Supporting information VI

This supporting information document includes two tables: Table SVI-1 and Table3. Table SVI-1 shows model performance outcomes after software updates of April 10, 2020 were applied. Details on software versions are provided after the second table below, Table 3. This latter table (Table 3) summarizes the findings from the original published work (https://www.frontiersin.org/articles/10.3389/fneur.2020.00364/full).

The model performance outcome with the recent software updates (sTable SVI-1 immediately below) had the same general pattern but performance was slightly improved for the PD vs. HC (control) GAM, random forest, and XGBoost classifiers. Performance was also improved for the SWEDD vs. PD random forest, decision tree, and XGBoost classifiers. The models were independently run several times; results were always reproducible. An R file (Mods.R) is available with code for all the analyses. If you would like the original R code for all models please contact the lead author (Charles Leger: cslfalcon@gmail.com). The data sets (derived from PPMI data) are available from Frontiers in Neurology (see the above link) and from https://github.com.

TABLE SVI-1: Performance summary, based on software updated April 2020

Early PD versus HC

Models	*Train*			*Test* (cross-validation)					
Metric	AUC (95% CI)	SN	SP	Opt.Thr	AUC (95% CI)	ACC	Kappa	SN	SP
GLM	.920 (0.888-0.953)	.912	.812	.462	.907 (0.849-0.964)	.898	.764	.909	.872
GAM	.946 (0.922-0.970)	.923	.850	.534	**.961 (0.930-0.991)**	**.905**	**.790**	**.886**	**.948**
Tree [a]	.827 (0.778-0.877)	.875	.795	.805	.857 (0.789-0.925)	.866	.696	.875	.846
RF [a]	.999 (0.999-1.00)	1.00	.900	.534	.944 (0.904-0.985)	.913	.806	.909	.872
XGB [a]	.952 (0.928-0.975)	.913	. 857	.660	.938 (0.895-0.981)	.905	.784	.909	.897

Early PD versus SWEDD

Models	*Train*			*Test* (cross-validation)					
Metric	AUC (95% CI)	SN	SP	Opt.Thr.	AUC (95% CI)	ACC	Kappa	SN	SP
GLM [b]	.938 (0.863-0.972)	.909	.841	.504	.779 (0.677-0.880)	.744	.265	.667	.755
GAM [b]	.955 (0.916-0.994)	.886	.909	.437	.787 (0.689-0.886)	.756	.299	.714	.762
Tree [a, b]	.932 (0.894-0.971)	.864	.920	.486	.882 (0.824-0.937)	.839	.471	.809	.843
RF [a, b]	1.00 (1.00-1.00)	1.00	1.00	.599	**.911 (0.852-0.967)**	**.839**	**.486**	**.857**	**.837**
XGB [a, b]	.999 (0.998-1.00)	1.00	.997	.599	.902 (0.840-0.965)	.839	.500	.905	.829

Note: the GLM and decision tree results were unchanged, but all other results marginally changed due to software package updates. Values altered by the updated software are dark red. Superscript a = 10-fold, 5 repeats resampling of the model tuning parameter(s), whereby the optimal hyper-parameter setting was determined by the AUC; ACC = accuracy; superscript b = synthetic minority oversampling technique (SMOTE); AUC = receiver operating characteristic area under the curve; CI = DeLong confidence interval; Kappa = Cohen's Kappa; SP = specificity; SN = sensitivity**;** GAM = general additive model; GLM = logistic regression generalized linear model; RF = random forest; Tree = decision tree; XGBoost = Extreme gradient boosting; thr= threshold; Bold model names = highest cross-validated AUC

TABLE 3: Performance summary based on original January 2020 software versions used (reported in the paper)

Early PD versus HC

Models	*Train*			*Test* (cross-validation)					
Metric	AUC (95% CI)	SN	SP	Opt.Thr	AUC (95% CI)	ACC	Kappa	SN	SP
GLM	.920 (0.888-0.953)	.912	.812	.462	.907 (0.849-0.964)	.898	.764	.909	.872
GAM	.946 (0.922-0.970)	.923	.850	.534	**.928** (0.878-0.978)	.898	.768	.898	.897

Tree [a]	.872 (0.831-0.913)	.857	.879	.586	.860 (0.799-0.922)	.842	.659	.818	.897
RF [a]	.999 (0.999-1.00)	.990	1.00	.534	.913 (0.858-0.968)	.898	.764	.909	.872
XGB [a]	.958 (0.937-0.979)	.898	. 901	.660	.923 (0.875-0.972)	.882	.736	.875	.897

Early PD versus SWEDD

Models

	Train			*Test* (cross-validation)					
Metric	AUC (95% CI)	SN	SP	Opt.Thr.	AUC (95% CI)	ACC	Kappa	SN	SP
GLM [b]	.938 (0.863-0.972)	.909	.841	.504	.779 (0.677-0.880)	.744	.265	.667	**.**755
GAM [b]	.955 (0.916-0.994)	.886	.909	.437	.787 (0.689-0.886)	.756	.299	.714	.762
Tree [a, b]	.932 (0.894-0.971)	.864	.920	.486	.743 (0.617-0.869)	.798	.343	.667	.816
RF [a, b]	1.00 (1.00-1.00)	1.00	1.00	.461	.822 (0.746-0.899)	.732	.302	.809	**.**721
XGB [a, b]	.997 (0.993-1.00)	.977	.954	.542	**.863** (0.777-0.948)	.768	.381	.905	**.**748

Note: Superscript a = 10-fold, 5 repeats resampling of the model tuning parameter(s), whereby the optimal hyper-parameter setting was determined by the AUC; ACC = accuracy; superscript b = synthetic minority oversampling technique (SMOTE); AUC = receiver operating characteristic area under the curve; CI = DeLong confidence interval; Kappa = Cohen's Kappa; SP = specificity; SN = sensitivity**;** GAM = general additive model; GLM = logistic regression generalized linear model; RF = random forest; Tree = decision tree; XGBoost = Extreme gradient boosting; thr= threshold; Bold model names = highest cross-validated AUC

Software session information

Current session information (April 19, 2020)

This section lists the up to date session information regarding software packages used to build the models. These updated packages were used to again re-run the same five models originally run in January 1, 2020. Neither the models nor the original data were altered but a number of software packages were updated during the four-month hiatus. With the exception of the logistic regression classifier, all models had slight improvements in performance. We attribute this slight change to largely to updates in the caret, random forest, and mgcv (GAM) packages. The current session information software package version is listed immediately below. This is followed by the session information from the original running of the models in January.

Current updated session information

R version 3.6.3 (2020-02-29)

Platform: x86_64-apple-darwin15.6.0 (64-bit)

Running under: macOS High Sierra 10.13.6

attached base packages:

[1] stats graphics grDevices utils datasets methods base

other attached packages:

[1] **mgcv_1.8-31** nlme_3.1-145 rpart_4.1-15 **randomForest_4.6-14**

[5] **caret_6.0-86** ggplot2_3.3.0 lattice_0.20-38 car_3.0-7

[9] carData_3.0-3

loaded via a namespace (and not attached):

[1] Rcpp_1.0.4.6 lubridate_1.7.8 class_7.3-15 assertthat_0.2.1

[5] ipred_0.9-9 foreach_1.5.0 R6_2.4.1 cellranger_1.1.0

[9] plyr_1.8.6 stats4_3.6.3 pillar_1.4.3 rlang_0.4.5

[13] curl_4.3 readxl_1.3.1 rstudioapi_0.11 data.table_1.12.8

[17] Matrix_1.2-18 splines_3.6.3 gower_0.2.1 stringr_1.4.0

[21] foreign_0.8-75 munsell_0.5.0 compiler_3.6.3 pkgconfig_2.0.3

[25] nnet_7.3-12 tidyselect_1.0.0 tibble_3.0.0 prodlim_2019.11.13

[29] rio_0.5.16 codetools_0.2-16 fansi_0.4.1 crayon_1.3.4

[33] dplyr_0.8.5 withr_2.1.2 ModelMetrics_1.2.2.2 MASS_7.3-51.5

[37] recipes_0.1.10 grid_3.6.3 gtable_0.3.0 lifecycle_0.2.0

[41] magrittr_1.5 pROC_1.16.2 scales_1.1.0 zip_2.0.4

[45] cli_2.0.2 stringi_1.4.6 reshape2_1.4.4 timeDate_3043.102

[49] ellipsis_0.3.0 generics_0.0.2 vctrs_0.2.4 openxlsx_4.1.4

[53] lava_1.6.7 iterators_1.0.12 tools_3.6.3 forcats_0.5.0

[57] glue_1.4.0 purrr_0.3.3 hms_0.5.3 abind_1.4-5

[61] survival_3.1-8 colorspace_1.4-1 haven_2.2.0

Original session information

Below is the Session information for the software versions used in the original research published in *Frontiers in neurology;* Manuscript ID 525605*,* May 11, 2020.

R version 3.4.0 (2017-04-21)

Platform: x86_64-apple-darwin15.6.0 (64-bit)

Running under: macOS 10.13.6

[1] DMwR_0.4.1 **xgboost_0.6.4.6** pROC_1.13.0

[4] **mgcv_1.8-27** nlme_3.1-131 randomForest_4.6-14

[7] **caret_6.0-78** lattice_0.20-35 rpart_4.1-13

[10] QuantPsyc_1.5 MASS_7.3-48 boot_1.3-20

[13] ggplot2_2.2.1 psych_1.7.8 car_2.1-6

loaded via a namespace (and not attached):

[1] bitops_1.0-6 pbkrtest_0.4-7 xts_0.11-1

[4] lubridate_1.7.1 dimRed_0.1.0 tools_3.4.0

[7] R6_2.2.2 KernSmooth_2.23-15 lazyeval_0.2.1

[10] colorspace_1.3-2 nnet_7.3-12 withr_2.1.2

[13] tidyselect_0.2.5 mnormt_1.5-5 curl_3.1

[16] compiler_3.4.0 quantreg_5.34 SparseM_1.77

[19] labeling_0.3 caTools_1.17.1 scales_0.5.0

[22] sfsmisc_1.1-1 DEoptimR_1.0-8 robustbase_0.92-8

[25] stringr_1.2.0 digest_0.6.13 foreign_0.8-69

[28] minqa_1.2.4 pkgconfig_2.0.1 lme4_1.1-15

[31] rlang_0.3.1 TTR_0.23-4 ddalpha_1.3.1

[34] quantmod_0.4-13 bindr_0.1 zoo_1.8-0

[37] gtools_3.5.0 dplyr_0.7.4 ModelMetrics_1.1.0

[40] magrittr_1.5 Matrix_1.2-12 Rcpp_0.12.14

[43] munsell_0.4.3 abind_1.4-5 stringi_1.1.6

[46] gplots_3.0.1 plyr_1.8.4 recipes_0.1.2

[49] parallel_3.4.0 gdata_2.18.0 **splines_3.4.0**

[52] reshape2_1.4.3 codetools_0.2-15 stats4_3.4.0

[55] CVST_0.2-1 glue_1.3.0 data.table_1.10.4-3

[58] nloptr_1.0.4 foreach_1.4.4 MatrixModels_0.4-1

[61] gtable_0.2.0 purrr_0.3.2 tidyr_0.7.2

[64] kernlab_0.9-25 assertthat_0.2.0 DRR_0.0.3

[67] gower_0.1.2 prodlim_1.6.1 broom_0.4.3

[70] class_7.3-14 survival_2.41-3 timeDate_3042.101

[73] RcppRoll_0.2.2 tibble_1.3.4 iterators_1.0.9

[76] bindrcpp_0.2 lava_1.6 **ROCR_1.0-7**

[79] ipred_0.9-6