**Supplemental material to the article “EEG/ERP-based biomarker/neuroalgorithms in adults with ADHD: Development, reliability, and application in clinical practice”**

***Supplemental material 1: Description of the parameter grids***

5 classification algorithms were applied in the framework:

Regularised Logistic Regression, SVM with linear kernel, SVM with RBF kernel, XGBoost, and Random Forest. Within each of these types the framework tested all possible combinations of hyperparameters defined as follows:

Logistic Regression:

Penalty type: “L1” (Lasso regression) or “L2” (Ridge regression).

Regularization strength C: 0.001, 0.01, 0.1, 1, 10, 100, 1000.

Linear SVM:

Penalty parameter C of the error term: 0.001, 0.01, 0.1, 1, 10, 100, 1000.

RBF SVM:

Penalty parameter C of the error term: 0.001, 0.01, 0.1, 1, 10, 100, 1000.

Kernel coefficient gamma: 0.001, 0.01, 0.1, 1, 10, 100, 1000.

XGBoost:

Number of estimators: 50, 250, 1000.

Random Forest:

Number of estimators: 50, 250, 1000.

Function measuring quality of a split: either “gini” (Gini impurity) or “entropy” (information gain).

For example: for the Logistic Regression there are 7 different values of C and two types of penalty which totals in 14 possible versions of Logistic Regression.

In addition to these parameters, the framework tested each version of the model with two possible kinds of input features: the original set of features and the PCA components of the original feature set.

The PCA transform was used as a form of compression due to the fact that EEG/ERP features are often correlated.

It totals in 158 different versions of the model.

***Supplemental material 2: Final feature set used for classification***

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| --- | --- |
| ERP\_GO&NOGO\_ST1\_Pz\_pos\_amp\_416 | ERP\_NOGO-GO\_ST2\_T5\_pos\_amp\_240 |
| ERP\_GO\_ST2\_Cz\_pos\_lat\_168 | ERP\_NOGO-GO\_ST2\_T5\_pos\_lat\_148 |
| ERP\_GO\_ST2\_Fz\_neg\_lat\_268 | ERP\_NOGO-GO\_ST2\_T6\_neg\_amp\_352 |
| ERP\_GO\_ST2\_O1\_neg\_amp\_148 | IC\_IGNORE&NOVELTY\_ST1\_ICP1N1P2vO\_neg\_amp\_144 |
| ERP\_GO\_ST2\_O2\_pos\_lat\_228 | IC\_IGNORE&NOVELTY\_ST1\_ICP1N1P2vO\_pos\_amp\_236 |
| ERP\_GO\_ST2\_Pz\_pos\_lat\_320 | IC\_IGNORE&NOVELTY\_ST1\_ICP1N1P2vTL\_neg\_amp\_196 |
| ERP\_GO\_ST2\_ST2\_Cz\_neg\_lat\_096 | IC\_IGNORE&NOVELTY\_ST1\_ICP1N1P2vTR\_neg\_amp\_160 |
| ERP\_GO\_ST2\_T5\_pos\_lat\_232 | IC\_NOGO\_ST2\_ICP1N1P2vTL\_neg\_lat\_160 |
| ERP\_GO\_ST2\_T6\_neg\_amp\_352 | IC\_NOGO\_ST2\_ICP1N1P2vTR\_pos\_lat\_108 |
| ERP\_GO\_ST2\_T6\_pos\_lat\_104 | IC\_NOGO\_ST2\_ICP3NOGOearly\_neg\_amp\_236 |
| ERP\_GO\_ST2\_T6\_pos\_lat\_236 | PS\_EC\_C3\_02-04 |
| ERP\_IGNORE&NOVELTY\_ST1\_O1\_pos\_amp\_240 | PS\_EC\_C4\_40-50 |
| ERP\_IGNORE&NOVELTY\_ST1\_O1\_pos\_lat\_104 | PS\_EC\_C4\_04-07 |
| ERP\_IGNORE&NOVELTY\_ST1\_O1\_pos\_lat\_240 | PS\_EC\_Cz\_20-30 |
| ERP\_IGNORE&NOVELTY\_ST1\_O2\_pos\_amp\_240 | PS\_EC\_Pz\_20-30 |
| ERP\_IGNORE\_ST2\_Cz\_neg\_lat\_108 | PS\_EO\_C3\_02-04 |
| ERP\_NOGO\_ST2\_Cz\_pos\_amp\_168 | PS\_EO\_C4\_40-50 |
| ERP\_NOGO\_ST2\_Fz\_pos\_lat\_164 | PS\_EO\_Cz\_40-50 |
| ERP\_NOGO\_ST2\_Pz\_neg\_lat\_188 | PS\_EO\_T5\_03-06 |
| ERP\_NOGO\_ST2\_T5\_pos\_lat\_108 | PS\_VCPT\_C3\_02-04 |
| ERP\_NOGO\_ST2\_T6\_neg\_lat\_336 | PS\_VCPT\_C4\_04-07 |
| ERP\_NOGO-GO\_ST2\_Pz\_pos\_lat\_236 | PS\_VCPT\_F4\_18-21 |
| ERP\_NOGO-GO\_ST2\_T5\_neg\_lat\_340 | PS\_VCPT\_P3\_30-40 |
| ERP\_NOGO-GO\_ST2\_T5\_pos\_amp\_148 |  |

The feature names are composed of different elements. The first element points to the general feature type (“ERP” standing for “event-related potential”, “IC” for “independent ERP component”, and “PS” for “power spectrum”).

In case of an ERP or IC feature, the subsequent name elements are composed of 1) the VCPT trial category (“GO”, “GO&NOGO”, “GO-NOGO”, “NOGO”, “IGNORE”, “IGNORE&NOVELTY”), 2) the stimulus (“ST1” standing for “stimulus 1”, “ST2” for “stimulus 2”), 3) the electrode/component name, 4) peak polarity (“pos” standing for “positive”, “neg” for “negative”), 5) ERP feature type (“amp” standing for “amplitude”, “lat” standing for “latency”), 6) average peak latency.

In case of a PS feature, the subsequent name elements are composed of 1) the task type (“EC” standing for “eyes-closed resting state”, “EO” for “eyes-open resting state”, and “VCPT” for “visual continuous performance test”), 2) the electrode, 3) frequency band.

***Supplemental material 3: Example of applying a classifier in clinical work***

Age Group Adults: ADHD: 79%

*Clinical tool output*

The feature set of this individual case shows the highest significance on the ERP feature at Pz in GO condition. This reflects an activation component in the information processing process. Further important features reflect the energization of control and monitoring (ERP NOGO Cz P3) as well as sensitivity (ERP GO O2 P2).

That way, the right questions can be quickly asked in the diagnostic process (in this case, reduced activation, reduced energization of impulse control as well as the influence of sensitivity can be addressed).

***Supplementary material 4: Recommendations***

Recommendations for the development of guidelines for the application of Big Data/Machine Learning models to support the diagnostic process (based on Thome et al. 2012):

1. The data recording of the patient group is crucial. In order to take into account the variability with regard to the diagnostic experts, a multicenter study must always be the basis for the data set. A minimum of 5 centers should be considered.
2. The size of the patient group should not be less than 80-100 patients, these must be compared with a matched control group of at least half the size of the patient group.
3. Sensitivity and specificity must each be 80%, so that a sufficiently reliable statement can be made in the diagnosis.
4. Linear models are preferable due to better interpretability and robustness unless non-linear alternatives provide significantly better performance.
5. The classifiers must be checked for reliability after 12/24 months.
6. The validation of classifiers on the basis of new data sets must be ensured, the new data must contain subjects of both patient and control groups.
7. The distinction between different patient groups should be targeted.