Supplementary to
LSTMs and resting-state fMRI for classification and understanding of Parkinson's disease

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1 Analysis of important regions-of-interest and their relevance to existing literature on Parkinson's disease

Using the procedure described in Section 2.5, importance weights are computed and thresholded to determine ROIs that were identified as salient in discriminating HDs from PDs.

As similarly done in [17], we employed a threshold t of 2 standard deviations from the absolute mean of the weights. This threshold corresponds to finding ROIs whose absolute weights are greater than 95% of those of all other ROIs. After aggregrating the weights derived over all units and all cross-validation

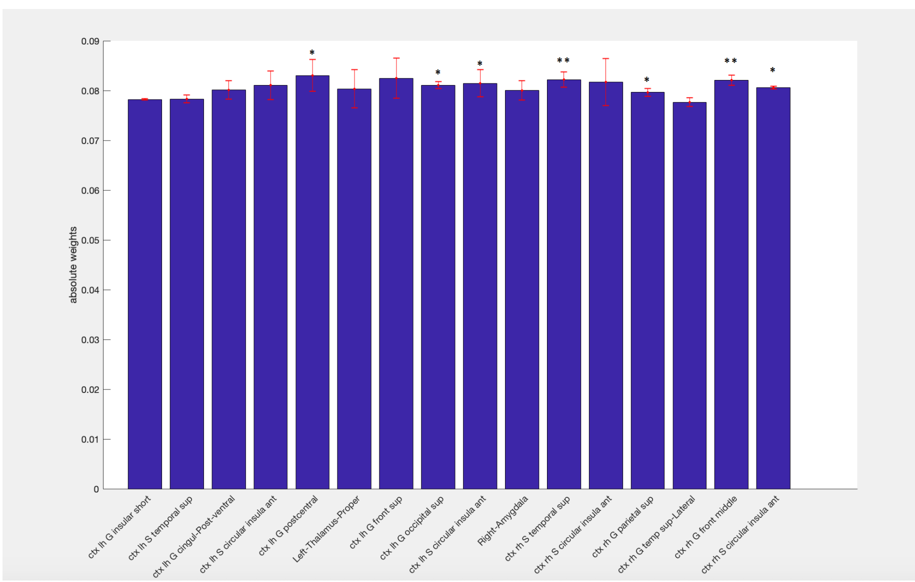

Fig. 1. Measured mean absolute weights of different ROIs that were greater than 2 standard deviations from the absolute means. ROIs whose importance weights are greater than standard deviations from the mean are marked with **; those whose importance weights that are greater than 2.5 standard deviations from the mean are marked with *.

Gate	ROIs	Functions	Relevance
Input	Left short insular gyrus [7]	Emotions, cognition	Non-motor symptoms of PD
	Left superior temporal sulcus [15]	Motion perception	Motion perception is impaired in PD
Forget	Left Posterior ventral cingulate [2]	Cognitive processing, executive performance	Part of default mode network, cognitive impairment in PD
	Left anterior circular insula [7, 14]	Autonomic processes	Part of salience network, Non-motor symptoms
Control	Left postcentral gyrus [12]	sensory receptive area for the sense of touch	sensory deficits like touch and smell in PD
Output	Left Thalamus [3]	Relaying motor signals to the cerebral cortex	Motor pathways affected in PD
	Left superior frontal gyrus [19]	cognitive control and executive control	Part of frontoparietal network
	Left superior occipital gyrus [13, 16]	Process visual information	worsened visuo-perceptual processing in Parkinson's disease
	Left anterior circular insula [7, 14]	subjective emotional experience	Part of salience network, Non-motor symptoms
Input	Right Amygdala [1]	Emotion processing	Depression in PD
	Right superior temporal sulcus [15]	Motion perception	Motion perception is impaired in PD
Forget	Right anterior circular insula [6]	Emotional experience and subjective feeling	Part of salience network
Control	Right superior parietal gyrus [10]	Spatial orientation	Part of frontoparietal network
	Right lateral superior temporal gyrus [5]	Auditory processing, including language, social cognition	Motion perception is impaired in PD
Output	Right middle frontal [19]	Executive attention	Part of frontoparietal network
	Right anterior circular insula [6]	Emotional experience and subjective feeling	Part of salience network

Table 1. ROIs that were shown to be important for PD-HC classification in our study and their relevance to existing studies.

folds, 14 ROIs were found to be important using this threshold. Fig. 1 shows a barplot of the mean and standard deviation of the absolute value of the weights of these 14 important ROIs. The low standard deviations shown on the barplot reflect that the derived feature weights remain fairly similar across trials.

In addition, we identified in Fig. 1 the ROIs whose mean absolute weights are greater than t standard deviations (STD) from the mean, with * and ** corresponding to t=2.5 and t=3, respectively. From Fig. 1, one could see that 7 ROIs exceeded 2.5 standard deviations from the mean, and that 2 of these stood out: the *right-superior temporal sulcus* and the *right-middle frontal gyrus*. According to the literature, the superior temporal sulcus is linked to the motion perception, which has been shown to be more commonly impaired in PDs than HCs [15]. On the other hand, the superior frontal gyrus (along with the mid-frontal and superior parietal gyrus) is known to be the main components of the fronto-parietal network, which is essential for cognitive control and executive control, whose impairments are commonly reported in PDs [8, 11].

Literature findings related to the rest of the ROIs that were identified as important (using t=2 STDs from the mean) are summarized in Table 1. The first column notes the gate type of the LSTM model from which the feature weights were derived; the third column identifies which functions have been attributed to the corresponding ROIs; the last column highlights the specific conclusions the corresponding articles have described that relate to the impairment of these ROIs and/or their associated functions in PD patients.

For instance, one of the identified important ROI is the *short insular gyrus*, which is known to be associated to non-motor symptoms of PD, such as apathy, blunted emotional responses and cognitive impairment [9]. Similarly, *anterior insula* is known to be responsible for autonomic processes. Dysfunction in these area could contribute to PD non-motor symptoms such as orthostatic hypotension, gastrointestinal dysfunction, and urinary dysfunction [18].

Another ROI deemed important is the *posterior ventral cingulate*, which is part of the default mode network that is known to be associated with cognitive processing and executive performance [2]. The integrity and function of default mode network have been widely reported to be impaired in PD, especially in patients with mild cognitive impairment and dementia [2].

The other important ROIs that have relevance to the PD literature are those in the gyrus: postcentral gyrus, superior occipital gyrus, and lateral superior temporal gyrus. The *postcentral gyrus* is part of the sensorimotor cortex and is known to be associated to the sensory receptive area for the sense of touch; dysfunction in this region could explain the sensory deficits like touch and smell [4] suffered by PD patients. Similarly, the *superior occipital gyrus* is known to process visual information; impairments of this region may explain how PD patients experience vision problems [16] and suffer from worsening of visuo-perceptual processing [16]. Lastly, the *lateral superior temporal gyrus*, which is known to be involved in auditory processing, has been shown to be attributed to PD patients' slowness in thought and in use of language, as well as memory difficulties.

In summary, 14 out of 200 ROIs have been identified in our study as important for HC-PD classification via LSTM's unsupervised feature extraction process. Many of these 14 ROIs are associated with the brain networks that are commonly found to be symptomatic in PDs (i.e., default mode network, salience network and frontoparietal network). Furthermore, of the 14 important ROIs, 8 of them have been shown to be related to PD's functional impairment in previous studies as introduced above.

2 Sensitivity analysis to p

Table 2 shows the performance scores as we decrease the keep probability p from 0.7 to 0.5 for the case of a single LSTM. In general, the performance scores are very similar between the two values. However, with p=0.5, we see slight improvement in the scores, albeit the improvement was not statistical significant, with a p-value of 0.408 when subjected to a paired t-test and a p-value of 0.2857 when subjected to Wilcoxon's rank-sum test.

l=2, u=40, p=0.5	F1-score	Precision	Recall
Proposed 2-component	0.6868 ± 0.030785	0.73 ± 0.028284	0.676 ± 0.073348
Single LSTM - all ROIs	0.6702 ± 0.02151	0.74 ± 0.025495	0.674 ± 0.094499
l=2, u=50, p=0.5	F1-score	Precision	Recall
Proposed 2-component	0.7004 ± 0.038371	0.724 ± 0.030496	0.692 ± 0.048166
Single LSTM - all ROIs	0.6794 ± 0.022744	0.72 ± 0.027386	0.658 ± 0.055408
l=2, u=60, p=0.5	F1-score	Precision	Recall
Proposed 2-component	0.6946 ± 0.041519	0.724 ± 0.018166	0.686 ± 0.054129
Single LSTM - all ROIs	0.674 ± 0.02509	0.726 ± 0.034351	0.666 ± 0.041593
l=3, u=40, p=0.5	F1-score	Precision	Recall
Proposed 2-component	0.6854 ± 0.030312	0.726 ± 0.038471	0.71 ± 0.07
Single LSTM - all ROIs	0.6784 ± 0.028219	0.702 ± 0.052631	0.686 ± 0.021909
l=3, u=50, p=0.5	F1-score	Precision	Recall
Proposed 2-component	0.6926 ± 0.0377	0.746 ± 0.015166	0.676 ± 0.063482
Single LSTM - all ROIs	0.6686 ± 0.029348	0.734 ± 0.023022	0.626 ± 0.063087
l=3, u=60, p=0.5	F1-score	Precision	Recall
Proposed 2-component	0.7038 ± 0.065308	0.758 ± 0.037683	0.688 ± 0.088431
Single LSTM - all ROIs	0.6706 ± 0.033598	0.736 ± 0.031305	0.662 ± 0.11278

Table 2. Shown are the mean and standard deviation of F1-score, precision and recall of various frameworks tested with keep probability (p) set to 0.5.

3 Increasing the number of layers

Table 3 shows the performance when we employ 4 layers. The results are very similar to those reported from the comparison table shown in the main submission, i.e. results of using 3 layers are very similar to those using 4 layers, suggesting that performance gains saturated when l=3.

l=4, u=40	F1-score	Precision	Recall
Proposed 2-component, p=0.7	0.691 ± 0.049244	0.746 ± 0.019494	0.668 ± 0.080125
Proposed 2-component, p=0.5	0.6728 ± 0.033789	0.744 ± 0.0251	0.622 ± 0.076616
l=4, u=50	F1-score	Precision	Recall
Proposed 2-component, p=0.7	0.6804 ± 0.028501	0.736 ± 0.036469	0.672 ± 0.075299
Proposed 2-component, p=0.5	0.6792 ± 0.042763	0.752 ± 0.013038	0.628 ± 0.085264
l=4, u=60	F1-score	Precision	Recall
Proposed 2-component, p=0.7	0.7046 ± 0.060186	0.738 ± 0.061806	0.704 ± 0.060249
Proposed 2-component, p=0.5	0.6628 ± 0.020167	0.758 ± 0.0044721	0.628 ± 0.085264

Table 3. Shown are the mean and standard deviation of F1-score, precision and recall of various frameworks tested with p =0.7 and 0.5.

4 Comparison of number of parameters

Table 4 presents the number of parameters employed by each model variant. We designed our comparison presented in the paper according to this table, which allowed us to identify the model variants that have comparable number of parameters.

Model	Hyper-parameters	Total # of model parameters
Proposed 2-component model	NL=2, HS=40	85,442
Proposed 2-component model	NL=2, HS=50	118,802
Proposed 2-component model	NL=2, HS=60	156,962
Proposed 2-component model	NL=3, HS=40	111,362
Proposed 2-component model	NL=3, HS=50	159,202
Proposed 2-component model	NL=3, HS=60	215,042
Single LSTM - all ROIs	NL=2, HS=40	58,722
Single LSTM - all ROIs	NL=2, HS=50	79,402
Single LSTM - all ROIs	NL=2, HS=60	102,482
Single LSTM - all ROIs	NL=3, HS=40	71,682
Single LSTM - all ROIs	NL=3, HS=50	99,602
Single LSTM - all ROIs	NL=3, HS=60	131,522
Single LSTM - 2x params	NL=2, HS=40	155,842
Single LSTM - 2x params	NL=2, HS=50	218,802
Single LSTM - 2x params	NL=2, HS=60	291,362
Single LSTM - 2x params	NL=3, HS=40	207,362
Single LSTM - 2x params	NL=3, HS=50	299,202
Single LSTM - 2x params	NL=3, HS=60	407,042
Single LSTM - only left ROIs	NL=2, HS=40	42,722
Single LSTM - only left ROIs	NL=2, HS=50	59,402
Single LSTM - only left ROIs	NL=2, HS=60	78,482
Single LSTM - only left ROIs	NL=3, HS=40	55,682
Single LSTM - only left ROIs	NL=3, HS=50	79,602
Single LSTM - only left ROIs	NL=3, HS=60	107,522
Single LSTM - only right ROIs	NL=2, HS=40	42,722
Single LSTM - only right ROIs	NL=2, HS=50	59,402
Single LSTM - only right ROIs	NL=2, HS=60	78,482
Single LSTM - only right ROIs	NL=3, HS=40	55,682
Single LSTM - only right ROIs	NL=3, HS=50	79,602
Single LSTM - only right ROIs	NL=3, HS=60	107,522

Table 4. Comparison of number of parameters in each model.

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