* 1. Review on techniques of Parkinson’s, exercises on graphics tablet and use evolutionary algorithm. Capturing degree of motor and cognitive dysfunction and compare linear models compared to polynomial models [12]. Measure instabilities by measuring punches/kicks M.V, J.C, “Exploring Diagnostic Models of Parkinson’s Disease with Multi-Objective Regression”IEEE 2016.
     1. Autonomated method, figure copying exercise using a multi-objective evolutionary algorithm to predict cognitive deficit. Tries to tackle this problem as diagnosis of PD is usually clinical, based on history & Exampniation of motor features [7]. D. A. Heldman, J. P. Giuffrida, R. Chen, M. Payne, F. Mazzella, A. P. Duker, A. Sahay, S. J. Kim, F. J. Revilla, and A. J. Espay, “The modiﬁed bradykinesia rating scale for parkinson’s disease: reliability andcomparisonwithkinematicmeasures,”MovementDisorders,vol.26, no. 10, pp. 1859–1863, 2011.
     2. Also deep brain simulation outcome for those with PD is different to those without in a study of 51 PD patients , with significance.
     3. Also has similar works, clock drawing [10] and rey-osterreith [11] and machine learning techniques used before [13] with reasonable discrimination what value is reasonable? E. Pinto and R. Peters, “Literature review of the clock drawing test as a tool for cognitive screening,” Dementia and geriatric cognitive disorders, vol. 27, no. 3, pp. 201–213, 2009. [11] M.-S. Shin, S.-Y. Park, S.-R. Park, S.-H. Seol, and J. S. Kwon, “Clinical and empirical applications of the rey–osterrieth complex ﬁgure test,” Nature protocols, vol. 1, no. 2, pp. 892–899, 2006.
     4. Concludes that multiple bursts of acceleration might be an indicator, does not have statistical significance. Diagnosis is significant, but to the degree is not
     5. Also, unknown medical value, so this will be basis to not pursue this method. Could be more important with the rise of wearable devices
  2. As well as analysing festinating gait (another method) with accelerometer-based sensing systems and analyse step symmetry [2]. W.Y.L,”An Accelerometer-based Festinating Gait Detection Algorithm and Its Application to Parkinson’s Disease Development,” IEEE International Conference on Systems,oct 2016. Rapid shuffling steps and trunk flex, no tool for monitoring its development. Also look for flexed forward upper trunk. This paper fails to determine the accuracy of this method, it just discusses the possibilities.
     1. Assesses movement of body in all directions Awful diagrams. How did this pass peer review, wtf? Several typo’s too. Also, doesn’t discuss how many people were in the study and accuracy. May need an overall assessment of related works in this category
     2. Several other methods, EMG (up to 76% so not that great) [31] Ruonala, V.; Meigal, A.; Rissanen, S.; Airaksinen, O.; Kankaanpaa, M.; Karjalainen, P. EMG signal morphology in essential tremor and parkinsonʼs disease. In Proceedings of the 35th Annual International Conference of the Engineering in Medicine and Biology Society (EMBC), Osaka, Japan, 3–7 July 2013; pp. 5765–5768, EEG was difficult to perform feature extraction for healthy controls. Possibly obtain 76.7% accuracy but was questionable. Brain imaging seemed most significant with SVM having best accuracy of 86.87%, sensitivity of 78.95% and specificity of 92.59% [41] Long, D.; Wang, J.; Xuan, M.; Gu, Q.; Xu, X.; Kong, D.; Zhang, M. Automatic classification of early parkinsonʼs disease with multi-modal mr imaging. PLoS ONE 2012 so seems very promising. The one above by Long D is very promising, high quality data acquisition with fixed imaging <https://www.fil.ion.ucl.ac.uk/spm/> used to analyse fMRI. Parameters
        1. Convert to frequency domain, then square root of each frequency. Thus reducing the global effects. T-tests to determine differences between PD and normal groups, leave one out cross-validation seems popular. Found changes in frontal and temporal lobes. Beats clinical which is typically 75% accurate, can improve to 90% [23], [24]. Hughes AJ, Daniel SE, Kilford L, Lees AJ (1992) Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 55: 181–184. Spetsieris PG, Ma Y, Dhawan V, Eidelberg D (2009) Differential diagnosis of parkinsonian syndromes using PCA-based functional imaging features. Neuroimage 45: 1241–1252. Thus showing structural changes in brain does occur to PD patients, consistent with another study [41] Tir M, Delmaire C, le Thuc V, Duhamel A, Destee A, et al. (2009) Motor-related circuit dysfunction in MSA-P: Usefulness of combined whole-brain imaging analysis. Mov Disord 24: 863–870.. May be changes due to low freq drifts and high freq noise. Also various types of MRI to consider
     3. <https://www.mdpi.com/1424-8220/15/9/21710> Sensors paper suggests all these other methods. More comprehensive view wit h Gait assessment also. Large number of assessments, all quite successful from gait to audio. Not much about imaging so there is a window of opportunity to discover more, suggest there could be something significant in exploring speech and wearable combined.
     4. Also analysed physical activity with fuzzy classifiers, achieving classification for basic activities between healthy and PD patients of i.e., walking, standing, siting and lying had a sensitivity of 85%, 83.6%, 86.3%, and 91.8%, respectively, and specificity of 97.8%, 96.5%, 98.0%, and 99.8%, respectively [46, 47]
  3. Also voice destruction, using extreme machine learning. UCI Repository, 90.76& accuracy, using Neural Networks and SVM [4]. Noisy, breathy speech, [7], increased vibration[8] and more abnormalities [9] including pauses [11] and rapid repetition of words/syllables . There has also been analysis on the prognosis of scientific rating scales, calculating the severity. Being able to differentiate between healthy and patient with PD. Consult my papers from overleaf in this
     1. Hui Ling et al (My lit rev) in a study of 31 people, 23/31 with pD and 10-fold used fuzzy KNN following PCA on UCI ML repository with accuracy 96.25%
  4. Overall this paper only talked about 3 methods, sure there are many more. How did this make it onto peer review? Doesn’t even compare the SVM to NN and assess strengths/weaknesses
  5. <https://search.proquest.com/docview/1912629314/?pq-origsite=primo>
  6. Talks about importance of early diagnosis as when motor symptoms are observed, it is considered too late for disease modifying therapy to be implemented because Dopamine neurons in SN are lost <https://link.springer.com/article/10.1007/s00702-012-0840-9>, <https://www.sciencedirect.com/science/article/pii/B9780444534866000491> so urgent need to identify in early stages as non-motor symptoms can develop before motor symptoms. Stating the importance of a imaging test which is cost effective and widely available. Next step would be one that can provide information about lead time and progression of prodromal neurodegeneration
     1. One way is by scanning dopamine transporters (DAT) scan or Single Proton Emission computed tomography (SPECT) for early diagnosis
     2. ‘Techniques such as high resolution MRI of the SN had functional imaging of PD brain networks have great potential to facilitate early diagnosis’ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5429242/> again important has >50% dopaminergic neurons and 80% of nigrostriatal synaptic activity lost by the time motor phenotype emerges Fearnley J.M., Lees A.J. Ageing and Parkinson's disease: substantia nigra regional selectivity. Brain. 1991;114:2283–2301. Fuente-Fernandez R. Age-specific progression of nigrostriatal dysfunction in Parkinson's disease. Ann. Neurol. 2011;69:803–810.
     3. Currently SPECT to identify DAT is the only imaging method to be approved by the US FDA and the NICE (National Institute for Health and Care Excellence), with sensitivity 95% and specificity of 93% rate from initial tremor and significantly better than clinical diagnosis in uncertain cases Benamer T.S., Patterson J., Grosset D.G. Accurate differentiation of parkinsonism and essential tremor using visual assessment of [123I]-FP-CIT imaging: the [123I]-FP-CIT study group. Mov. Disord. 2000;15:503–510 Then this can be a gateway to talk about the power of MRI as being the next approved imaging method (Difference is SPECT analyses pathways and connections but MRI is structural, so combined could be even more powerful!)
        1. In a large study of DAT SPECT, Iranzo and colleagues found pathologically reduced 123IFP-CIT binding in 17 out of 43 individuals with RBD (rapid eye movement, sleep behaviour disorder) Benamer T.S., Patterson J., Grosset D.G. Accurate differentiation of parkinsonism and essential tremor using visual assessment of [123I]-FP-CIT imaging: the [123I]-FP-CIT study group. Mov. Disord. 2000;15:503–510
        2. Quantifying the SN tissue with structural cross-sectional imaging has been limited by lack of spatial resolution and ability to detect subtle signal change in this area, though with MRI methodology improving, there is promise to overcome. Transcranial Ultrasound has been used for many years on the other hand, identifying key abonormalities in the echogenic properties in up to 90% of patients with PD Berg D., Siefker C., Becker G. Echogenicity of the substantia nigra in Parkinson's disease and its relation to clinical findings. J. Neurol. 2001;248:684–689, Ressner P., Skoloudik D., Hlustik P., Kanovsky P. Hyperechogenicity of the substantia nigra in Parkinson's disease. J. Neuroimaging. 2007;17:164–167
        3. T2 Weighted MRI can detect fluctuation in activity from changes in blood oxygen level Beckmann C.F., DeLuca M., Devlin J.T., Smith S.M. Investigations into resting-state connectivity using independent component analysis. Philos. Trans. R. Soc. Lond. Ser. B Biol. Sci. 2005 May 29;360(1457):1001–1013
           1. Using resting state MRI examiniation and measuring functional connectivity (FC) differentiated PD patients from controls with 100% sensitivity and 89.5% specificity. Robust to methodological variations Szewczyk-Krolikowski K., Menke R.A., Rolinski M., Duff E., Salimi- Khorshidi G, Filippini N, et al. Functional connectivity in the basal ganglia network differentiates PD patients from controls. Neurology. 2014;83:208–214 So we know that there is huge potential in this region..
        4. Is still cautious, important obstacles to overcome such as reproducibility and moving away from small subsets to the wider population before it can be as popular as DAT SPECT.
  7. For SPECT Imaging, <https://neuro.psychiatryonline.org/doi/pdf/10.1176/jnp.23.1.jnp63> SPET showed a significant uptake of 99mTC-TRODAT-1 binding in basal ganglia of the brain for PD patients than Non-PD. So dopamine transporter is deficient for those with PD. Linking to wider problems, such as lack of dopamine and depressive symptoms Laine TP, Ahonen A, Rasanen P, et al: Dopamine transporteravailability and depressive symptoms during alcohol with-drawal. Psychiatry Res 1999; 90:153–157 and a possible correlation of PD and major depressive disorders.

1. <https://www-karger-com.libproxy.kcl.ac.uk/Article/Abstract/314495> MRI significance in diagnosis and differential diagnosis of PD (one of the hardest diseases to diagnose). Conventional MRI is already well established.
   1. Neurodegenerative processes characterised by cell loss, increased deposition of iron and microglial proliferation. Leading to signal changes in MRI sequences [24-26], Duguid JR, De La PR, DeGroot J: Magnetic resonance imaging of the midbrain in Par-kinson’s disease. Ann Neurol 1986; 20: 74 4 –747. Hirsch EC, Hunot S: Neuroinf lammation in Parkinson’s disease: a target for neuropro-tection? Lancet Neurol 2009; 8: 382–397. T2 is sensitive to changes in tissue properties or t2 decay, less intense t2 may point to non-heme iron or no intensity in t1. [27] Brass SD, Chen NK, Mulkern RV, Bakshi R: Magnetic resonance imaging of iron deposi-t i o n i n n e u r o l o g i c a l d i s o r d e r s . To p M a g n R e -son Imaging 2006; 17: 31– 4 0.
      1. 1.5T usually yields obtainable results, quite popular. Though not strong enough typically. T1 is good for anatomical details, providing good grey matter/white matter contrast, improved with inversion pulse [33] Brant-Zawadzki M, Gillan GD, Nitz WR: MP RAGE: a three-dimensional, T1-weighted, gradient-echo sequence – initial experience in the brain. Radiology 1992; 182: 769–775. Authors were more able to distinguish changes in SN for PD patients [34, 35, 42, 43] Hutchinson M, Raff U: Parkinson’s disease: a novel MRI method for determining struc-tural changes in the substantia nigra. J Neu-rol Neurosurg Psychiatry 1999; 67: 815–818 Hu MT, White SJ, Herlihy AH, Chaudhuri KR, Hajnal JV, Brooks DJ: A comparison of (18)F-dopa PET and inversion recovery MRI in the diagnosis of Parkinson’s disease. Neu-rology 2001; 56: 1195 –120 0. Minati L, Grisoli M, Carella F, De ST, Bruz-zone MG, Savoiardo M: Imaging degenera-tion of the substantia nigra in Parkinson dis-ease with inversion-recovery MR imaging. AJNR Am J Neuroradiol 2007; 28: 309–313. Hinting at promising results. However, at early stages still unable to reliably exclude other possibilities, such as brain tumors, normal pressure hydrocephalus etc..
      2. With changes in fronteoparietal and asymmetric regions of the brain [68, 75] Soliveri P, Monza D, Paridi D, Radice D, Grisoli M, Testa D, et al: Cognitive and mag-netic resonance imaging aspects of cortico-basal degeneration and progressive supranu-clear palsy. Neurology 1999; 53: 502–507 Hauser RA, Murtaugh FR, Akhter K, Gold M, Olanow CW: Magnetic resonance imag-ing of corticobasal degeneration. J Neuroim-aging 1996; 6: 222–226.
      3. A higher resolution with 3T can be used to evaluate rostral, middle and caudal ROI within the SN [117] Vaillancourt DE, Spraker MB, Prodoehl J, Abraham I, Corcos DM, Zhou XJ, et al: High-resolution diffusion tensor imaging in the substantia nigra of de novo Parkin-son disease. Neurology 2009; 72: 1378–1384. to separate PD patients from the control group. Using the volume of SN for PD and control could be used, though there is considerable overlap, though volume of SN and connectivity with thalamus can result in sensitivity of 100% and specificity 80% for PD [90] Menke RA, Scholz J, Miller KL, Deoni S, Jbabdi S, Matthews PM, et al: MRI charac-teristics of the substantia nigra in Parkin-son’s disease: a combined quantitative T1 and DTI study. Neuroimage 2009; 47: 435–441. Use this to justify having selected T2 from the dataset and picking 3T as a determining factor for greater resolution. Also keep to the same slice size as it may be harder to classify different types of PD otherwise (AXIAL is most common, so go with that – a benchmark is there to compare our results to). [112] Blain CR, Barker GJ, Jarosz JM, Coyle NA, Landau S, Brown RG, et al: Measuring brain stem and cerebellar damage in par-kinsonian syndromes using diffusion ten-sor MRI. Neurology 2006; 67: 2199–2205
      4. Also mentions how certain genes being present can increase the probability of getting pd
   2. <https://www.frontiersin.org/articles/10.3389/fneur.2015.00146/full> Could use for the image of PD progression. MR-based techniques are recommended for diagnosis and treatment of PD. There have been ways to analyse neural activity and blood oxygenation, but this is not entirely characterised (13) Arias-Carrion O, Poppel E. Dopamine, learning, and reward-seeking behavior. *Acta Neurobiol Exp (Wars)* (2007) **67**:481–8.Can direct this to how Structural has been more effective and how we will use this.. Differences between PD and alzheimers disease (AD) are not that dissimilar in terms of blood flow (40) Le Heron CJ, Wright SL, Melzer TR, Myall DJ, Macaskill MR, Livingston L, et al. Comparing cerebral perfusion in Alzheimer’s disease and Parkinson’s disease dementia: an ASL-MRI study. *J Cereb Blood Flow Metab* (2014) **34**:964–70. doi:10.1038/jcbfm.2014.40. Acknowledges that some techniques requires stronger magnetic fields to get measurable signals from compounds, reducing the availability and usefulness. States that it’s overall effectiveness will be the ability to provide efficacy, safety and long-lasting improvements to the quality of life to patients.
   3. Recent: Review of MRI in PD diagnosis Also talks about how it can affect sleeping MRI is non-invasive, better over time as technology will improve (magnetic field strength) as signal-to-noise ratio (SNR) increases with field strength so has future benefits too.   
      Acknowledges that PET and SPECT are the most common, MRI has shown promise for detecting pathological changes in SN.  
      Hard to distinguish SN effectively , though SNc and SNr were clearly visualised and delineated by combining PD-weighted and short inversion time [31] **The substantia nigra in Parkinson disease: proton density-weighted spin-echo and fast short inversion time inversion-recovery MR findings** by Oikawa et al. Structures of the basal forebrain have been studied with T1 and T2 weighted, both revealed a significant decrease in volume by PD patients, especially in late stages compared to healthy controls. JAMA Neurol, 70 (2013), p. 241, [10.1001/jamaneurol.2013.597](https://doi.org/10.1001/jamaneurol.2013.597) Concludes that MRI is usually first line of approach for most neurological diseases, improvements in the technology results in higher spatial resolution to further diagnose PD. Though still needs to be standardised in terms of the technique on a wider scale
   4. <https://link.springer.com/article/10.1007%2Fs00702-017-1717-8> MRI allows quantitative evaluation of brain abnormalities (Rizzo et. Al 2016 Rizzo G, Copetti M, Arcuti S, Martino D, Fontana A, Logroscino G(2016a) Accuracy of clinical diagnosis of Parkinson disease: asystematic review and meta-analysis. Neurology 86(6):566–576; Mahlknecht et al.2010 Mahlknecht P, Hotter A, Hussl A, Esterhammer R, Schocke M, SeppiK (2010) Significance of MRI in diagnosis and differentialdiagnosis of Parkinson’s disease. Neuro Degener Dis7(5):300–318) . New imaging techniques at 7T will make diagnosing with MRI even better, as in advanced stages, smudging of the red nucleus borders towards the SN may occur (Hotter et al.2009 Hotter A, Esterhammer R, Schocke MF, Seppi K (2009) Potential ofadvanced MR imaging techniques in the differential diagnosis ofparkinsonism. Mov Disord Off J Mov Disord Soc 24(Suppl2):S711–S720; Mahlknecht et al.2010) This only adds to the fact that a recent meta-analysis with 364 patients with PD and 331 controls from 10 studies have a overall sensitivity and specificity of 98% and 95% respectively for 3T (Mahlkneecht et al. 2017) Mahlknecht P, Krismer F, Poewe W, Seppi K (2017) Meta-analysis ofdorsolateral nigral hyperintensity on MRI as a marker forParkinson’s disease. Mov Disord Off J Mov Disord Soc. doi:10.1002/mds.26932 . Talks about the evidence suggesting a paradigm shift in the diagnosis of PD (Poewe et al. 2017) Poewe W, Seppi K, Tanner CM, Halliday GM, Brundin P, VolkmannJ, Schrag AE, Lang AE, (2017) Parkinson disease. Nat Rev DisPrim. doi:10.1038/nrdp.2017.13 with prominence of image analysis algorithms such as SVM classification and other machine-learning derived classifications for quantitative MRI datasets (Huppertz et al. 2016 Huppertz HJ, Moller L, Sudmeyer M, Hilker R, Hattingen E, Egger Ket al (2016) Differentiation of neurodegenerative parkinsoniansyndromes by volumetric magnetic resonance imaging analysisand support vector machine classification. Mov Disord Off JMov Disord Soc 31(10):1506–1517; Scherfler et al. 2016 cherfler C, Gobel G, Muller C, Nocker M, Wenning GK, Schocke Met al (2016) Diagnostic potential of automated subcorticalvolume segmentation in atypical parkinsonism. Neurology86(13):1242–1249) suggesting another window being opened to large scale, automated image analysis
2. <https://www.ncbi.nlm.nih.gov/pubmed/27452874> 2016 study Used SVM to differentiate between 204 PD patients and 73 healthy controls with leave-one-out cross validation with a 79% sensitivity and up to 87% for PSP with MSA (multiple system atrophy), again confirming the midbrain, basal ganglia and cerebellar peduncles had the largest relevance for classification by examining the weighting factors. Though was inconsistent with T1 and T2, using both with both 1.5T and 3T so mixed resolutions, could effect weighting and did not adjust or homogenize between centres. Also has a section on image processing, statistical analysis and results of classification (good structure basically)
   1. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5610036/> Examines DAT scan using deep learning-based interpretation. Used PPMI database, 2017 at that time. 431 patients with PD, 193 controls and 77 with SWEDD (scans without evidence of dopaminergic deficit). Developed Training and test set, randomly divided and trained CNN.
      1. Baseline diagnosis was by clinical evaluation by UK PD Brain Bank Criteria Gibb W.R., Lees A.J. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. J. Neurol. Neurosurg. Psychiatry. 1988;51:745–752. Though we know that this can be up to 25% inaccurate
      2. Designed their own deep CNN framework, PD Net, rescaling from range [0, 255] and subtracted the mean. Applied 3d convolution, then pooling (was done 3 times) to get 1x1x2 vector Figure 1 is very nice to see how the overall classifier may work, good structure
      3. Used ReLU activation layer and max-pooling layer, stride size of 2. This produced 256 feature vectors, connected to two output labels. Trained with stochastic gradient descent, 90%/10% ratio Would need to state which framework and methodology used as well as show understanding of it’s architecture
      4. Sensitivity, specificity and accuracy was used to evaluate, could also use ROC curve (DeLong et al 1988)
      5. Got 94.2% with PD Net for PD vs NC with overall accuracy of PD Net higher than individual readers (96.0% vs 90.7% and 84%; with p=0.008 and 0.001. Could also include confusion matrix as a better measure of accuracy and strength of classification. Though this seems very powerful and applicable to MRI
      6. So deep learning can be very powerful in accurately diagnosing patients, with potential for practical use in a clinical setting, typically higher than other quantification methods. Though further validation of deep learning techniques are required this is where MRI could come in.. Also mentioning of the 3 misclassified by the PD Convnet, 2/3 were misclassified clinically also. This is an improvement on other machine-learning methods for SPET scans with accuracies 90-96% Huertas-Fernandez I., Garcia-Gomez F.J., Garcia-Solis D., Benitez-Rivero S., Marin-Oyaga V.A., Jesus S., Caceres-Redondo M.T., Lojo J.A., Martin-Rodriguez J.F., Carrillo F., Mir P. Machine learning models for the differential diagnosis of vascular parkinsonism and Parkinson's disease using [(123)I]FP-CIT SPECT. Eur. J. Nucl. Med. Mol. Imaging. 2015;42:112–119 Illan I.A., Gorrz J.M., Ramirez J., Segovia F., Jimenez-Hoyuela J.M., Ortega Lozano S.J. Automatic assistance to Parkinson's disease diagnosis in DaTSCAN SPECT imaging. Med. Phys. 2012;39:5971–5980. Prashanth R., Roy S.D., Mandal P.K., Ghosh S. Automatic classification and prediction models for early Parkinson's disease diagnosis from SPECT imaging. Expert Syst. Appl. 2014;41:3333–3342
      7. Benefit also is no feature selection, PD Net finds patterns itself, though doesn’t reflect actual reality. PPMI has a \*gold standard\* When it comes to quality of data and collection methods. Thus suggesting promise for Deep NN and MRI Scans
   2. <http://jnm.snmjournals.org/content/59/supplement_1/29> DATScan images from PPMI also, different methodology,
   3. In a non peer-reviewed paper, End-to-End Parkinson Disease Diagnosis using Brain MR-Images by 3D-CNN [Esmaeilzadeh, Soheil](https://search.proquest.com/indexinglinkhandler/sng/au/Esmaeilzadeh,+Soheil/$N?accountid=11862); [Yang, Yao](https://search.proquest.com/indexinglinkhandler/sng/au/Yang,+Yao/$N?accountid=11862); [Adeli, Ehsan](https://search.proquest.com/indexinglinkhandler/sng/au/Adeli,+Ehsan/$N?accountid=11862). **arXiv.org**, Jun 13, 2018
      1. Significance of iron-sensitive and Field strength of at least 3T to demonstrate absence of swallow tail in dorsolateral SN, which is indicative of PD and dementia with Lewy bodies Schwarz ST, Afzal M, Morgan PS et-al. The 'swallow tail' appearance of the healthy nigrosome - a new accurate test of Parkinson's disease: a case-control and retrospective cross-sectional MRI study at 3T. PLoS ONE. 2014;9 (4): e93814. [doi:10.1371/journal.pone.0093814](http://dx.doi.org/10.1371/journal.pone.0093814)
      2. Baseline for state of the art using MR-images, by Ahmed et al. M. N. Ahmed and A. A. Farag, “Two-stage neural network for volume segmentation of medical images,” Neural Networks, International Conference on pp 1373- 1378 vol.3. which combined ANN and SVM to get an accuracy 86.96%, with human- engineered feature extraction. Otherwise just an ANN accuracy if 70% is achieved. Set baseline here
      3. Also uses PPMI dataset, states cut and image size, thus number of pixels (which will be our visual features) Also the distribution of males, females, average age and max age.
      4. Skill stripping used to remove non-cerebral tissue like skull, scalp and dura (increases speed and removes redundancies), Uses algorithms to delineate brain, such as Smith in 2002 [13], reducing pixel size
      5. Augment the data, flip left and right hemispheres and keep everything else the same; doubling the dataset size, uses Precision, Recall and F-score.
      6. Very nice architectural diagram. Dropout Layer Paper: http://jmlr.org/papers/v15/srivastava14a.html
      7. Following each convolution, used normalization method (both batch and regular was attempted) Y. Wu and K. He, “Group normalization.” https://github. com/taki0112/Group\_Normalization-Tensorflow, journal: arXiv:1803.08494v2 [cs.CV] 24 Apr 2018.
      8. Also experimented adding/removing age/gender of patients as extra two features in last FC layer
      9. 77.1% on validation set after training till training set had 100% accuracy with learning rate 0.00005, simplified model had 82%, possibly due to overfitting data. Adding age and gender increased validation accuracy by 5% and 2.5%, also trained faster. Note that simple logistic regression with age, neglecting MR-images has 72% accuracy.
      10. Normalisation led to faster convergence and better accuracy
      11. Sensitivity analysis on heat-map R. F. Matthew D. Zeiler, “Visualizing and understanding convolutional networks,” arXiv:1311.2901v3 [cs.CV] 28 Nov 2013, 2013.
      12. 100%, very impressive..