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Bodily maps of symptoms and emotions in Parkinson's disease

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Abstract

Background: Emotions are reflected in bodily sensations and these reflections are abnormal in psychiatric conditions. However, emotion-related bodily sensations have not been studied in neurological disorders.

Objectives: To investigate whether Parkinson's disease is associated with altered bodily presentations of emotions.

Methods: Symptoms and emotion-related sensations were investigated in 380 patients with PD and 79 controls, using a topographical self-report method, termed body sensation mapping. The bodily mapping data was analyzed with pixelwise generalized linear models and principal component analyses.

Results: Bodily maps of symptoms showed characteristic patterns of PD motor symptom distributions. Compared to controls, PD patients showed decreased parasternal sensation of anger, and longer PD symptom duration was associated with increased abdominal sensation of anger (P_{FWE}<0.05). The PD-related sensation patterns were abnormal across all basic emotions (P<0.05).

Conclusions: The results demonstrate altered bodily maps of emotions in Parkinson's disease, providing novel insight into the non-motor effects of Parkinson's disease.

Introduction

Emotions tune our bodies for different situations. They modulate attention, decision-making and cognitive functions to ensure survival and during everyday life. Emotions are associated with physical responses, mediated by the sensorimotor and autonomic nervous systems. For example, when a worker hears about layoffs with simultaneous bonuses to the CEO, a hiker faces a grizzly bear, or a mother sees her newborn, emotions prepare them broadly for action.[1,2]

Body sensation mapping (BSM) is a relatively novel technique for quantitative, topographical mapping of bodily sensations associated with emotions.[2] The method has been shown to yield consistent results across cultures and developmental stages, independent from sex.[3,4] (Neuro)psychiatric disorders, such as schizophrenia and autism, affect emotion processing, reflected in the bodily maps of emotions.[5,6] However, it is unclear if neurodegenerative disorders alter the bodily representations of emotions.

Parkinson's disease (PD) is a common, diffuse neurodegenerative disorder defined and diagnosed by the motor symptoms.[7] Yet, PD is also associated with substantial non-motor symptom burden.[7] The symptoms of PD, especially in the advanced disease stage, are not stable but show considerable fluctuations, primarily linked with brain dopamine levels but are also modulated by emotional states.[8,9] Moreover, basal ganglia, the brain structures primarily affected in PD, play a crucial role in emotional processing.[10–12] Unsurprisingly, previous studies have suggested abnormalities in the recognition of emotional prosody and facial expressions in PD.[13,14]

In this study, we investigated bodily sensations of motor and sensory symptoms and emotions in individuals with PD and controls. We hypothesized that PD is associated with abnormal bodily maps of emotions corresponding to the known autonomic deficits caused by the disease.

Methods

Study sample

380 individuals with PD and 79 controls participated in the study. The study protocol was approved by Turku University Hospital Clinical Research Services Board. The need for separate ethics board review was waived. Written informed consent was obtained and the study conducted according to the principles of the declaration of Helsinki. Participants were recruited through the Finnish Movement Disorders Association via email. The inclusion criterion for the PD group was an established diagnosis of PD by a neurologist, and for the control group, no evidence of PD or other neurodegenerative parkinsonism syndrome. Data collection was conducted online on a platform hosting the BSM tool and a questionnaire about demographic and clinical information, including age, sex, education, alcohol consumption, and smoking, and PD disease duration (from diagnosis), duration of motor symptoms (self-reported), dopaminergic medications, and device-aided treatments.[15]

Bodily sensation maps

The BSM maps (resolution 171 x 522 pixels) were collected with emBODY-tool[2]. The participants were asked to color 1) the bodily locations of the currently experienced motor and sensory symptoms (clumsiness, stiffness, tremor, numbness, and pain) and 2) bodily sensations associated with basic emotions (anger, disgust, fear, happiness, sadness, surprise, and neutral) on an outline of the human body. **(Supplementary Figure 1)** With emotions, the participants were instructed to think carefully what they feel in their body while feeling the emotion in question, and separately color the areas of the body in which they feel the activity increasing or decreasing. Coloring was performed by pressing the mouse button and simultaneously dragging the cursor on the body template. As in the previous studies using this method, emotions were mapped to a body outline without separating front and back side, as emotions are typically localized inside the body rather than superficially.[2,5,6] The raw data matrices were converted to NIfTI (Neuroimaging Informatics Technology Initiative) format to facilitate the preprocessing, and the data were smoothed with Gaussian kernel smoothing ($\sigma = 20$) respecting the body outline boundaries, to control for possible minor anatomical imprecision in the drawings. The preprocessing of the BSM data is described in detail in the **Supplementary Methods**.

Statistics

Statistical analyses were performed with R 4.3.2 (https://www.r-project.org), and pixelwise generalized linear model analyses with Statistical Parametric Mapping software (SPM12, https://www.fil.ion.ucl.ac.uk/spm/software/spm12/). Group differences in demographic and clinical data were investigated using Mann-Whitney U test or Fisher's exact test, as appropriate.

First, to evaluate focal between-group differences and clinical associations of the bodily maps of symptoms and sensations, the BSM data was analyzed with pixelwise generalized linear models applying family-wise error (FWE) correction to correct for multiple comparisons across the whole-body template. The bodily maps of symptoms and emotions were visualized by calculating pixelwise Cohen's D maps for each group separately.

Second, to characterize patterns of symptoms and emotion-associated sensations in PD more generally, principal component analysis (PCA) was used to identify the two components best explaining the overall variance. In this analysis, more positive/negative expression of a component indicates more/less prevalent presence of the component loading pattern in a group compared to the other. Statistical significance of these components was evaluated using permutation tests. The between-group comparisons of the pattern expression values were conducted using Mann-Whitney U test and binary logistic regression. *P* values less than 0.05 were considered significant across all analyses. For the covariance pattern expression values, median and 95% bootstrapped CI of median (10,000 iterations) were chosen as descriptive statistics.

Finally, to evaluate the robustness of the observed covariance patterns, we created random forest classification models for the reclassification of data to control and PD groups. Differences between classification model performance scores were tested using Mann-Whitney U test. More details are available in the **Supplementary Methods**.

Data availability

The emBODY-tool is available at https://version.aalto.fi/gitlab/eglerean/embody and group-level maps at https://github.com/kajuni/Bodily-maps-of-symptoms-and-emotions-in-PD. All other data are available from the corresponding author upon reasonable request, subject to the national and institutional regulations.

Results

There were no significant differences in age, alcohol use, or smoking status. However, the PD group had more males and lower education levels compared to controls **(Table 1)**. There were significant differences between the groups in both the pixelwise linear models (P_{FWE}<0.05) and PCA analysis identifying the two main covariance patterns (P<0.001) of which the first component showed more positive expression in PD (P<0.05) and second in controls (P<0.05) (**Supplementary Tables 1–2**). Adding sex or education as a covariate did not change the significance of any of the findings (**Supplementary Tables 1–2**).

Maps of the motor and sensory symptoms

The bodily maps of the controls were used as reference for motor and sensory symptoms associated with PD (**Fig. 1A**). In PD, clumsiness mapped primarily to distal limbs, stiffness to torso and limbs, and tremor to hands, aligning with clinically expected localization of bradykinesia, rigidity and tremor, respectively (**Fig. 1B**). In the linear models, there were significant differences in bodily maps of symptoms corresponding to the motor symptoms of PD (clumsiness, stiffness, tremor) but not with sensory symptoms (numbness, pain) in individuals with PD compared to controls (P_{FWE} < 0.05, **Fig. 1C**). The principal component analysis revealed more extensive PD-related patterns of all studied motor and sensory symptoms (**Fig. 1D, Supplementary Figure 3)**.

Maps of the emotion-related sensations

Visually, emotion-associated maps of the groups showed tendency towards overall weaker sensations in PD compared to controls, i.e. the bodily sensations associated with emotions in controls were absent or less intensive in the PD group (**Fig. 2A–B**). In the linear models, individuals with PD showed reduced anger-related parasternal sensations compared to controls (P_{FWE} < 0.05, **Fig. 2C**). Adding sex or education as a covariate (**Supplementary Fig. 4**), or balancing the group analysis with random oversampling (**Supplementary Fig. 5**) did not change the significance of these findings. Motor symptom duration was significantly associated with anger-related sensation in the abdomen (P_{FWE} < 0.05) but not with other emotion-related sensations, with or without the covariates (**Supplementary Fig. 6**). None of the emotion-related sensations were associated with LEDD.

Similar to the motor and sensory symptoms, the principal component analysis revealed more widespread PD-related covariance patterns of emotion-related sensations, localizing anger to the abdomen rather than chest (**Figure 2D**). In addition to anger, PD-related patterns of disgust, fear and surprise localized to different body regions, whereas the patterns of happiness and sadness were mostly more restricted compared to control-related patterns (**Supplementary Figure 7**).

Classification with random forest models

The main classification model, including BSM pattern expression and demographic data had a reasonable performance in the reclassification task. Across the 1,000 repeats of first training a model and then testing it with a test dataset, this model had a median area under the curve (*AUC*) of 0.745, 86.3 % median sensitivity, and 100 % median specificity, and performed better than the reference models without BSM pattern expression data ($P < 0.0001$). (**Supplementary Table 3**)

Discussion

The present study is the first to investigate the bodily sensations of motor and sensory symptoms and emotions in a neurological disorder, PD. The bodily maps of the motor symptoms corresponding to the parkinsonian cardinal motor symptoms matched well with clinical localization of these symptoms, demonstrating feasibility of this technique for topographical mapping of symptoms in PD. We further show that PD is associated with abnormal patterns of emotion-related bodily sensations. The bodily mapping data seems robust based on the reasonable performance in the reclassification task between individuals with PD and controls. Overall, our findings add novel information to the non-motor symptoms of PD by showing that a neurodegenerative disorder can affect physical sensations of emotions.

The most prominent abnormality was decreased parasternal sensation related to anger with shift towards the abdomen along with disease progression. This finding may be related to cardiac sympathetic denervation, which is one of the major autonomic features in PD, contributing to the cardiovascular response defects in PD[16]. The cardiac sympathetic denervation process is typically present already early in the disease process and can be detected using [^{123}I]-meta-iodobenzylguanidine (MIBG) scintigraphy.[17] The results from previous studies of basic emotions and their autonomic counterparts in non-PD populations have also shown that anger

has the strongest association with hemodynamic responses[1], which may also be relevant for cardiovascular health[18–20].

Our study is limited by the fact that the reported bodily sensations related to emotions are subjective and it is not known how strongly they correlate with actual physiological responses or abilities experiencing or detecting emotions, which should be confirmed in an independent study with objective measures. In addition, as the previous studies using BSM[2,3,6], this study was conducted online and therefore we were unable to clinically confirm the diagnoses. Although all individuals with PD reported to have an established diagnosis, some of the diagnoses are likely inaccurate as differential diagnostics of parkinsonism syndromes can be challenging even for neurologists[21]. However, this would only bias us against the present group differences. We also cannot exclude possible selection bias in our study population. For example, it is possible that patients with less cognitive impairment may be more likely to participate in this kind of a study. In addition, more severe motor symptoms and cognitive impairment could be reflected in the accuracy of the drawings. However, as the motor symptom maps aligned well with the known clinical symptom distribution, systematic bias in the observed group differences can be considered unlikely.

In conclusion, we show that PD is associated with altered emotion-related bodily sensations, demonstrating that these sensations are abnormal not only in psychiatric and neuropsychiatric disorders but also in a neurodegenerative disorder. Our study also demonstrates the feasibility of bodily sensation mapping technique in PD that could also be useful in other neurological disorders. However, the neurobiological and potential clinical relevance of these findings remain to be determined.

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Authors' Roles

A.H., E.J., E.G. L.N. and J.J. designed research; A.H., E.J. and E.G. collected data; K.J.N., L.N. and J.J. analyzed data; and K.J.N. and J.J. wrote the paper; all authors reviewed and critically revised the paper.

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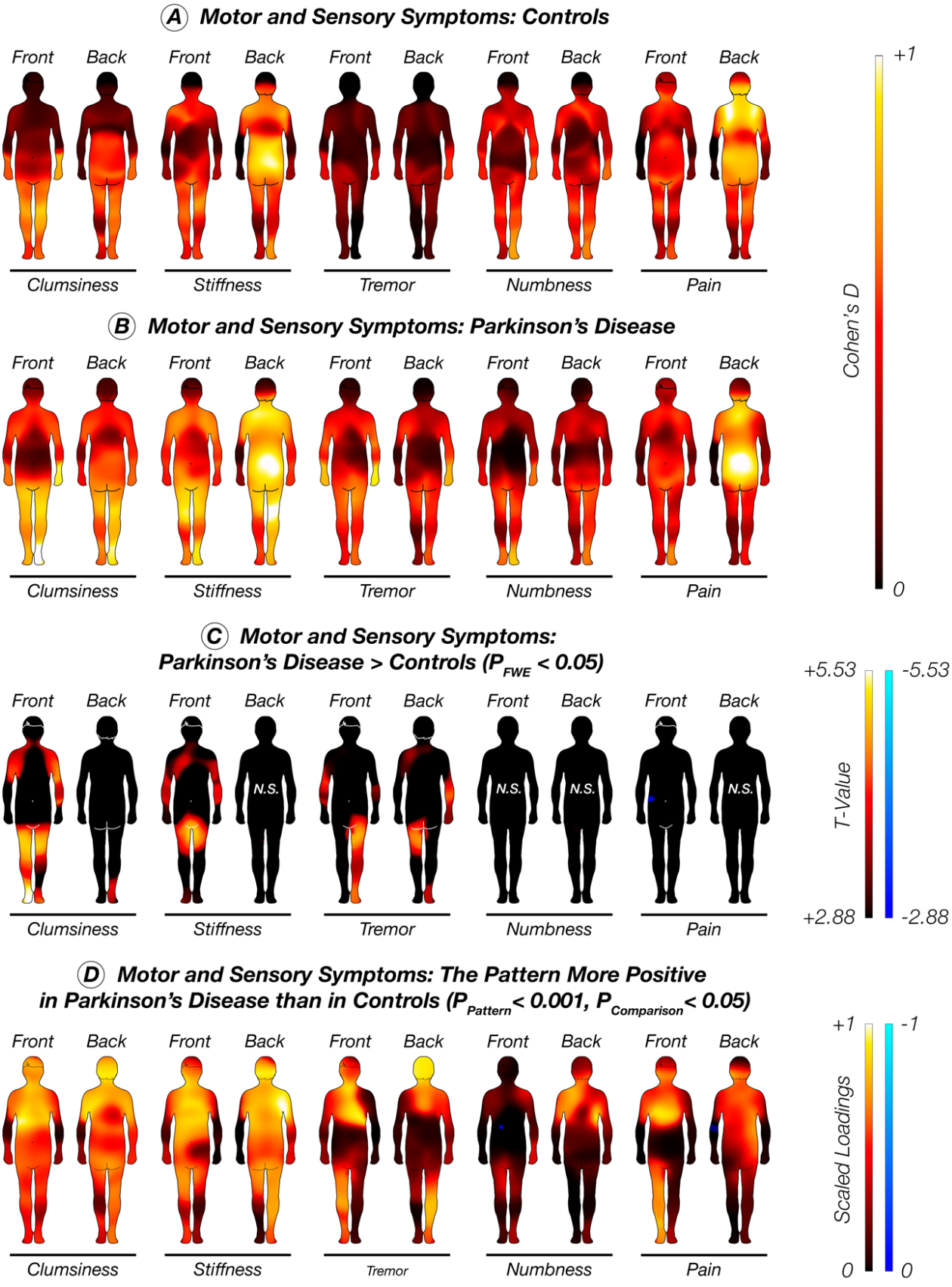
A Motor and Sensory Symptoms: Controls
Front
Back
Clumsiness
Stiffness
Tremor
Numbness
Pain
+1
Cohen's D
0
B Motor and Sensory Symptoms: Parkinson's Disease
C Motor and Sensory Symptoms:
Parkinson's Disease > Controls ($P_{FWE} < 0.05$)
N.S.
+5.53
-5.53
T-Value
+2.88
-2.88
D Motor and Sensory Symptoms: The Pattern More Positive
in Parkinson's Disease than in Controls ($P_{Pattern} < 0.001$, $P_{Comparison} < 0.05$)
+1
-1
Scaled Loadings
0
0

Figure 1. Symptom-related bodily maps. The pixelwise effect sizes in controls (A) and individuals with Parkinson's disease (B), significant differences between groups in the linear model (P_{FWE}<0.05) (C), and PD-related pattern (P < 0.001 for the pattern, P < 0.05 for expression compared to controls) (D). In Parkinson's disease, clumsiness, stiffness, and tremor map to the body regions commonly affected by bradykinesia, rigidity and tremor, respectively (B). These motor, but not sensory, symptoms also showed significant regional differences compared to the controls (C). The PCA analysis showed similar but clearly more widespread patterns associated with Parkinson's disease (D). Red - yellow scale indicates positive values, and blue – light blue scale indicates negative values. N.S. = non-significant.

Supplementary Methods

Bodily sensation maps: Data preprocessing

The emBODY data were first converted to NIfTI (Neuroimaging Informatics Technology Initiative) format for further processing. To control the effect caused by minor errors in drawing and clinically insignificant topographical differences in localization, the data were smoothed using Gaussian smoothing kernel. The smoothing kernel sigma was selected based on visual inspection of the colored maps to best reflect the primary body part (e.g. lower part of the face or distal lower limb) (**Supplementary Fig. 1**). Smoothing with $\sigma = 20$ resulted in the most reasonable anatomical resolution and was selected for the statistical analyses. To prevent spillover across distinct anatomical regions (e.g. from hand to hip, which are anatomically distinct but in close proximity in the body outline used in this study), the original maps in anatomical position were nonlinearly warped to a map space with moderately abducted extremities using ANTs (http://stnava.github.io/ANTs/). Finally, the smoothed maps were returned to the original anatomical position and masked with the body outline.

Statistics: Pixelwise generalized linear models

Pixelwise analyses were conducted with SPM12 (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/) using generalized linear models. First, pixelwise one-sample *T*-tests were performed to create bodily maps for each sensorimotor symptom and emotion. To facilitate visual comparison of the PD and control group maps, the obtained *T*-maps were converted to Cohen's D effect size maps with R 4.3.2. Second, pixelwise two-sample *T*-tests between the groups were performed to identify abnormalities associated with PD. Third, the pixelwise association of each map and i) patient-reported motor symptom duration and ii) levodopa equivalent daily dose (LEDD), were evaluated with univariate linear regression models.

To ensure that the findings were not driven by differences in demographical characteristics between the PD and control group, the two-sample *T*-tests and regression analyses of emotions were repeated with sex and education levels as additional covariates. Pixelwise family-wise error corrected *P* values (P_{FWE}) < 0.05 were considered significant. Finally, to account for the imbalance of the group sizes in the comparative analyses, we conducted additional analyses by randomly oversampling the control group. In this approach, the control group data was

augmented to the sample size of the PD group by duplicating control subjects with random replaceable sampling. For each comparison analysis, the resampling and pixelwise statistical tests with balanced groups were repeated 10,000 times. From these analyses, the mean together with 2.5th and 97.5th percentile *T*-maps were extracted. These maps were thresholded to the *T*-value corresponding to $P_{FWE} < 0.05$.

Statistics: Principal component analyses

The covariance patterns from the BSM data were analyzed with principal component analyses (PCA), across both groups and across all pixels, including both symptom and emotion maps, in R 4.3.2 (https://www.r-project.org). The pixelwise values were centered to the pixelwise mean and scaled to unity. Pixels with all-zero observations were excluded. This PCA analysis resulted in the typical covariance patterns of symptoms and emotion-related sensations for both the groups, as indicated by the two first principal components, accounting for 13.4% of the total variance across the pixelwise BSM data. The statistical significance of the principal components were evaluated with permutation tests (1,000 iterations), using *PCAtest* package.[1] A component value for an individual subject was interpreted as the amount of expression of the corresponding covariance pattern, i.e. the pattern expression value.

Differences in the pattern expression values between the groups were tested using Mann-Whitney U test and binary logistic regression with sex or education as covariates. Finally, to provide additional descriptive information, these models were run with data balanced with random oversampling the control group (10,000 iterations), as with the linear analyses.

Statistics: Classification with random forest models

We trained random forest models with *caret*[2] package in R 4.3.2 for reclassification to PD and control groups, with 10 times repeated, 10-fold cross-validation. The main model had the expression values of the two first principal components, age, sex, education level and smoking status as explanatory variables. The models were trained with 50% of the data and tested on the remaining 50% 1,000 times with group-proportion-saving random data partitioning. Area under the curve (AUC), sensitivity, specificity, and kappa values of these runs were calculated to evaluate the performance of the models. For comparison, similar models were run excluding part of the explanatory variables.

Supplementary Table 1. Expression of the covariance patterns.

	PD Group -Related Covariance Pattern	Control Group -Related Covariance Pattern
Control Group Median [95% CI]	-114.2 [-137.6, -79.2]	0.22 [-11.46, 24.92]
PD Group Median [95% CI]	-79.0 [-92.5, -60.8]	-18.98 [-20.87, -15.10]
Mann-Whitney U-test: P value	0.004†	0.000‡
Univariate Binary Logistic Regression: Odds Ratio [Per Difference in Medians]	1.068	0.949
Univariate Binary Logistic Regression: P value	0.022*	0.001†
Binary Logistic Regression, Education as Additional Covariates: Odds Ratio [Per Difference in Medians]	1.069	0.948
Binary Logistic Regression, Education as Additional Covariates: P value	0.027*	0.002†
Binary Logistic Regression, Sex as Additional Covariate: Odds Ratio [Per Difference in Medians]	1.069	0.946
Binary Logistic Regression, Sex as Additional Covariate: P value	0.022*	0.001‡

For the group medians of pattern expression, the median value with its bootstrapping-derived 95 % confidence interval [in square brackets] are reported. *$P < 0.05$, † $P < 0.01$, ‡ $P < 0.001$

Supplementary Table 2. Expression of the covariance patterns between the groups

	PD Group -Related Covariance Pattern	Control Group -Related Covariance Pattern
Univariate Binary Logistic Regression: Odds Ratio (Per Difference in Medians) [95% CI]	1.062* [1.037, 1.093]	0.938* [0.926, 0.945]
Binary Logistic Regression, Education as Additional Covariates: Odds Ratio (Per Difference in Medians) [95% CI]	1.064* [1.038, 1.096]	0.936* [0.924, 0.947]
Binary Logistic Regression, Sex as Additional Covariate: Odds Ratio (Per Difference in Medians) [95% CI]	1.069* [1.032, 1.091]	0.936* [0.923, 0.947]

The odds ratios per difference in medians are calculated from the binary logistic regression coefficients. The bootstrapping-derived (10,000 iterations) 95% confidence intervals [in square brackets] for each test are reported. *Significant with α threshold of < 0.05.

Supplementary Table 3. Random forest model classification performance.

	Model 1: Age, Sex, Smoking, Education, and the 1st and 2nd Principal Components	**Model 2: Age, Sex, Smoking, Education**	**Model 3: Age, Sex, and the 1st and 2nd Principal Components**	**Model 4: Age, Sex**
Median AUC [IQR]	0.7452*†‡ [0.7208, 0.7690]	0.6910 [0.6614, 0.7163]	0.6790 [0.6554, 0.7048]	0.6330 [0.6045, 0.6557]
Median Sensitivity [IQR]	0.8634*†‡ [0.8578, 0.8680]	0.8676 [0.8607, 0.8750]	0.8465 [0.8411, 0.8519]	0.2759 [0.8350, 0.8465]
Median Specificity [IQR]	1.0000*†‡ [0.8000, 1.0000]	0.7500 [0.5833, 1.0000]	0.3920 [0.3333, 0.4667]	0.8408 [0.2222, 0.3333]
Median Kappa [IQR]	0.3340*†‡ [0.2785, 0.3799]	0.3467 [0.2935, 0.3813]	0.1446 [0.1000, 0.1879]	0.0846 [0.0440, 0.1275]

Significance of the comparisons between the model 1 and the reference models: $P < 0.0001$ in Mann-Whitney U-test with *model 2, †model 3, ‡model 4. IQR = interquartile range

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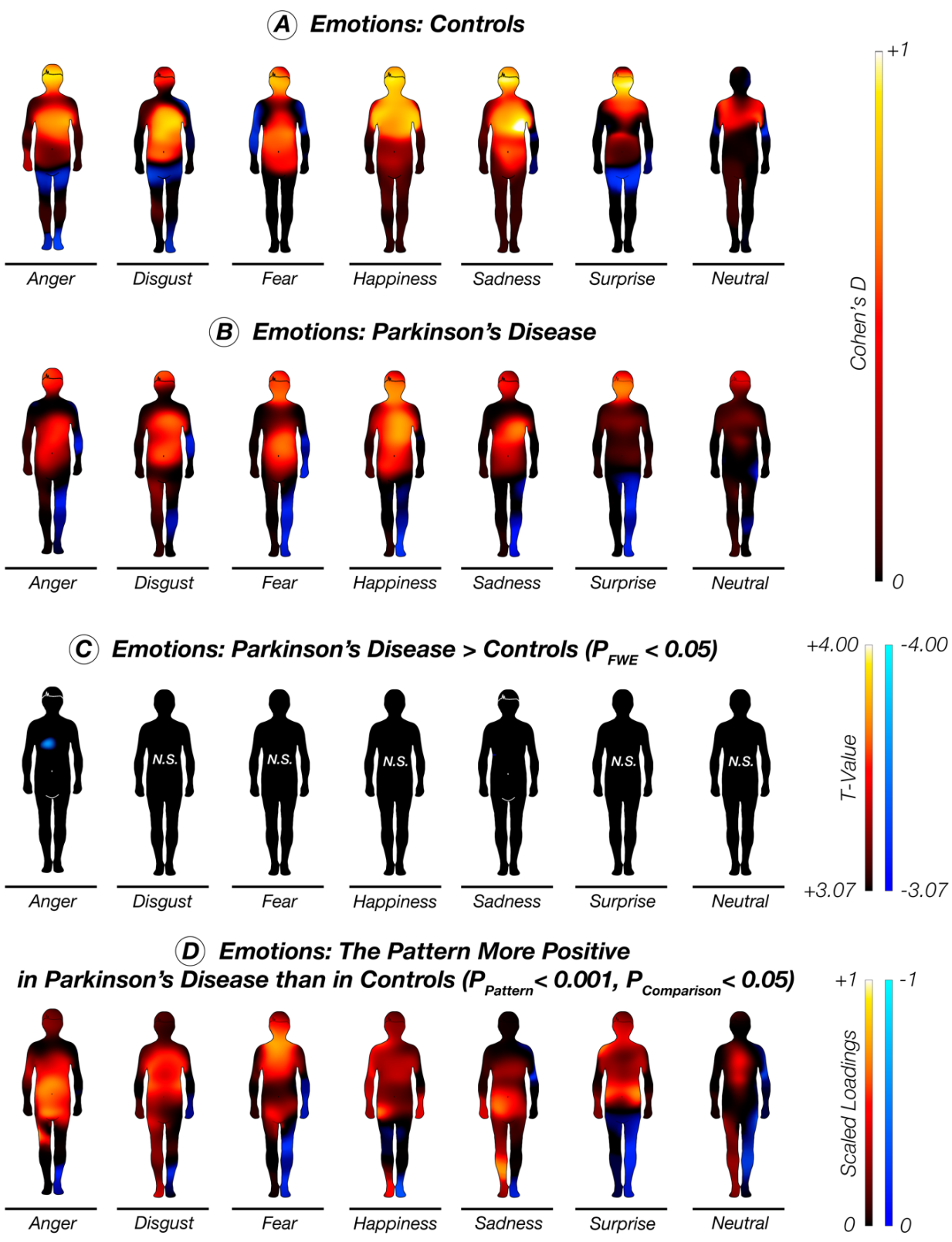
A Emotions: Controls
Anger
Disgust
Fear
Happiness
Sadness
Surprise
Neutral
+1
Cohen's D
0
B Emotions: Parkinson's Disease
Anger
Disgust
Fear
Happiness
Sadness
Surprise
Neutral
C Emotions: Parkinson's Disease > Controls (P_{FWE} < 0.05)
N.S.
+4.00
-4.00
T-Value
+3.07
-3.07
Anger
Disgust
Fear
Happiness
Sadness
Surprise
Neutral
D Emotions: The Pattern More Positive in Parkinson's Disease than in Controls ($P_{Pattern}$ < 0.001, $P_{Comparison}$ < 0.05)
+1
-1
Scaled Loadings
0
0
Anger
Disgust
Fear
Happiness
Sadness
Surprise
Neutral

Figure 2. Emotion-related bodily maps. The pixelwise effect sizes in controls (A) and individuals with Parkinson's disease (B), significant differences between groups in the linear model (P_{FWE}<0.05) (C), and PD-related pattern (P < 0.001 for the pattern, P < 0.05 for expression compared to controls) (D). Visually, the bodily sensations associated with emotions show absent or less intensive expression in Parkinson's disease (B) compared to controls (A) with a significant difference between the groups in anger-related sensations (C). The PCA analysis revealed more widespread PD-related patterns across all emotions, localizing anger to the abdomen rather than chest in line with the linear model findings (D). Red - yellow scale indicates positive values, and blue – light blue scale indicates negative values. N.S. = non-significant.