, Shozo Furumoto, Drs Ryuichi Harada, Michelle Fodero-Tavoletti, William P. Blatty, Mrs Svetlana Pejoska-Bozinovski, Ms Fiona Lamb, and the Brain Research Institute for their assistance with this study. This review was supported in part by NHMRC Project Grant 1044361. VLV is supported by NHMRC Research Fellowship 1046471. The funding sources had no input into the design of this study, the analysis of data, or writing of the manuscript.

V.L.V. has received speaker honoraria from GE Healthcare, Piramal Imaging, and Avid Radiopharmaceuticals and consulting honoraria from Novartis and Lundbeck. N.O. has received research support from Clino Co. Ltd. THK compounds have been licensed to GE Healthcare. C.C.R. has received speaker honoraria from received speaker and consulting honoraria from GE Healthcare, Piramal Imaging, Avid Radiopharmaceuticals, Navidea, and AstraZeneca.

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http://dx.doi.org/10.1016/j.dadm.2016.05.001
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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.dadm.2016.05.001.

Reference mentioned in this video article can be found here.

References

[1] Chen-Plotkin AS, Lee VM, Trojanowski JQ. TAR DNA-binding protein 43 in neurodegenerative disease. Nat Rev Neurol 2010; 6:211–20.

[2] Rabinovici GD, Miller BL. Frontotemporal lobar degeneration: epidemiology, pathophysiology, diagnosis and management. CNS Drugs 2010;24:375–98.

[3] Seelaar H, Rohrer JD, Pijnenburg YA, Fox NC, van Swieten JC. Clinical, genetic and pathological heterogeneity of frontotemporal dementia: a review. J Neurol Neurosurg Psychiatry 2011;82:476–86.

[4] Klunk WE, Engler H, Nordberg A, Wang Y, Blomqvist G, Holt DP, et al. Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. Ann Neurol 2004;55:306–19.

[5] Rowe CC, Ackerman U, Browne W, Mulligan R, Pike KL, O'Keefe G, et al. Imaging of amyloid beta in Alzheimer's disease with 18F-BAY94-9172, a novel PET tracer: proof of mechanism. Lancet Neurol 2008;7:129–35.

[6] Rowe CC, Pejoska S, Mulligan RS, Jones G, Chan JG, Svensson S, et al. Head-to-head comparison of 11C-PiB and 18F-AZD4694 (NAV4694) for beta-amyloid imaging in aging and dementia. J Nucl Med 2013;54:880–6.

[7] Vandenberghe R, Van Laere K, Ivanoiu A, Salmon E, Bastin C, Triau E, et al. 18F-flutemetamol amyloid imaging in Alzheimer disease and mild cognitive impairment: a phase 2 trial. Ann Neurol 2010;68:319–29.

[8] Wong DF, Rosenberg PB, Zhou Y, Kumar A, Raymont V, Ravert HT, et al. In vivo imaging of amyloid deposition in Alzheimer disease using the radioligand 18F-AV-45 (florbetapir [corrected] F 18). J Nucl Med 2010;51:913–20.

[9] Buee L, Bussiere T, Buee-Scherrer V, Delacourte A, Hof PR. Tau protein isoforms, phosphorylation and role in neurodegenerative disorders. Brain Res Brain Res Rev 2000;33:95–130.

[10] Maas T, Eidenmuller J, Brandt R. Interaction of tau with the neural membrane cortex is regulated by phosphorylation at sites that are modified in paired helical filaments. J Biol Chem 2000;275:15733–40.

[11] Li X, Kumar Y, Zempel H, Mandelkow EM, Biernat J, Mandelkow E. Novel diffusion barrier for axonal retention of Tau in neurons and its failure in neurodegeneration. EMBO J 2011;30:4825–37.

[12] Hernandez F, Avila J. Tauopathies. Cell Mol Life Sci 2007; 64:2219–33.

[13] Arima K. Ultrastructural characteristics of tau filaments in tauopathies: immuno-electron microscopic demonstration of tau filaments in tauopathies. Neuropathology 2006;26:475–83.

[14] Zempel H, Luedtke J, Kumar Y, Biernat J, Dawson H, Mandelkow E, et al. Amyloid-beta oligomers induce synaptic damage via Tau-dependent microtubule severing by TTLL6 and spastin. EMBO J 2013;32:2920–37.

[15] Zempel H, Thies E, Mandelkow E, Mandelkow EM. Abeta oligomers cause localized Ca(2+) elevation, missorting of endogenous Tau into dendrites, Tau phosphorylation, and destruction of microtubules and spines. J Neurosci 2010;30:11938–50.

[16] Braak H, Braak E. Evolution of neuronal changes in the course of Alzheimer's disease. J Neural Transm Suppl 1998;53:127–40.

[17] Delacourte A, David JP, Sergeant N, Buee L, Wattez A, Vermersch P, et al. The biochemical pathway of neurofibrillary degeneration in aging and Alzheimer's disease. Neurology 1999;52:1158–65.

[18] Braak H, Braak E. Frequency of stages of Alzheimer-related lesions in different age categories. Neurobiol Aging 1997;18:351–7.

[19] Serrano-Pozo A, Frosch MP, Masliah E, Hyman BT. Neuropathological Alterations in Alzheimer Disease. Cold Spring Harb Perspect Med 2011;1:a006189.

[20] Guo JL, Lee VM. Seeding of normal Tau by pathological Tau conformers drives pathogenesis of Alzheimer-like tangles. J Biol Chem 2011;286:15317–31.

[21] Mohorko N, Bresjanac M. Tau Protein And Human Tauopathies: An Overview. Zdrav Vestn 2008;77:35–41.

[22] Lee VM, Goedert M, Trojanowski JQ. Neurodegenerative tauopathies. Annu Rev Neurosci 2001;24:1121–59.

[23] McKee AC, Cantu RC, Nowinski CJ, Hedley-Whyte ET, Gavett BE, Budson AE, et al. Chronic traumatic encephalopathy in athletes: progressive tauopathy after repetitive head injury. J Neuropathol Exp Neurol 2009;68:709–35.

[24] Masters CL, Selkoe DJ. Biochemistry of amyloid beta-protein and amyloid deposits in Alzheimer disease. Cold Spring Harb Perspect Med 2012;2:a006262.

[25] Arriagada PV, Growdon JH, Hedley-Whyte ET, Hyman BT. Neurofibrillary tangles but not senile plaques parallel duration and severity of Alzheimer's disease. Neurology 1992;42:631–9.

[26] Rowe CC, Ng S, Ackermann U, Gong SJ, Pike K, Savage G, et al. Imaging beta-amyloid burden in aging and dementia. Neurology 2007; 68:1718–25.

[27] McLean CA, Cherny RA, Fraser FW, Fuller SJ, Smith MJ, Beyreuther K, et al. Soluble pool of Abeta amyloid as a determinant of severity of neurodegeneration in Alzheimer's disease. Ann Neurol 1999;46:860–6.

[28] Zempel H, Mandelkow EM. Linking amyloid-beta and tau: amyloid-beta induced synaptic dysfunction via local wreckage of the neuronal cytoskeleton. Neurodegener Dis 2012;10:64–72.

[29] Ittner LM, Ke YD, Gotz J. Phosphorylated Tau interacts with c-Jun N-terminal kinase-interacting protein 1 (JIP1) in Alzheimer disease. J Biol Chem 2009;284:20909–16.

[30] Price JL, Morris JC. Tangles and plaques in nondemented aging and "preclinical" Alzheimer's disease. Ann Neurol 1999;45:358–68.

[31] Villemagne VL, Fodero-Tavoletti MT, Pike KE, Cappai R, Masters CL, Rowe CC. The ART of Loss: Aβ Imaging in the Evaluation of Alzheimer's Disease and other Dementias. Mol Neurobiol 2008;38:1–15.

[32] Jack CR Jr, Knopman DS, Jagust WJ, Petersen RC, Weiner MW, Aisen PS, et al. Tracking pathophysiological processes in Alzheimer's disease: an updated hypothetical model of dynamic biomarkers. Lancet Neurol 2013;12:207–16.

[33] Jack CR Jr, Knopman DS, Weigand SD, Wiste HJ, Vemuri P, Lowe V, et al. An operational approach to National Institute on Aging-Alzheimer's Association criteria for preclinical Alzheimer disease. Ann Neurol 2012;71:765–75.

[34] Dutra JR, Cortes EP, Vonsattel JP. Update on Hippocampal Sclerosis. Curr Neurol Neurosci Rep 2015;15:592.

[35] Crary JF, Trojanowski JQ, Schneider JA, Abisambra JF, Abner EL, Alafuzoff I, et al. Primary age-related tauopathy (PART): a common pathology associated with human aging. Acta Neuropathol 2014; 128:755–66.

[36] Villemagne VL, Furumoto S, Fodero-Tavoletti MT, Harada R, Mulligan RS, Kudo T, et al. The Challenges of Tau Imaging. Future Neurol 2012;7:409–21.

[37] Villemagne VL, Okamura N. In vivo tau imaging: Obstacles and progress. Alzheimers Dement 2014;10:S254–64.

[38] Villemagne VL, Fodero-Tavoletti MT, Masters CL, Rowe CC. Tau imaging: early progress and future directions. Lancet Neurol 2015; 14:114–24.

[39] Wegmann S, Jung YJ, Chinnathambi S, Mandelkow EM, Mandelkow E, Muller DJ. Human Tau isoforms assemble into ribbon-like fibrils that display polymorphic structure and stability. J Biol Chem 2010;285:27302–13.

[40] Sergeant N, Bretteville A, Hamdane M, Caillet-Boudin ML, Grognet P, Bombois S, et al. Biochemistry of Tau in Alzheimer's disease and related neurological disorders. Expert Rev Proteomics 2008; 5:207–24.
[41] Martin L, Latypova X, Terro F. Post-translational modifications of tau protein: implications for Alzheimer's disease. Neurochem Int 2011; 58:458–71.
[42] Spillantini MG, Goedert M. Tau protein pathology in neurodegenerative diseases. Trends Neurosci 1998;21:428–33.
[43] Rosen RF, Walker LC, Levine H 3rd. PIB binding in aged primate brain: enrichment of high-affinity sites in humans with Alzheimer's disease. Neurobiol Aging 2011;32:223–34.
[44] Ni R, Gillberg PG, Bergfors A, Marutle A, Nordberg A. Amyloid tracers detect multiple binding sites in Alzheimer's disease brain tissue. Brain 2013;136:2217–27.
[45] Scaravilli T, Tolosa E, Ferrer I. Progressive supranuclear palsy and corticobasal degeneration: lumping versus splitting. Mov Disord 2005;20 Suppl 12:S21–8.
[46] Khatoon S, Grundke-Iqbal I, Iqbal K. Levels of normal and abnormally phosphorylated tau in different cellular and regional compartments of Alzheimer disease and control brains. FEBS Lett 1994;351:80–4.
[47] Mukaetova-Ladinska EB, Harrington CR, Roth M, Wischik CM. Biochemical and anatomical redistribution of tau protein in Alzheimer's disease. Am J Pathol 1993;143:565–78.
[48] Naslund J, Haroutunian V, Mohs R, Davis KL, Davies P, Greengard P, et al. Correlation between elevated levels of amyloid beta-peptide in the brain and cognitive decline. JAMA 2000;283:1571–7.
[49] Laruelle M, Slifstein M, Huang Y. Relationships between radiotracer properties and image quality in molecular imaging of the brain with positron emission tomography. Mol Imaging Biol 2003;5:363–75.
[50] Pike VW. PET radiotracers: crossing the blood-brain barrier and surviving metabolism. Trends Pharmacol Sci 2009;30:431–40.
[51] Villemagne VL, Klunk WE, Mathis CA, Rowe CC, Brooks DJ, Hyman BT, et al. Aβ Imaging: feasible, pertinent, and vital to progress in Alzheimer's disease. Eur J Nucl Med Mol Imaging 2012;39:209–19.
[52] Shoghi-Jadid K, Small GW, Agdeppa ED, Kepe V, Ercoli LM, Siddarth P, et al. Localization of neurofibrillary tangles and beta-amyloid plaques in the brains of living patients with Alzheimer disease. Am J Geriatr Psychiatry 2002;10:24–35.
[53] Smid LM, Kepe V, Vinters HV, Bresjanac M, Toyokuni T, Satyamurthy N, et al. Postmortem 3-D Brain Hemisphere Cortical Tau and Amyloid-beta Pathology Mapping and Quantification as a Validation Method of Neuropathology Imaging. J Alzheimers Dis 2013;36:261–74.
[54] Taghavi A, Nasir S, Pickhardt M, Heyny-von Haussen R, Mall G, Mandelkow E, et al. N'-benzylidene-benzohydrazides as novel and selective tau-PHF ligands. J Alzheimers Dis 2011;27:835–43.
[55] Jensen JR, Cisek K, Funk KE, Naphade S, Schafer KN, Kuret J. Research towards tau imaging. J Alzheimers Dis 2011;26 Suppl 3:147–57.
[56] Honson NS, Johnson RL, Huang W, Inglese J, Austin CP, Kuret J. Differentiating Alzheimer disease-associated aggregates with small molecules. Neurobiol Dis 2007;28:251–60.
[57] Kemp S, Storey L, Storey J, Rickard J, Harrington C, Wischik C, inventors; Ligands for aggregated tau molecules. International patent 2010/034982 patent 2010/034982. 2010.
[58] Ono M, Hayashi S, Matsumura K, Kimura H, Okamoto Y, Ihara M, et al. Rhodanine and thiohydantoin derivatives for detecting tau pathology in Alzheimer's brains. ACS Chem Neurosci 2011;2:269–75.
[59] Watanabe H, Ono M, Kimura H, Matsumura K, Yoshimura M, Okamoto Y, et al. Synthesis and biological evaluation of novel oxindole derivatives for imaging neurofibrillary tangles in Alzheimer's disease. Bioorg Med Chem Lett 2012;22:5700–3.
[60] Matsumura K, Ono M, Yoshimura M, Kimura H, Watanabe H, Okamoto Y, et al. Synthesis and biological evaluation of novel styryl benzimidazole derivatives as probes for imaging of neurofibrillary tangles in Alzheimer's disease. Bioorg Med Chem 2013; 21:3356–62.
[61] Bolander A, Kieser D, Voss C, Bauer S, Schon C, Burgold S, et al. Bis(arylvinyl)pyrazines, -pyrimidines, and -pyridazines as imaging agents for tau fibrils and beta-amyloid plaques in Alzheimer's disease models. J Med Chem 2012;55:9170–80.
[62] Honson NS, Jensen JR, Darby MV, Kuret J. Potent inhibition of tau fibrillization with a multivalent ligand. Biochem Biophys Res Commun 2007;363:229–34.
[63] Kudo Y, Furumoto S, Okamura N, inventors; Benzoxazole derivatives. U.S. Patent 2010/0021385 patent 2010.
[64] Szardenings AK, Zhang W, Kolb HC, Cashion DK, Chen G, Kasi D, et al., inventors; Siemens Medical Solutions USA, Inc., assignee. Imaging Agents for Detecting Neurological Disorders. US Patent 2011/0182812 A1 patent 2011/0182812 A1. 2011.
[65] Kudo Y, Susuki M, Suemoto T, Okamura N, Shiomitzu T, Shimazu H, inventors; Quinoline derivative as diagnostic probe for disease with tau protein accumulation. U.S. Patent 7,118,730 patent 2006.
[66] Shao XM, Carpenter GM, Desmond TJ, Sherman P, Quesada CA, Fawaz M, et al. Evaluation of [11C]N-Methyl Lansoprazole as a Radiopharmaceutical for PET Imaging of Tau Neurofibrillary Tangles. ACS Med Chem Lett 2012;3:936–41.
[67] Fawaz MV, Brooks AF, Rodnick ME, Carpenter GM, Shao X, Desmond TJ, et al. High affinity radiopharmaceuticals based upon lansoprazole for PET imaging of aggregated tau in Alzheimer's disease and progressive supranuclear palsy: synthesis, preclinical evaluation, and lead selection. ACS Chem Neurosci 2014;5:718–30.
[68] Maruyama M, Shimada H, Suhara T, Shinotoh H, Ji B, Maeda J, et al. Imaging of Tau Pathology in a Tauopathy Mouse Model and in Alzheimer Patients Compared to Normal Controls. Neuron 2013; 79:1094–108.
[69] Hashimoto H, Kawamura K, Igarashi N, Takei M, Fujishiro T, Aihara Y, et al. Radiosynthesis, photoisomerization, biodistribution, and metabolite analysis of 11C-PBB3 as a clinically useful PET probe for imaging of tau pathology. J Nucl Med 2014;55:1532–8.
[70] Xia CF, Arteaga J, Chen G, Gangadharmath U, Gomez LF, Kasi D, et al. [(18)F]T807, a novel tau positron emission tomography imaging agent for Alzheimer's disease. Alzheimers Dement 2013;9:666–76.
[71] Chien DT, Bahri S, Szardenings AK, Walsh JC, Mu F, Su MY, et al. Early clinical PET imaging results with the novel PHF-tau radioligand [F-18]-T807. J Alzheimers Dis 2013;34:457–68.
[72] Vieira M, Saraiva MJ. Transthyretin: a multifaceted protein. Biomol Concepts 2014;5:45–54.
[73] Johnson KA, Schultz A, Betensky RA, Becker JA, Sepulcre J, Rentz D, et al. Tau positron emission tomographic imaging in aging and early Alzheimer disease. Ann Neurol 2016;79:110–9.
[74] Okamura N, Suemoto T, Furumoto S, Suzuki M, Shimadzu H, Akatsu H, et al. Quinoline and benzimidazole derivatives: candidate probes for in vivo imaging of tau pathology in Alzheimer's disease. J Neurosci 2005;25:10857–62.
[75] Okamura N, Furumoto S, Harada R, Tago T, Yoshikawa T, Fodero-Tavoletti M, et al. Novel 18F-Labeled Arylquinoline Derivatives for Noninvasive Imaging of Tau Pathology in Alzheimer Disease. J Nucl Med 2013;54:1420–7.
[76] Fodero-Tavoletti MT, Okamura N, Furumoto S, Mulligan RS, Connor AR, McLean CA, et al. 18F-THK523: a novel in vivo tau imaging ligand for Alzheimer's disease. Brain 2011;134:1089–100.
[77] Harada R, Okamura N, Furumoto S, Tago T, Maruyama M, Higuchi M, et al. Comparison of the binding characteristics of [18F]THK-523 and other amyloid imaging tracers to Alzheimer's disease pathology. Eur J Nucl Med Mol Imaging 2013;40:125–32.
[78] Fodero-Tavoletti MT, Furumoto S, Taylor L, McLean CA, Mulligan RS, Birchall I, et al. Assessing THK523 selectivity for tau deposits in Alzheimer's disease and non-Alzheimer's disease tauopathies. Alzheimers Res Ther 2014;6:11.
[79] Villemagne VL, Furumoto S, Fodero-Tavoletti MT, Mulligan RS, Hodges J, Harada R, et al. In vivo evaluation of a novel tau imaging tracer for Alzheimer's disease. Eur J Nucl Med Mol Imaging 2014; 41:816–26.

[80] Okamura N, Furumoto S, Fodero-Tavoletti MT, Mulligan RS, Harada R, Yates P, et al. Non-invasive assessment of Alzheimer's disease neurofibrillary pathology using 18F-THK5105 PET. Brain 2014; 137:1762–71.

[81] Villemagne VL, Burnham S, Bourgeat P, Brown B, Ellis KA, Salvado O, et al. Amyloid beta deposition, neurodegeneration, and cognitive decline in sporadic Alzheimer's disease: a prospective cohort study. Lancet Neurol 2013;12:357–67.

[82] Roberson ED, Scearce-Levie K, Palop JJ, Yan F, Cheng IH, Wu T, et al. Reducing endogenous tau ameliorates amyloid beta-induced deficits in an Alzheimer's disease mouse model. Science 2007;316:750–4.

[83] Giacobini E, Becker RE. One hundred years after the discovery of Alzheimer's disease. A turning point for therapy? J Alzheimers Dis 2007; 12:37–52.

[84] Zhang B, Maiti A, Shively S, Lakhani F, McDonald-Jones G, Bruce J, et al. Microtubule-binding drugs offset tau sequestration by stabilizing microtubules and reversing fast axonal transport deficits in a tauopathy model. Proc Natl Acad Sci U S A 2005;102:227–31.

[85] Wischik C, Staff R. Challenges in the conduct of disease-modifying trials in AD: practical experience from a phase 2 trial of Tau-aggregation inhibitor therapy. J Nutr Health Aging 2009; 13:367–9.

[86] Duyckaerts C, Braak H, Brion JP, Buee L, Del Tredici K, Goedert M, et al. PART is part of Alzheimer disease. Acta Neuropathol 2015; 129:749–56.

[87] Jellinger KA, Alafuzoff I, Attems J, Beach TG, Cairns NJ, Crary JF, et al. PART, a distinct tauopathy, different from classical sporadic Alzheimer disease. Acta Neuropathol 2015;129:757–62.