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Accessible False Discovery Rate Computation

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OBJECTIVES/GOALS: To improve the implementation of FDRs in translation research. Current statistical packages are hard to use and fail to adequately convey strong assumptions. We developed a software package that allows the user to decide on assumptions and choose the hey desire. We encourage wider reporting of FDRs for observed findings. METHODS/STUDY POPULATION: We developed a user-friendly R function for computing FDRs from observed p-values. A variety of methods for FDR estimation and for FDR control are included so the user can select the approach most appropriate for their setting. Options include Efron's Empirical Bayes FDR, Benjamini-Hochberg FDR control for multiple testing, Lindsey's method for smoothing empirical distributions, estimation of the mixing proportion, and central matching. We illustrate the important difference between estimating the FDR for a particular finding and adjusting a hypothesis test to control the false discovery propensity. RESULTS/ANTICIPATED RESULTS: We performed a comparison of the capabilities of our new p.fdr function to the popular p.adjust function from the base stats-package. Specifically, we examined multiple examples of data coming from different unknown mixture distributions to highlight the null estimation methods p.fdr includes. The base package does not provide the optimal FDR usage nor sufficient estimation options. We also compared the step-up/step-down procedure used in adjusted p-value hypothesis test and discuss when this is inappropriate. The p.adjust function is not able to report raw-adjusted values and this will be shown in the graphical results. DISCUSSION/SIGNIFICANCE OF IMPACT: FDRs reveal the propensity for an observed result to be incorrect. FDRs should accompany observed results to help contextualize the relevance and potential impact of research findings. Our results show that previous methods are not sufficient rich or precise in their calculations. Our new package allows the user to be in control of the null estimation and step-up implementation when reporting FDRs.

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Acral, Head and Neck Melanoma Subtype Classification Performance Using A Convolutional Neural Network (CNN) Trained On a Public Dataset

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OBJECTIVES/GOALS: Composition of demographics or image types in publicly available datasets may detract from deep learning (DL) diagnosis performance of underrepresented melanoma subtypes. We evaluate a DL model's performance on melanoma subtypes (acral; head and neck) that have known association with poor prognosis. METHODS/STUDY POPULATION: We trained a CNN using a single InceptionV3 model for 30 epochs on dermoscopic images of pigmented lesions from the International Skin Imaging Collaboration (ISIC). The ISIC 2018 challenge training set had 10008 total images, with 1113 total nevi, 6705 total melanomas, 97 acral nevi, 10 acral melanomas, 256 head and neck (H&N) nevi, and 164 H&N melanomas. The non-acral test set had 117 melanomas and 200 nevi. The acral test set had 201 melanomas and 161 nevi. The H&N test set had 199 melanomas and 128 nevi. Area under the receiver operating curve (AUC) was calculated. The model was retrained with acral lesion oversampling (10x) and performance on the acral test set was re-evaluated. RESULTS/ANTICIPATED RESULTS: The model performed on the non-acral test with an AUC of 80.5%, on the acral test with an AUC of 76.3%, and on the head and neck test with an AUC of 83.8% After oversampling acral lesions within the training set, the model showed nearly the same performance as without oversampling on acral lesions: AUC of 75.6%. DISCUSSION/SIGNIFICANCE OF IMPACT: Diagnosis of high-risk melanoma subsets (acral; H&N) remains reliable despite underrepresentation during training, increasing validity for broad implementation of DL technology. Datasets for individual subtypes may not be warranted as findings suggest features may be learned from other skin lesions.

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Age-related Changes in the Functional Connectivity within the Default Mode Network*

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OBJECTIVES/GOALS: To evaluate whether the default mode network experiences age-related changes in functional connectivity and to identify these patterns of progression across seven decades of life. The overall goal is to evaluate whether quantifying these functional changes can serve as potential neurobiomarkers of aging for further quantitative genetic analyses. METHODS/STUDY POPULATION: Scans were performed at the RII on a 3T Siemens Trio scanner with an 8-channel head coil. Whole-brain, rsfMR imaging was performed using a gradient-echo EPI sequence sensitive to the BOLD effect (TE/TR = 30/3000 ms; flip angle = 90°; isotropic 1.72 mm^2). Subjects were instructed to lie in dimmed light with their eyes open and try not to fall asleep. Image analysis was performed with FMRIB's Software Library tools (www.fmrib.ox.ac.uk/fsl). Preprocessing of resting state data includes motion correction, brain extraction, spatial smoothing, and high-pass temporal filtering. Time series data was extracted from 9 DMN ROIs using FSL's Featquery tool with 6mm radius spherical ROI masks created in Mango. After extraction, DMN connectivity was assess using structural equation modeling implemented in Amos 22.0 (IBM, Inc.). RESULTS/ANTICIPATED RESULTS: The exploratory SEM (eSEM) default mode network (DMN) model used consists of 9 regions of interest and 13 functional connectivity paths. The eSEM DMN model exhibited exceptional model fit to a primary resting state data set of 1169 subjects from the Genetics of Brain Structure project (1R01MH078111-01, David Glahn PI) with an RMSEA of 0.037. This model also had excellent model fit in 7 cohorts that were grouped by decade age (10s – RMSEA: 0.058, 20s – 0.051, 30s – 0.045, 40s – 0.048, 50s – 0.043, 60s – 0.035, 70s – 0.037). Analysis of the decade group-wise path coefficients identified 7 of the 13 paths (pC -> LMTG, pC -> PCC, PCC -> MPFG, PCC -> vACC, MPFG -> vACC, LIPL -> RIPL, LMTG -> RMTG) significantly negatively correlated with age-related changes. As early as the 1st decade of life, the functional connectivity within the DMN decreases. DISCUSSION/SIGNIFICANCE OF IMPACT: The DMN experiences progressive age-related decreases in connectivity, beginning in the first decade of life. Our results suggest that DMN path coefficients can serve as biomarkers of cognitive aging, which can then be used as quantitative traits for genetic analyses to identify genes associated with normal aging and age-related cognitive diseases.

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