Classification and early detection of dementia and cognitive decline with magnetic resonance imaging
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Citation
Schouten, T. M. (2019, September 18). *Classification and early detection of dementia and cognitive decline with magnetic resonance imaging*. Retrieved from https://hdl.handle.net/1887/78450

Note: To cite this publication please use the final published version (if applicable).

Cover Page

Universiteit Leiden

The handle http://hdl.handle.net/1887/78450 holds various files of this Leiden University dissertation.

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**Issue Date**: 2019-09-18

Appendix A

Cross-validation confidence intervals

In section 6.3 I discussed the unknown confidence intervals of cross-validation estimates of generalization performance. Here I have replicated the simulation by Varoquaux (2018). The goal of this study was to estimate the confidence intervals of a typical neuroimaging study that uses machine learning predictions. In order to see how these findings apply to our research I have adjusted the simulation to resemble the situation in this thesis more closely. Specifically, instead of using accuracy, I use AUC. To allow this, I used the distances to the decision boundary for the support vector classifier instead of predicted class. The separation between classes have been tuned to approximate 90% AUC, whereas the original study used 75% accuracy. Furthermore, as we used repeated cross-validation in our studies, I used repeated 10 fold cross-validation with 10 repeats instead of leave-one-out. This allows an additional comparison between repeated cross-validation that we used, and repeated hold-out testing that was used in the original simulation.

The resulting 90% confidence intervals are similar in size, but slightly skewed to the left due to a ceiling effect of the AUC compared to the results in Varoquaux (2018). The differences between repeated 10-fold cross-validation and repeated hold-out testing are small (see Figure A.1a).

To explore how these findings generalize to unbalanced data, I have repeated the simulation with a 77/173 ratio between classes, the same as the ratio in chapters 2 and 3. The resulting confidence intervals are slightly wider. In the case of 250 samples they increase from $[-4.7\%, 4.1\%]$ to $[-5.0\%, 4.3\%]$ (see Figure A.1b).
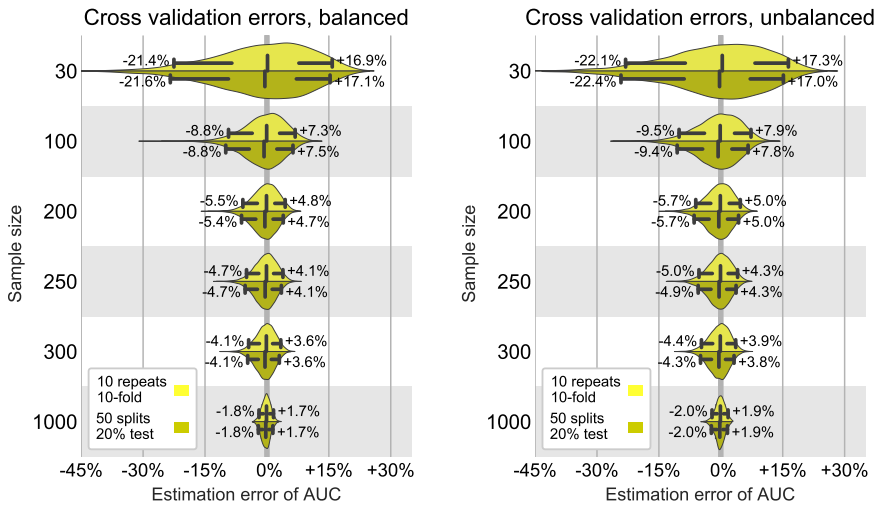
(a) Balanced 50/50 class labels   (b) Unbalanced 77/173 class labels

Figure A.1: Differences between validation performance on a sample of 10000 and estimated generalization performance by 10 repeats 10 fold cross-validation or 50 repeats 80/20 split hold-out validation. The decision function of a support vector classifier was used without tuning hyperparameters. Whiskers represent 5th and 95th percentile values, and the black vertical stripe indicates the median. The simulation was repeated 1000 times for sample size of 1000, and 10000 times for smaller sample sizes.

Bibliography

Adaszewski, S., Dukart, J., Kherif, F., Frackowiak, R., and Draganski, B. (2013). How early can we predict Alzheimer's disease using computational anatomy? *Neurobiology of Aging*, 34(12):2815–2826.

Agosta, F., Pievani, M., Geroldi, C., Copetti, M., Frisoni, G. B., and Filippi, M. (2012). Resting state fMRI in Alzheimer's disease: Beyond the default mode network. *Neurobiology of Aging*, 33(8):1564–1578.

Alonzo, N. C., Hyman, B. T., Rebeck, G. W., and Greenberg, S. M. (1998). Progression of cerebral amyloid angiopathy: accumulation of amyloid-beta40 in affected vessels. *Journal of neuropathology and experimental neurology*, 57(4):353–359.

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders, Fourth Edition, Text Revision.* American Psychiatric Association, Washington, DC.

Apostolova, L. G., Hwang, K. S., Kohannim, O., Avila, D., Elashoff, D., Jack, C. R., Shaw, L., Trojanowski, J. Q., Weiner, M. W., and Thompson, P. M. (2014). ApoE4 effects on automated diagnostic classifiers for mild cognitive impairment and Alzheimer's disease. *NeuroImage: Clinical*, 4:461–472.

Arbabshirani, M. R., Plis, S., Sui, J., and Calhoun, V. D. (2017). Single subject prediction of brain disorders in neuroimaging: Promises and pitfalls. *NeuroImage*, 145:137–165.

Arbuthnott, K. and Frank, J. (2000). Trail Making Test, Part B as a Measure of Executive Control: Validation Using a Set-Switching Paradigm. *Journal of Clinical and Experimental Neuropsychology*, 22(4):518–528.

Basser, P. J., Mattiello, J., and LeBihan, D. (1994a). Estimation of the effective self-diffusion tensor from the NMR spin echo.

Basser, P. J., Mattiello, J., and LeBihan, D. (1994b). MR diffusion tensor spectroscopy and imaging. *Biophysical journal*, 66(1):259–267.

Bassett, D. S., Bullmore, E., Verchinski, B. a., Mattay, V. S., Weinberger, D. R., and Meyerlindenberg, A. (2008). Hierarchical Organization of Human Cortical Networks in Health and Schizophrenia. *J Neurosci*, 28(37):9239–9248.

Baykara, E., Gesierich, B., Adam, R., Tuladhar, A. M., Biesbroek, J. M., Koek, H. L., Ropele, S., Jouvent, E., Chabriat, H., Ertl-Wagner, B., Ewers, M., Schmidt, R., de Leeuw, F. E., Biessels, G. J., Dichgans, M., and Duering, M. (2016). A Novel Imaging Marker for Small Vessel Disease Based on Skeletonization of White Matter Tracts and Diffusion Histograms. *Annals of Neurology*, 80(4):581–592.

Beckmann, C. F. (2012). Modelling with independent components. *NeuroImage*, 62(2):891–901.

Beckmann, C. F. and Smith, S. M. (2004). Probabilistic independent component analysis for functional magnetic resonance imaging. *IEEE transactions on medical imaging*, 23(2):137–152.

Behrens, T. E. J., Berg, H. J., Jbabdi, S., Rushworth, M. F. S., and Woolrich, M. W. (2007). Probabilistic diffusion tractography with multiple fibre orientations: What can we gain? *NeuroImage*, 34(1):144–155.

Benedictus, M. R., Leeuwis, A. E., Binnewijzend, M. A., Kuijer, J. P., Scheltens, P., Barkhof, F., van der Flier, W. M., and Prins, N. D. (2017). Lower cerebral blood flow is associated with faster cognitive decline in Alzheimer's disease. *European Radiology*, 27(3):1169–1175.

Biffi, A. and Greenberg, S. M. (2011). Cerebral amyloid angiopathy: a systematic review. *Journal of clinical neurology (Seoul, Korea)*, 7(1):1–9.

Binnewijzend, M. A. A., Schoonheim, M. M., Sanz-Arigita, E., Wink, A. M., van der Flier, W. M., Tolboom, N., Adriaanse, S. M., Damoiseaux, J. S., Scheltens, P., van Berckel, B. N. M., and Barkhof, F. (2012). Resting-state fMRI changes in Alzheimer's disease and mild cognitive impairment. *Neurobiology of aging*, 33(9):2018–2028.

Bobinski, M., de Leon, M. J., Wegiel, J., Desanti, S., Convit, A., Saint Louis, L. A., Rusinek, H., and Wisniewski, H. M. (2000). The histological validation of post mortem magnetic resonance imaging-determined hippocampal volume in Alzheimer's disease. *Neuroscience*, 95(3):721–5.

Bornebroek, M., Haan, J., Maat-Schieman, M. L., Van Duinen, S. G., and Roos, R. a. (1996). Hereditary cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D): I–A review of clinical, radiologic and genetic aspects. *Brain pathology (Zurich, Switzerland)*, 6(2):111–4.

Bouts, M. J., Möller, C., Hafkemeijer, A., van Swieten, J. C., Dopper, E. G., van der Flier, W. M., Vrenken, H., Wink, A. M., Pijnenburg, Y. A., Scheltens, P., Barkhof, F., Schouten, T. M., de Vos, F., Feis, R. A., van der Grond, J., de Rooij, M., and Rombouts, S. A. (2018). Single subject classification of Alzheimer's disease and behavioral variant frontotemporal dementia using anatomical, diffusion tensor, and resting-state functional magnetic resonance imaging. *Journal of Alzheimer's Disease*, 62(4):1827–1839.

Boyle, P. A., Wilson, R. S., Yu, L., Barr, A. M., Honer, W. G., Schneider, J. A., and Bennett, D. A. (2013). Much of late life cognitive decline is not due to common neurodegenerative pathologies. *Annals of Neurology*, 74(3):478–489.

Breiman, L., Friedman, J., Stone, C., and Olshen, R. A. (1984). *Classification and regression trees*. Taylor & Francis.

Bron, E. E., Smits, M., van der Flier, W. M., Vrenken, H., Barkhof, F., Scheltens, P., Papma, J. M., Steketee, R. M., Méndez Orellana, C., Meijboom, R., Pinto, M., Meireles, J. R., Garrett, C., Bastos-Leite, A. J., Abdulkadir, A., Ronneberger, O., Amoroso, N., Bellotti, R., Cárdenas-Peña, D., Álvarez-Meza, A. M., Dolph, C. V., Iftekharuddin, K. M., Eskildsen, S. F., Coupé, P., Fonov, V. S., Franke, K., Gaser, C., Ledig, C., Guerrero, R., Tong, T., Gray, K. R., Moradi, E., Tohka, J., Routier, A., Durrleman, S., Sarica, A., Di Fatta, G., Sensi, F., Chincarini, A., Smith, G. M., Stoyanov, Z. V., Sørensen, L., Nielsen, M., Tangaro, S., Inglese, P., Wachinger, C., Reuter, M., van Swieten, J. C., Niessen, W. J., and Klein, S. (2015). Standardized evaluation of algorithms for computer-aided diagnosis of dementia based on structural MRI: The CADDementia challenge. *NeuroImage*, 111:562–579.

Chao, L. L., Buckley, S. T., Kornak, J., Schuff, N., Madison, C., Yaffe, K., Miller, B. L., Kramer, J. H., and Weiner, M. W. (2010). ASL perfusion MRI predicts cognitive decline and conversion from MCI to dementia. *Alzheimer Disease and Associated Disorders*, 24(1):19–27.

Charidimou, A., Gang, Q., and Werring, D. J. (2012). Sporadic cerebral amyloid angiopathy revisited: recent insights into pathophysiology and clinical spectrum. *Journal of neurology, neurosurgery, and psychiatry*, 83(2):124–137.

Charidimou, A., Jaunmuktane, Z., Baron, J.-c., and Jäger, R. (2014). White matter perivascular spaces. *Neurology*, 82:57–62.

Charidimou, A., Meegahage, R., Fox, Z., Peeters, A., Vandermeeren, Y., Laloux, P., Baron, J.-c., Jäger, H. R., and Werring, D. J. (2013). Enlarged perivascular spaces as a marker of underlying arteriopathy in intracerebral haemorrhage: a multicentre MRI cohort study. *Journal of neurology, neurosurgery, and psychiatry*, 84(6):624–9.

Cui, Y., Liu, B., Luo, S., Zhen, X., Fan, M., Liu, T., Zhu, W., Park, M., Jiang, T., and Jin, J. S. (2011). Identification of conversion from mild cognitive impairment to alzheimer's disease using multivariate predictors. *PLoS ONE*, 6(7):2–11.

Cuingnet, R., Gerardin, E., Tessieras, J., Auzias, G., Lehéricy, S., Habert, M.-O., Chupin, M., Benali, H., and Colliot, O. (2011). Automatic classification of patients with Alzheimer's disease from structural MRI: a comparison of ten methods using the ADNI database. *NeuroImage*, 56(2):766–781.

Cummings, J. L., Morstorf, T., and Zhong, K. (2014). Alzheimer's disease drug-development pipeline: Few candidates, frequent failures. *Alzheimer's Research and Therapy*, 6(4):1–7.

Dai, Z., Yan, C., Wang, Z., Wang, J., Xia, M., Li, K., and He, Y. (2012). Discriminative analysis of early Alzheimer's disease using multi-modal imaging and multi-level characterization with multi-classifier (M3). *NeuroImage*, 59(3):2187–2195.

de Vos, F., Koini, M., Schouten, T. M., Seiler, S., van der Grond, J., Lechner, A., Schmidt, R., de Rooij, M., and Rombouts, S. A. (2018). A comprehensive analysis of resting state fMRI measures to classify individual patients with Alzheimer's disease. *NeuroImage*, 167(December 2016):62–72.

de Vos, F., Schouten, T. M., Hafkemeijer, A., Dopper, E. G. P., van Swieten, J. C., de Rooij, M., van der Grond, J., and Rombouts, S. A. R. B. (2016). Combining multiple anatomical MRI measures improves Alzheimer's disease classification. *Human Brain Mapping*.

Desikan, R. S., Ségonne, F., Fischl, B., Quinn, B. T., Dickerson, B. C., Blacker, D., Buckner, R. L., Dale, A. M., Maguire, R. P., Hyman, B. T., Albert, M. S., and Killiany, R. J. (2006). An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage*, 31(3):968–980.

Dickerson, B. C. and Wolk, D. a. (2012). MRI cortical thickness biomarker predicts AD-like CSF and cognitive decline in normal adults. *Neurology*, 78(2):84–90.

Dietterich, T. G. (1998). Approximate Statistical Tests for Comparing Supervised Classification Learning Algorithms.

Dipasquale, O., Griffanti, L., Clerici, M., Nemni, R., Baselli, G., and Baglio, F. (2015). High-Dimensional ICA Analysis Detects Within-Network Functional Connectivity Damage of Default-Mode and Sensory-Motor Networks in Alzheimerâ€™s Disease. *Frontiers in Human Neuroscience*, 9(February):1–7.

Douaud, G., Jbabdi, S., Behrens, T. E. J., Menke, R. a., Gass, A., Monsch, A. U., Rao, A., Whitcher, B., Kindlmann, G., Matthews, P. M., and Smith, S. (2011). DTI measures in crossing-fibre areas: increased diffusion anisotropy reveals early white matter alteration in MCI and mild Alzheimer's disease. *NeuroImage*, 55(3):880–890.

Duan, J.-H., Wang, H.-Q., Xu, J., Lin, X., Chen, S.-Q., Kang, Z., and Yao, Z.-B. (2006). White matter damage of patients with Alzheimer's disease correlated with the decreased cognitive function. *Surgical and radiologic anatomy : SRA*, 28(2):150–156.

Dyrba, M., Ewers, M., Wegrzyn, M., Kilimann, I., Plant, C., Oswald, A., Meindl, T., Pievani, M., Bokde, A. L. W., Fellgiebel, A., Filippi, M., Hampel, H., Kl??ppel, S., Hauenstein, K., Kirste, T., and Teipel, S. J. (2013). Robust Automated Detection of Microstructural White Matter Degeneration in Alzheimer's Disease Using Machine Learning Classification of Multicenter DTI Data. *PLoS ONE*, 8(5).

Dyrba, M., Grothe, M., Kirste, T., and Teipel, S. J. (2015). Automated detection of functional and structural disconnection in AD using multiple kernels SVM. *Hum. Brain Mapp.*, 36(6):2118–2131.

Fawcett, T. (2006). An introduction to ROC analysis. *Pattern Recognition Letters*, 27(8):861–874.

Ferreira, L. K., Diniz, B. S., Forlenza, O. V., Busatto, G. F., and Zanetti, M. V. (2011). Neurostructural predictors of Alzheimer's disease: a meta-analysis of VBM studies. *Neurobiology of aging*, 32(10):1733–1741.

Fox, N. C., Scahill, R. I., Crum, W. R., and Rossor, M. N. (1999). Correlation between rates of brain atrophy and cognitive decline in AD. *Neurology*, 52(8):1687–1687.

Friedman, J., Hastie, T., and Tibshirani, R. (2008). Sparse inverse covariance estimation with the graphical lasso. *Biostatistics (Oxford, England)*, 9(3):432–441.

Friedman, J., Hastie, T., and Tibshirani, R. (2010). Regularization Paths for Generalized Linear Models via Coordinate Descent. *Journal of statistical software*, 33(1):1–22.

Frisoni, G. B., Fox, N. C., Jack, C. R., Scheltens, P., and Thompson, P. M. (2010). The clinical use of structural MRI in Alzheimer disease. *Nature reviews. Neurology*, 6(2):67–77.

Gour, N., Felician, O., Didic, M., Koric, L., Gueriot, C., Chanoine, V., Confort-Gouny, S., Guye, M., Ceccaldi, M., and Ranjeva, J. P. (2014). Functional connectivity changes differ in early and late-onset alzheimer's disease. *Human Brain Mapping*, 35(7):2978–2994.

Grabner, G., Janke, A. L., Budge, M. M., Smith, D., Pruessner, J., and Collins, D. L. (2006). Symmetric atlasing and model based segmentation: an application to the hippocampus in older adults. *Med Image Comput Comput Assist Interv Int Conf Med Image Comput Comput Assist Interv*, 9:58–66.

Greenberg, S. M. (1998). Cerebral amyloid angiopathy: Prospects for clinical diagnosis and treatment. *Neurology*, 51(3):690–694.

Greenberg, S. M. (2002). Cerebral amyloid angiopathy and vessel dysfunction. *Cerebrovascular Diseases*, 13(SUPPL. 2):42–47.

Greicius, M. D., Srivastava, G., Reiss, A. L., and Menon, V. (2004). Default-mode network activity distinguishes Alzheimer ' s disease from healthy aging : Evidence from functional MRI. *PNAS*, 101(13):4637–4642.

Grieve, S. M., Williams, L. M., Paul, R. H., Clark, C. R., and Gordon, E. (2007). Cognitive aging, executive function, and fractional anisotropy: a diffusion tensor MR imaging study. *AJNR Am J Neuroradiol*, 28(2):226–235.

Groves, A. R., Beckmann, C. F., Smith, S. M., and Woolrich, M. W. (2011). Linked independent component analysis for multimodal data fusion. *NeuroImage*, 54(3):2198–2217.

Hardy, J. and Allsop, D. (1991). Amyloid deposition as the central event in the aetiology of Alzheimer's disease. *Trends in Pharmacological Sciences*, 12:383–388.

Hartz, A. M., Bauer, B., Soldner, E. L., Wolf, A., Boy, S., Backhaus, R., Mihaljevic, I., Bogdahn, U., Klünemann, H. H., Schuierer, G., and Schlachetzki, F. (2012). Amyloid-β contributes to blood-brain barrier leakage in transgenic human amyloid precursor protein mice and in humans with cerebral amyloid angiopathy. *Stroke*, 43(2):514–523.

Hoerl, A. E. and Kennard, R. W. (1970). Ridge Regression: Biased Estimation for Nonorthogonal Problems. *Technometrics*, 12(1):55–67.

Houx, P. J., Jolles, J., and Vreeling, F. W. (1993). Stroop interference: Aging effects assessed with the stroop color-word test.

Hua, K., Zhang, J., Wakana, S., Jiang, H., Li, X., Reich, D. S., Calabresi, P. a., Pekar, J. J., van Zijl, P. C. M., and Mori, S. (2008). Tract probability maps in stereotaxic spaces: analyses of white matter anatomy and tract-specific quantification. *NeuroImage*, 39(1):336–347.

Jack, C. R., Knopman, D. S., Jagust, W. J., Petersen, R. C., Weiner, M. W., Aisen, P. S., Shaw, L. M., Vemuri, P., Wiste, H. J., Weigand, S. D., Lesnick, T. G., Pankratz, V. S., Donohue, M. C., and Trojanowski, J. Q. (2013). Tracking pathophysiological processes in Alzheimer's disease: an updated hypothetical model of dynamic biomarkers. *The Lancet Neurology*, 12(2):207–216.

Jack, C. R., Knopman, D. S., Jagust, W. J., Shaw, L. M., Aisen, P. S., Weiner, M. W., Petersen, R. C., and Trojanowski, J. Q. (2010). Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. *The Lancet Neurology*, 9:119–128.

Jenkinson, M., Bannister, P., Brady, M., and Smith, S. (2002). Improved Optimization for the Robust and Accurate Linear Registration and Motion Correction of Brain Images. *NeuroImage*, 17(2):825–841.

Jenkinson, M., Beckmann, C. F., Behrens, T. E. J., Woolrich, M. W., and Smith, S. M. (2012). Fsl. *NeuroImage*, 62(2):782–790.

Karran, E., Mercken, M., and Strooper, B. D. (2011). The amyloid cascade hypothesis for Alzheimer's disease: An appraisal for the development of therapeutics. *Nature Reviews Drug Discovery*, 10(9):698–712.

Klöppel, S., Stonnington, C. M., Chu, C., Draganski, B., Scahill, R. I., Rohrer, J. D., Fox, N. C., Jack, C. R., Ashburner, J., and Frackowiak, R. S. J. (2008). Automatic classification of MR scans in Alzheimer's disease. *Brain : a journal of neurology*, 131:681–689.

Koch, W., Teipel, S., Mueller, S., Benninghoff, J., Wagner, M., Bokde, A. L. W., Hampel, H., Coates, U., Reiser, M., and Meindl, T. (2012). Diagnostic power of default mode network resting state fMRI in the detection of Alzheimer's disease. *Neurobiology of aging*, 33(3):466–478.

Kriegeskorte, N., Simmons, W. K., Bellgowan, P. S. F., and Baker, C. I. (2009). Circular analysis in systems neuroscience: the dangers of double dipping. *Nature neuroscience*, 12(5):535–540.

Lecun, Y., Bengio, Y., and Hinton, G. (2015). Deep learning. *Nature*, 521(7553):436–444.

Lee, M. H., Smyser, C., and Shimony, J. (2013). Resting-state fMRI: a review of methods and clinical applications. *American Journal of Neuroradiology*, 35(11):1866–1872.

Levy, E., Carman, M. D., Fernandezmadrid, I. J., Power, M. D., Lieberburg, I., Vanduinen, S. G., Bots, G., Luyendijk, W., and Frangione, B. (1990). Mutation of the Alzheimers-Disease Amyloid Gene in Hereditary Cerebral-Hemorrhage, Dutch Type. *Science*, 248(4959):1124–1126.

Li, J., Pan, P., Huang, R., and Shang, H. (2012). A meta-analysis of voxel-based morphometry studies of white matter volume alterations in Alzheimer's disease. *Neuroscience and Biobehavioral Reviews*, 36(2):757–763.

Li, X.-y., Tang, Z.-c., Sun, Y., Tian, J., Liu, Z.-y., and Han, Y. (2016). White matter degeneration in subjective cognitive decline: a diffusion tensor imaging study. *Oncotarget*, 7(34).

Lindeboom, J., Schmand, B., Tulner, L., Walstra, G., and Jonker, C. (2002). Visual association test to detect early dementia of the Alzheimer type. *Journal of Neurology Neurosurgery and Psychiatry*, 73(2):126–133.

Lorenzi, M., Filippone, M., Frisoni, G. B., Alexander, D. C., and Ourselin, S. (2019). Probabilistic disease progression modeling to characterize diagnostic uncertainty: Application to staging and prediction in Alzheimer's disease. *NeuroImage*, 190(May 2017):56–68.

Maat-Schieman, M. L., van Duinen, S. G., Bornebroek, M., Haan, J., and Roos, R. a. (1996). Hereditary cerebral hemorrhage with amyloidosis-Dutch type (HCHWA-D): II–A review of histopathological aspects. *Brain pathology (Zurich, Switzerland)*, 6(2):115–20.

Martinez-Ramirez, S., Pontes-Neto, O. M., Dumas, A. P., Auriel, E., Halpin, A., Quimby, M., Gurol, M. E., Greenberg, S. M., and Viswanathan, A. (2013). Topography of dilated perivascular spaces in subjects from a memory clinic cohort. *Neurology*, 80(17):1551–1556.

McKhann, G. M., Drachman, D., Folstein, M., Katzman, R., Price, D., and Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force. *Neurology*, 34(7):939–944.

McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack, C. R., Kawas, C. H., Klunk, W. E., Koroshetz, W. J., Manly, J. J., Mayeux, R., Mohs, R. C., Morris, J. C., Rossor, M. N., Scheltens, P., Carrillo, M. C., Thies, B., Weintraub, S., and Phelps, C. H. (2011). 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*, 7(3):263–269.

Medina, D., DeToledo-Morrell, L., Urresta, F., Gabrieli, J. D., Moseley, M., Fleischman, D., Bennett, D. A., Leurgans, S., Turner, D. A., and Stebbins, G. T. (2006). White matter changes in mild cognitive impairment and AD: A diffusion tensor imaging study. *Neurobiology of Aging*, 27(5):663–672.

Mesrob, L., Sarazin, M., Hahn-barma, V., Souza, L. C. D., Dubois, B., Gallinari, P., and Kinkingnéhun, S. (2012). DTI and Structural MRI Classification in Alzheimer's Disease. *Advances in Molecular Imaging*, 2:12–20.

Miller, K. L., Alfaro-Almagro, F., Bangerter, N. K., Thomas, D. L., Yacoub, E., Xu, J., Bartsch, A. J., Jbabdi, S., Sotiropoulos, S. N., Andersson, J. L., Griffanti, L., Douaud, G., Okell, T. W., Weale, P., Dragonu, I., Garratt, S., Hudson, S., Collins, R., Jenkinson, M., Matthews, P. M., and Smith, S. M. (2016). Multimodal population brain imaging in the UK Biobank prospective epidemiological study. *Nature Neuroscience*, 19(11):1523–1536.

Moonen, J. E. F., Foster-Dingley, J. C., de Ruijter, W., van der Grond, J., Bertens, A. S., van Buchem, M. A., Gussekloo, J., Middelkoop, H. A., Wermer, M. J. H., Westendorp, R. G. J., de Craen, A. J. M., and van der Mast, R. C. (2015). Effect of Discontinuation of Antihypertensive Treatment in Elderly People on Cognitive Functioning - the DANTE Study Leiden. *JAMA Internal Medicine*, 175(10):1622.

Mori, S., Wakana, S., Van Zijl, P. C. M., and Nagae-Poetscher, L. M. (2005). *MRI atlas of human white matter*. Elsevier.

Mosconi, L., Berti, V., Glodzik, L., Pupi, A., De Santi, S., and de Leon, M. J. (2010). Pre-Clinical Detection of Alzheimer's Disease Using FDG-PET, with or without Amyloid Imaging. *Journal of Alzheimer's Disease*, 20(3):843–854.

Mudher, A. and Lovestone, S. (2002). Alzheimer's disease - Do tauists and baptists finally shake hands? *Trends in Neurosciences*, 25(1):22–26.

Nir, T. M., Villalon-Reina, J. E., Prasad, G., Jahanshad, N., Joshi, S. H., Toga, A. W., Bernstein, M. a., Jack, C. R., Weiner, M. W., and Thompson, P. M. (2014). Diffusion weighted imaging-based maximum density path analysis and classification of Alzheimer's disease. *Neurobiology of Aging*, 36:1–9.

O'Dwyer, L., Lamberton, F., Bokde, A. L. W., Ewers, M., Faluyi, Y. O., Tanner, C., Mazoyer, B., O'Neill, D., Bartley, M., Collins, D. R., Coughlan, T., Prvulovic, D., and Hampel, H. (2012). Using support vector machines with multiple indices of diffusion for automated classification of mild cognitive impairment. *PLoS ONE*, 7(2).

Ouyang, X., Chen, K., Yao, L., Wu, X., Zhang, J., Li, K., Jin, Z., and Guo, X. (2015). Independent Component Analysis-Based Identification of Covariance Patterns of Microstructural White Matter Damage in Alzheimer's Disease. *PLoS ONE*, 10(3):e0119714.

Patenaude, B., Smith, S. M., Kennedy, D. N., and Jenkinson, M. (2011). A Bayesian model of shape and appearance for subcortical brain segmentation. *NeuroImage*, 56(3):907–922.

Perneczky, R., Wagenpfeil, S., Komossa, K., Grimmer, T., Diehl, J., and Kurz, A. (2006). Mapping scores onto stages: mini-mental state examination and clinical dementia rating. *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry*, 14(2):139–44.

Plant, C., Teipel, S. J., Oswald, A., Böhm, C., Meindl, T., Mourao-Miranda, J., Bokde, A. W., Hampel, H., and Ewers, M. (2010a). Automated detection of brain atrophy patterns based on MRI for the prediction of Alzheimer's disease. *NeuroImage*, 50(1):162–174.

Plant, C., Teipel, S. J., Oswald, A., Böhm, C., Meindl, T., Mourao-Miranda, J., Bokde, A. W., Hampel, H., and Ewers, M. (2010b). Automated detection of brain atrophy patterns based on MRI for the prediction of Alzheimer's disease. *NeuroImage*, 50(1):162–174.

Prince, M., Bryce, R., and Ferri, C. (2011). World Alzheimer Report 2011. Technical report, Alzheimer's Disease International, London.

Pruim, R. H., Mennes, M., van Rooij, D., Llera, A., Buitelaar, J. K., and Beckmann, C. F. (2015). ICA-AROMA: A robust ICA-based strategy for removing motion artifacts from fMRI data. *NeuroImage*, 112:267–277.

Rathore, S., Habes, M., Iftikhar, M. A., Shacklett, A., and Davatzikos, C. (2017). A review on neuroimaging-based classification studies and associated feature extraction methods for Alzheimer's disease and its prodromal stages. *NeuroImage*, 155(March):530–548.

Reijmer, Y. D., Fotiadis, P., Charidimou, A., Veluw, S. J. V., Xiong, L., Riley, G. A., Martinez-ramirez, S., Schwab, K., Viswanathan, A., Gurol, M. E., and Greenberg, S. M. (2017). Relationship Between White Matter Connectivity Loss and Cortical Thinning in Cerebral Amyloid Angiopathy. *Human Brain Mapping*, 38(March):3723–3731.

Reijmer, Y. D., Fotiadis, P., Martinez-Ramirez, S., Salat, D. H., Schultz, A., Shoamanesh, A., Ayres, A. M., Vashkevich, A., Rosas, D., Schwab, K., Leemans, A., Biessels, G. J., Rosand, J., Johnson, K. A., Viswanathan, A., Gurol, M. E., and Greenberg, S. M. (2015). Structural network alterations and neurological dysfunction in cerebral amyloid angiopathy. *Brain*, 138(1):179–188.

Reijmer, Y. D., Fotiadis, P., Riley, G. A., Xiong, L., Charidimou, A., Boulouis, G., Ayres, A. M., Schwab, K., Rosand, J., Gurol, M. E., Viswanathan, A., and Greenberg, S. M. (2016a). Progression of Brain Network Alterations in Cerebral Amyloid Angiopathy. *Stroke*, 47(10):2470–2475.

Reijmer, Y. D., Van Veluw, S. J., and Greenberg, S. M. (2016b). Ischemic brain injury in cerebral amyloid angiopathy. *Journal of Cerebral Blood Flow and Metabolism*, 36(1):40–54.

Rose, S. E., McMahon, K. L., Janke, A. L., O'Dowd, B., De Zubicaray, G., Strudwick, M. W., and Chalk, J. B. (2006). Diffusion indices on magnetic resonance imaging and neuropsychological performance in amnestic mild cognitive impairment. *Journal of Neurology, Neurosurgery and Psychiatry*, 77(10):1122–1128.

Rowe, C. C., Ng, S., Ackermann, U., Gong, S. J., Pike, K., Savage, G., Cowie, T. F., Dickinson, K. L., Maruff, P., Darby, D., Smith, C., Woodward, M., Merory, J., Tochon-Danguy, H., O'Keefe, G., Klunk, W. E., Mathis, C. A., Price, J. C., Masters, C. L., and Villemagne, V. L. (2007). Imaging β-amyloid burden in aging and dementia. *Neurology*, 68(20):1718–1725.

Rubinov, M. and Sporns, O. (2010). Complex network measures of brain connectivity: uses and interpretations. *NeuroImage*, 52(3):1059–69.

Salat, D. H., Smith, E. E., Tuch, D. S., Benner, T., Pappu, V., Schwab, K. M., Gurol, M. E., Rosas, H. D., Rosand, J., and Greenberg, S. M. (2006). White Matter Alterations in Cerebral Amyloid Angiopathy Measured by Diffusion Tensor Imaging. *Stroke*, 37(7):1759 LP – 1764.

Salimi-Khorshidi, G., Douaud, G., Beckmann, C. F., Glasser, M. F., Griffanti, L., and Smith, S. M. (2014). Automatic denoising of functional MRI data: Combining independent component analysis and hierarchical fusion of classifiers. *NeuroImage*, 90:449–468.

Samper-González, J., Burgos, N., Bottani, S., Fontanella, S., Lu, P., Marcoux, A., Routier, A., Guillon, J., Bacci, M., Wen, J., Bertrand, A., Bertin, H., Habert, M. O., Durrleman, S., Evgeniou, T., and Colliot, O. (2018). Reproducible evaluation of classification methods in Alzheimer's disease: Framework and application to MRI and PET data. *NeuroImage*, 183(August):504–521.

Scheltens, P., Blennow, K., Breteler, M. M. B., Strooper, B. D., Frisoni, G. B., Salloway, S., and Flier, W. M. V. D. (2016). Alzheimer's disease. *The Lancet*, 388(10043):505–517.

Schouten, T. M., Koini, M., de Vos, F., Seiler, S., de Rooij, M., Lechner, A., Schmidt, R., van den Heuvel, M., van der Grond, J., and Rombouts, S. A. (2017). Individual Classification of Alzheimer's Disease with Diffusion Magnetic Resonance Imaging. *NeuroImage*, 152(March):476–481.

Schouten, T. M., Koini, M., de Vos, F., Seiler, S., van der Grond, J., Lechner, A., Hafkemeijer, A., Möller, C., Schmidt, R., de Rooij, M., and Rombouts, S. A. (2016). Combining anatomical, diffusion, and resting state functional magnetic resonance imaging for individual classification of mild and moderate Alzheimer's disease. *NeuroImage: Clinical*, 11:46–51.

Seiler, S., Schmidt, H., Lechner, A., and Benke, T. (2012). Driving cessation and dementia: results of the prospective registry on dementia in Austria (PRODEM). *PloS one*, 7(12):1–6.

Shaw, L. M., Vanderstichele, H., Knapik-Czajka, M., Clark, C. M., Aisen, P. S., Petersen, R. C., Blennow, K., Soares, H., Simon, A., Lewczuk, P., Dean, R., Siemers, E., Potter, W., Lee, V. M., and Trojanowski, J. Q. (2009). Cerebrospinal fluid biomarker signature in alzheimer's disease neuroimaging initiative subjects. *Annals of Neurology*, 65(4):403–413.

Sheline, Y. I. and Raichle, M. E. (2013). Resting state functional connectivity in preclinical Alzheimer's disease. *Biological Psychiatry*, 74(5):340–347.

Simon, N., Friedman, J., Hastie, T., and Tibshirani, R. (2013). A Sparse-Group Lasso. *Journal of Computational and Graphical Statistics*, 22(2):231–245.

Smith, R. E., Tournier, J. D., Calamante, F., and Connelly, A. (2012). Anatomically-constrained tractography: Improved diffusion MRI streamlines tractography through effective use of anatomical information. *NeuroImage*, 62(3):1924–1938.

Smith, R. E., Tournier, J. D., Calamante, F., and Connelly, A. (2015). The effects of SIFT on the reproducibility and biological accuracy of the structural connectome. *NeuroImage*, 104:253–265.

Smith, S. M., Jenkinson, M., Johansen-Berg, H., Rueckert, D., Nichols, T. E., Mackay, C. E., Watkins, K. E., Ciccarelli, O., Cader, M. Z., Matthews, P. M., and Behrens, T. E. J. (2006). Tract-based spatial statistics: Voxelwise analysis of multi-subject diffusion data. *NeuroImage*, 31(4):1487–1505.

Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E. J., Johansen-Berg, H., Bannister, P. R., De Luca, M., Drobnjak, I., Flitney, D. E., Niazy, R. K., Saunders, J., Vickers, J., Zhang, Y., De Stefano, N., Brady, J. M., and Matthews, P. M. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage*, 23:S208–S219.

Smith, S. M., Miller, K. L., Salimi-Khorshidi, G., Webster, M., Beckmann, C. F., Nichols, T. E., Ramsey, J. D., and Woolrich, M. W. (2011). Network modelling methods for FMRI. *NeuroImage*, 54(2):875–891.

Smith, S. M. and Nichols, T. E. (2009). Threshold-free cluster enhancement: Addressing problems of smoothing, threshold dependence and localisation in cluster inference. *NeuroImage*, 44(1):83–98.

Smith, S. M., Vidaurre, D., Beckmann, C. F., Glasser, M. F., Jenkinson, M., Miller, K. L., Nichols, T. E., Robinson, E. C., Salimi-Khorshidi, G., Woolrich, M. W., Barch, D. M., Uğurbil, K., and Van Essen, D. C. (2013). Functional connectomics from resting-state fMRI. *Trends in cognitive sciences*, 17(12):666–682.

Smyth, G. K. and Phipson, B. (2010). Permutation P-values should never be zero: calculating exact P-values when permutations are randomly drawn. *Statistical applications in genetics and molecular biology*, 9(1):Article 39.

Stone, M. (1974). Cross-Validatory Choice and Assessment of Statistical Predictions. *Journal of the Royal Statistical Society. Series B (Methodological)*, 36(2):111–147.

Sui, J., He, H., Pearlson, G. D., Adali, T., Kiehl, K. a., Yu, Q., Clark, V. P., Castro, E., White, T., Mueller, B. a., Ho, B. C., Andreasen, N. C., and Calhoun, V. D. (2013a). Three-way (N-way) fusion of brain imaging data based on mCCA+jICA and its application to discriminating schizophrenia. *NeuroImage*, 66:119–132.

Sui, J., He, H., Yu, Q., Chen, J., Rogers, J., Pearlson, G. D., Mayer, A., Bustillo, J., Canive, J., and Calhoun, V. D. (2013b). Combination of Resting State fMRI, DTI, and sMRI Data to Discriminate Schizophrenia by N-way MCCA + jICA. *Frontiers in human neuroscience*, 7(May):1–14.

Tax, C. M., Jeurissen, B., Vos, S. B., Viergever, M. A., and Leemans, A. (2014). Recursive calibration of the fiber response function for spherical deconvolution of diffusion MRI data. *NeuroImage*, 86:67–80.

Tibshirani, R. (1996). Regression Shrinkage and Selection via the Lasso. *Journal of the Royal Statistical Society. Series B (Methodological)*, 58(1):267–288.

Tournier, J.-D., , F. Calamante, and a. Connelly (2010). Improved probabilistic streamlines tractography by 2nd order integration over fibre orientation distributions. *Ismrm*, 88(2003):2010.

Tournier, J. D., Calamante, F., and Connelly, A. (2012). MRtrix: Diffusion tractography in crossing fiber regions. *International Journal of Imaging Systems and Technology*, 22(1):53–66.

Van Rooden, S., Van Opstal, A. M., Labadie, G., Terwindt, G. M., Wermer, M. J. H., Webb, A. G., Middelkoop, H. A. M., Greenberg, S. M., Van Der Grond, J., and Van Buchem, M. A. (2016). Early Magnetic Resonance Imaging and Cognitive Markers of Hereditary Cerebral Amyloid Angiopathy. *Stroke*, 47(12):3041–3044.

Varma, S. and Simon, R. (2006). Bias in error estimation when using cross-validation for model selection. *BMC bioinformatics*, 7:91.

Varoquaux, G. (2018). Cross-validation failure: Small sample sizes lead to large error bars. *NeuroImage*, 180(June 2017):68–77.

Varoquaux, G., Raamana, P., Engemann, D., Hoyos-Idrobo, A., Schwartz, Y., and Thirion, B. (2016). Assessing and tuning brain decoders: cross-validation, caveats, and guidelines. *arXiv:1606.05201 [stat.ML]*, 145(October):1–14.

Veraart, J., Novikov, D. S., Christiaens, D., Ades-aron, B., Sijbers, J., and Fieremans, E. (2016). Denoising of diffusion MRI using random matrix theory. *NeuroImage*, 142:394–406.

Vieira, S., Pinaya, W. H., and Mechelli, A. (2017). Using deep learning to investigate the neuroimaging correlates of psychiatric and neurological disorders: Methods and applications. *Neuroscience and Biobehavioral Reviews*, 74:58–75.

Vinters, H. V. (1987). Cerebral amyloid angiopathy. A critical review. *Stroke; a journal of cerebral circulation*, 18(2):311–24.

Wardlaw, J. M., Makin, S. J., Valdés Hernández, M. C., Armitage, P. A., Heye, A. K., Chappell, F. M., Muñoz-Maniega, S., Sakka, E., Shuler, K., Dennis, M. S., and Thrippleton, M. J. (2017). Blood-brain barrier failure as a core mechanism in cerebral small vessel disease and dementia: evidence from a cohort study. *Alzheimer's and Dementia*, 13(6):634–643.

Wee, C. Y., Yap, P. T., Li, W., Denny, K., Browndyke, J. N., Potter, G. G., Welsh-Bohmer, K. A., Wang, L., and Shen, D. (2011). Enriched white matter connectivity networks for accurate identification of MCI patients. *NeuroImage*, 54:1812–1822.

Wee, C. Y., Yap, P. T., Zhang, D., Denny, K., Browndyke, J. N., Potter, G. G., Welsh-Bohmer, K. A., Wang, L., and Shen, D. (2012). Identification of MCI individuals using structural and functional connectivity networks. *NeuroImage*, 59:2045–2056.

Weiner, M. W., Veitch, D. P., Aisen, P. S., Beckett, L. A., Cairns, N. J., Cedarbaum, J., Green, R. C., Harvey, D., Jack, C. R., Jagust, W., Luthman, J., Morris, J. C., Petersen, R. C., Saykin, A. J., Shaw, L., Shen, L., Schwarz, A., Toga, A. W., and Trojanowski, J. Q. (2015). 2014 Update of the Alzheimer's Disease Neuroimaging Initiative: A review of papers published since its inception. *Alzheimer's & Dementia*, 11(6):e1–e120.

Winkler, A. M., Ridgway, G. R., Douaud, G., Nichols, T. E., and Smith, S. M. (2016). Faster permutation inference in brain imaging. *NeuroImage*, 141:502–516.

Winkler, A. M., Ridgway, G. R., Webster, M. A., Smith, S. M., and Nichols, T. E. (2014). Permutation inference for the general linear model. *NeuroImage*, 92:381–397.

Wolk, D. A. and Detre, J. A. (2012). Arterial spin labeling MRI. *Current Opinion in Neurology*, 25(4):421–428.

Woodard, J. L., Seidenberg, M., Nielson, K. a., Smith, J. C., Antuono, P., Durgerian, S., Guidotti, L., Zhang, Q., Butts, A., Hantke, N., Lancaster, M., and Rao, S. M. (2010). Prediction of cognitive decline in healthy older adults using fMRI. *Journal of Alzheimer's disease : JAD*, 21(3):871–885.

Yang, Y. and Zou, H. (2015). A fast unified algorithm for solving group-lasso penalize learning problems. *Statistics and Computing*, 25(6):1129–1141.

Yeh, C. H., Smith, R. E., Liang, X., Calamante, F., and Connelly, A. (2016). Correction for diffusion MRI fibre tracking biases: The consequences for structural connectomic metrics. *NeuroImage*, 142:150–162.

Young, J., Modat, M., Cardoso, M. J., Mendelson, A., Cash, D., and Ourselin, S. (2013). Accurate multimodal probabilistic prediction of conversion to Alzheimer's disease in patients with mild cognitive impairment. *NeuroImage: Clinical*, 2(1):735–745.

Zhan, L., Zhou, J., Wang, Y., Jin, Y., Jahanshad, N., Prasad, G., Nir, T. M., Leonardo, C. D., Ye, J., and Thompson, P. M. (2015). Comparison of 9 tractography algorithms for detecting abnormal structural brain networks in Alzheimer's disease. *Frontiers in Aging Neuroscience*, 7(MAR):1–19.

Zhang, Y., Brady, M., and Smith, S. (2001). Segmentation of brain MR images through a hidden Markov random field model and the expectation-maximization algorithm. *IEEE transactions on medical imaging*, 20(1):45–57.

Zhang, Y., Schuff, N., Du, A. T., Rosen, H. J., Kramer, J. H., Gorno-Tempini, M. L., Miller, B. L., and Weiner, M. W. (2009). White matter damage in frontotemporal dementia and Alzheimers disease measured by diffusion MRI. *Brain*, 132(9):2579–2592.

Zhang-nunes, S. X., Maat-schieman, M. L. C., Duinen, S. G. V., Roos, R. A. C., and Frosch, M. P. (2006). The Cerebral β-Amyloid Angiopathies : Hereditary and Sporadic. *Brain Pathol*, 16(1):30–39.

Zhu, Y.-C., Chabriat, H., Godin, O., Dufouil, C., Rosand, J., Greenberg, S. M., Smith, E. E., Tzourio, C., and Viswanathan, A. (2012). Distribution of white matter hyperintensity in cerebral hemorrhage and healthy aging. *Journal of neurology*, 259(3):530–6.

Zou, H. and Hastie, T. (2005). Regularization and variable selection via the elastic net. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 67(2):301–320.