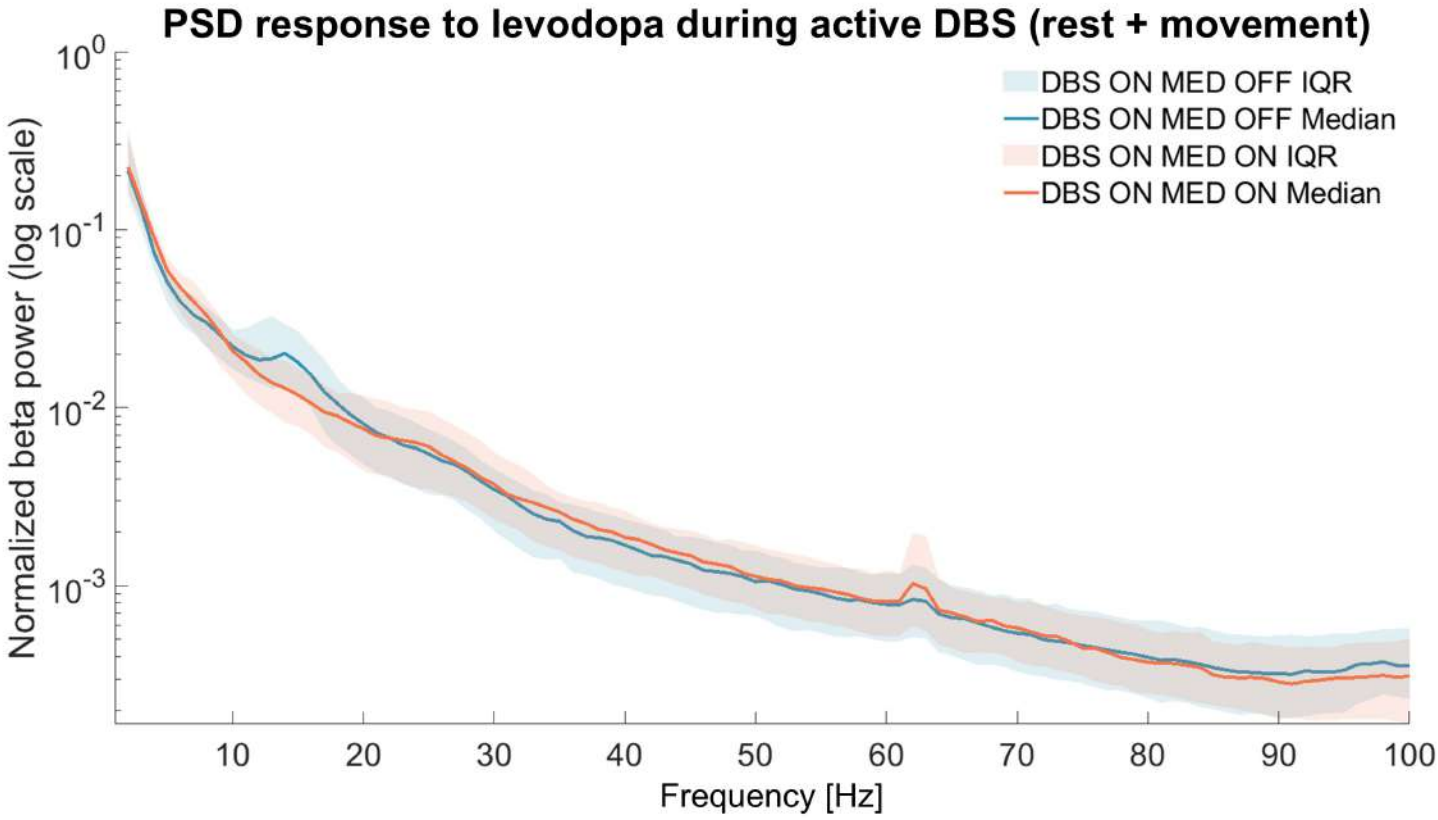
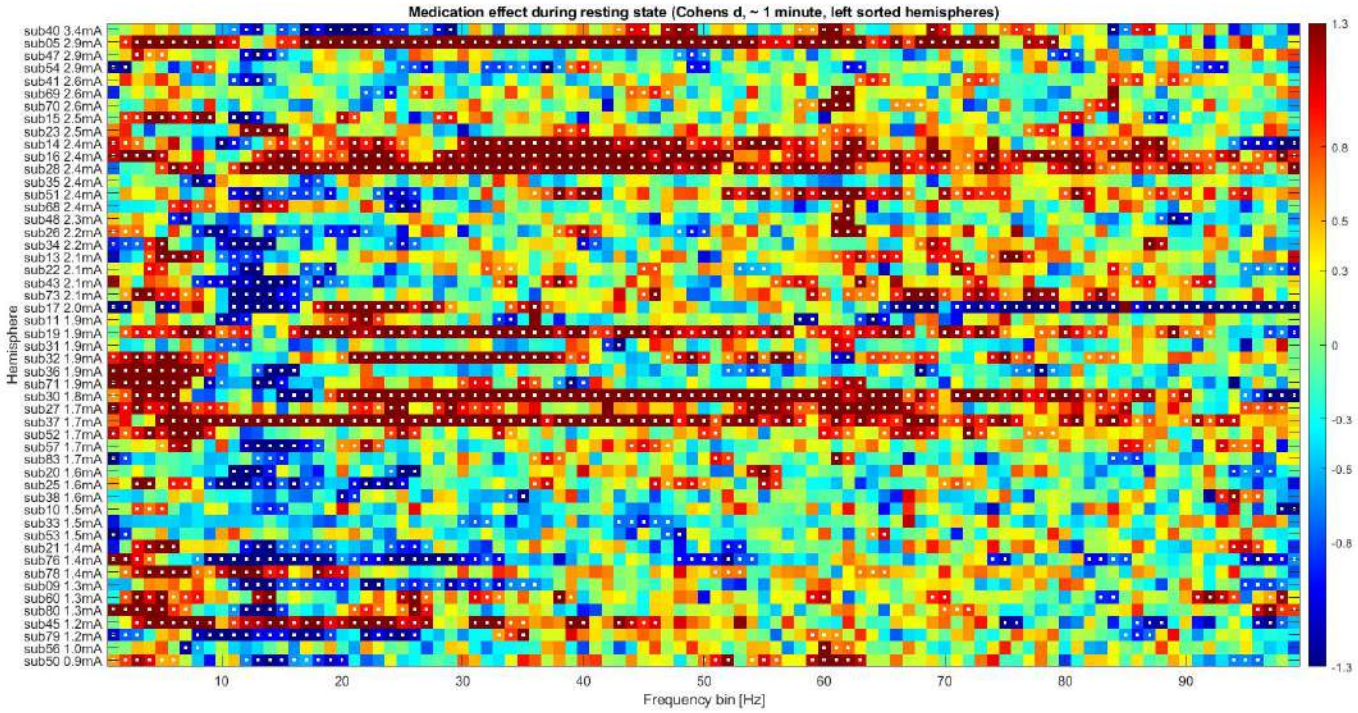
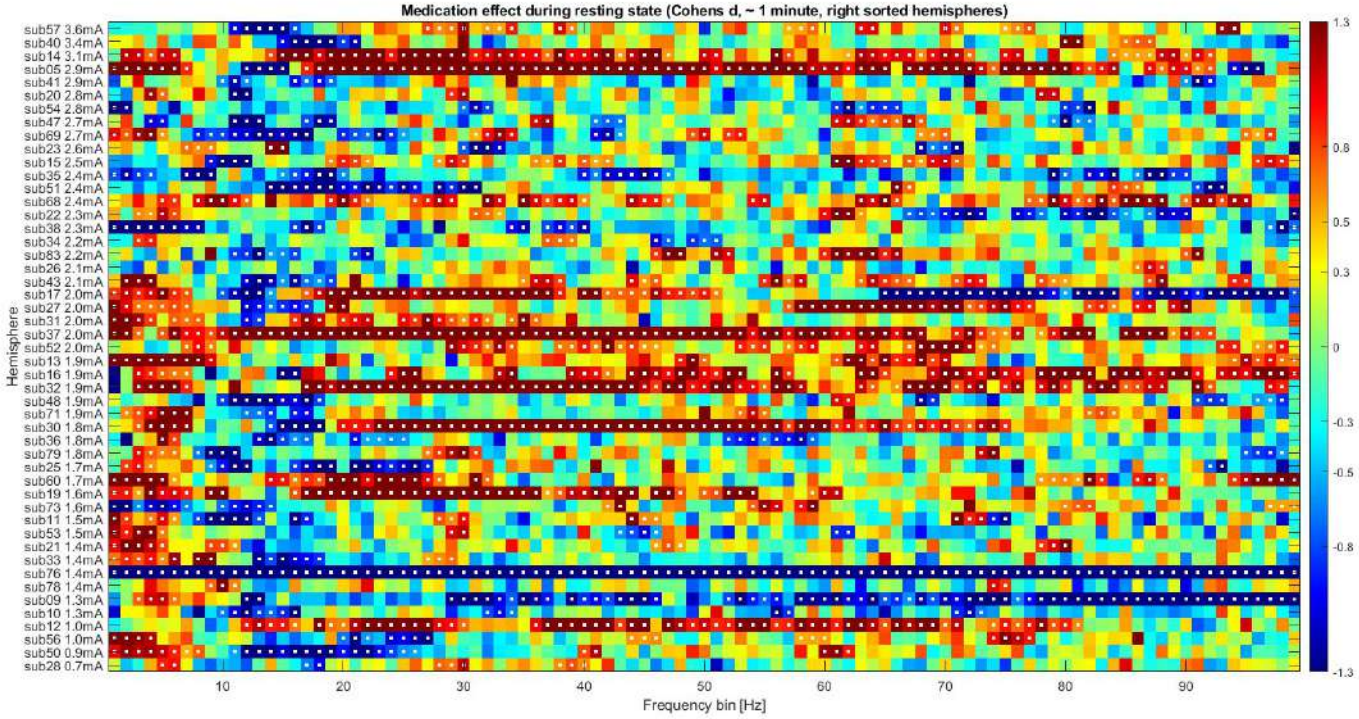

PSD response to levodopa during active DBS (rest + movement)
DBS ON MED OFF IQR
DBS ON MED OFF Median
DBS ON MED ON IQR
DBS ON MED ON Median
Normalized beta power (log scale)
$10^{0}$
$10^{-1}$
$10^{-2}$
$10^{-3}$
10
20
30
40
50
60
70
80
90
100
Frequency [Hz]

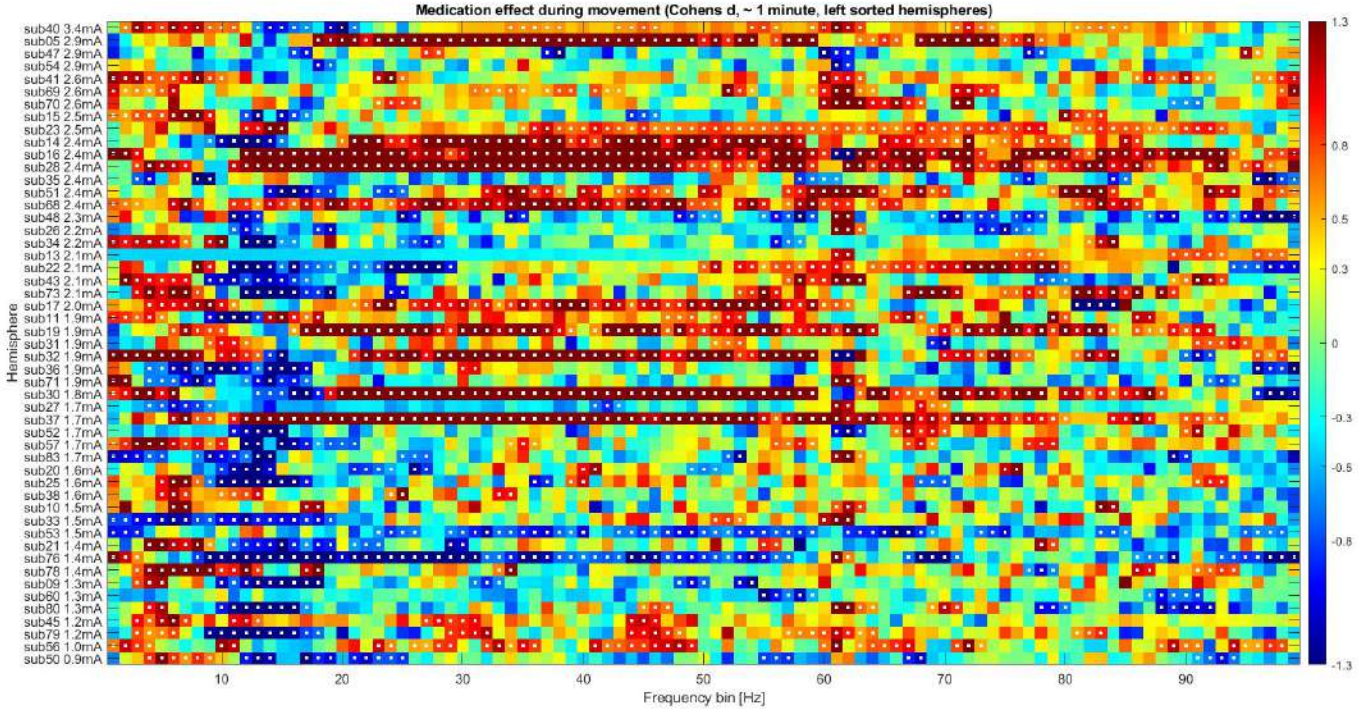
**Supplementary Figure S1 – Power response to levodopa across hemispheres.** Effect of levodopa intake on the power spectral density (PSD) of local field potential recordings obtained during deep brain stimulation after optimising stimulation amperage and medication schedule. Per hemisphere (n = 100) one PSD was computed for each medication state (MED OFF and MED ON) based on the total segment of available data (4 – 8 minutes). Shown are the median PSD and interquartile range (IQR) across hemispheres.


Medication effect during resting state (Cohens d, ~ 1 minute, left sorted hemispheres)
Hemisphere
sub40 3.4mA
sub05 2.9mA
sub47 2.9mA
sub54 2.9mA
sub41 2.6mA
sub69 2.6mA
sub70 2.6mA
sub15 2.5mA
sub23 2.5mA
sub14 2.4mA
sub16 2.4mA
sub28 2.4mA
sub35 2.4mA
sub51 2.4mA
sub68 2.4mA
sub48 2.3mA
sub26 2.2mA
sub34 2.2mA
sub13 2.1mA
sub22 2.1mA
sub43 2.1mA
sub73 2.1mA
sub17 2.0mA
sub11 1.9mA
sub19 1.9mA
sub31 1.9mA
sub32 1.9mA
sub36 1.9mA
sub71 1.9mA
sub30 1.8mA
sub27 1.7mA
sub37 1.7mA
sub52 1.7mA
sub57 1.7mA
sub83 1.7mA
sub20 1.6mA
sub25 1.6mA
sub38 1.6mA
sub10 1.5mA
sub33 1.5mA
sub53 1.5mA
sub21 1.4mA
sub76 1.4mA
sub78 1.4mA
sub09 1.3mA
sub60 1.3mA
sub80 1.3mA
sub45 1.2mA
sub79 1.2mA
sub56 1.0mA
sub50 0.9mA
10
20
30
40
50
60
70
80
90
Frequency bin [Hz]
1.3
0.8
0.5
0.3
0
-0.3
-0.5
-0.8
-1.3

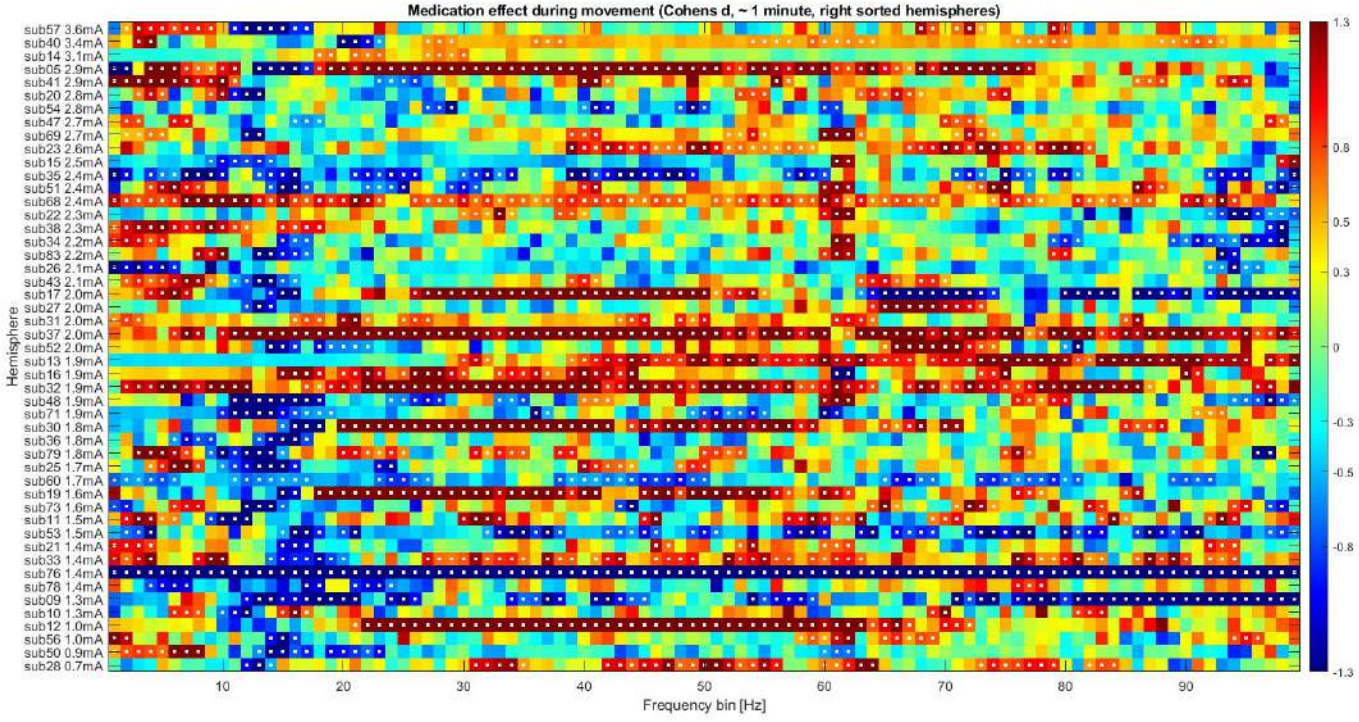
**Supplementary Figure S2 A – Effect sizes of medication-induced changes in LFP power of resting state recordings from left hemispheres.** For each of 51 hemispheres, effect sizes were calculated as Cohen's d (MED OFF > MED ON) for the full LFP spectrum as described in the methods and statistically tested with cluster-based permutation testing. White dots indicate frequency bins that are part of a significant cluster ($p < 0.05$). For visualisation, hemispheres were sorted based upon stimulation amplitude. SEG physiomarkers (~62,5 Hz) appeared at higher stimulation amplitudes, while alpha/low-beta (9-20 Hz) physiomarkers were spread across stimulation amplitudes. Some hemispheres showed strong broadband effects in the high beta and low gamma band without clear modulation of alpha/low-beta or SEG bands.


Medication effect during resting state (Cohens d, ~ 1 minute, right sorted hemispheres)
Hemisphere
sub57 3.6mA
sub40 3.4mA
sub14 3.1mA
sub05 2.9mA
sub41 2.9mA
sub20 2.8mA
sub54 2.8mA
sub47 2.7mA
sub69 2.7mA
sub23 2.6mA
sub15 2.5mA
sub35 2.4mA
sub51 2.4mA
sub68 2.4mA
sub22 2.3mA
sub38 2.3mA
sub34 2.2mA
sub83 2.2mA
sub26 2.1mA
sub43 2.1mA
sub17 2.0mA
sub27 2.0mA
sub31 2.0mA
sub37 2.0mA
sub52 2.0mA
sub13 1.9mA
sub16 1.9mA
sub32 1.9mA
sub48 1.9mA
sub71 1.9mA
sub30 1.8mA
sub36 1.8mA
sub79 1.8mA
sub25 1.7mA
sub60 1.7mA
sub19 1.6mA
sub73 1.6mA
sub11 1.5mA
sub53 1.5mA
sub21 1.4mA
sub33 1.4mA
sub76 1.4mA
sub78 1.4mA
sub09 1.3mA
sub10 1.3mA
sub12 1.0mA
sub56 1.0mA
sub50 0.9mA
sub28 0.7mA
10
20
30
40
50
60
70
80
90
Frequency bin [Hz]
1.3
0.8
0.5
0.3
0
-0.3
-0.5
-0.8
-1.3

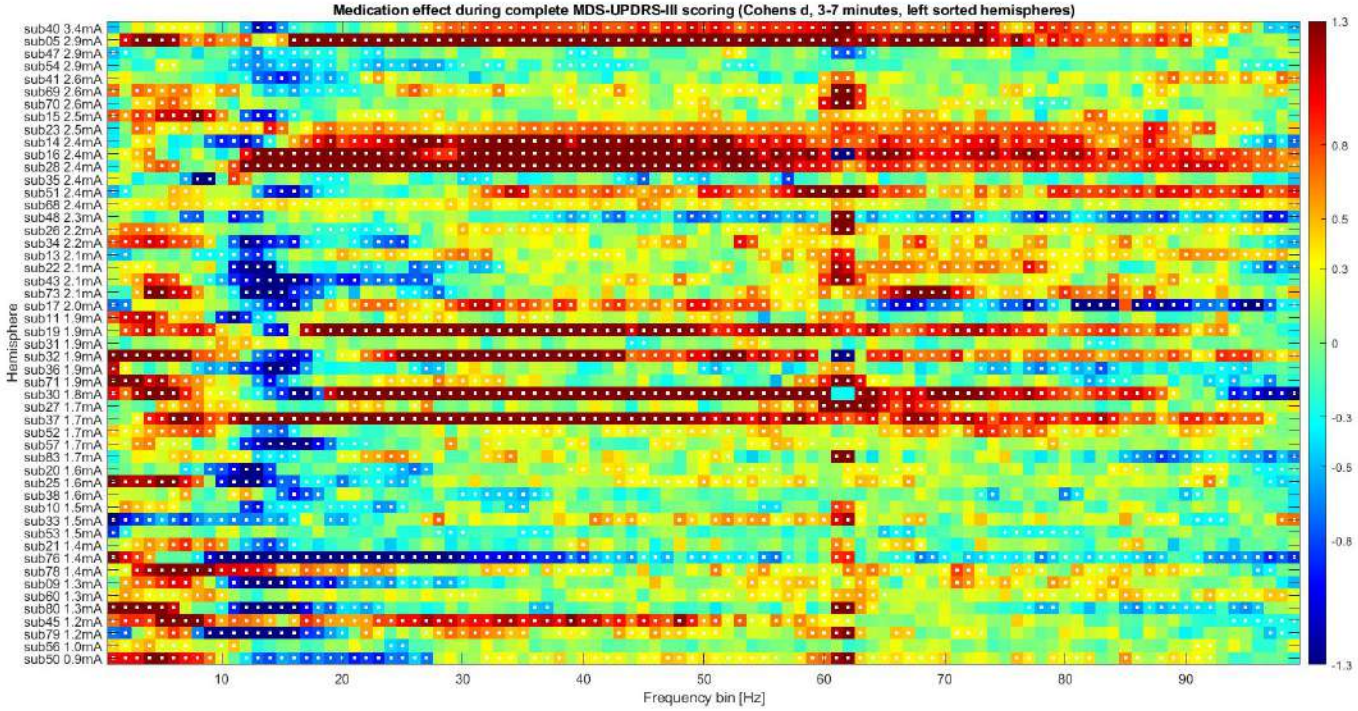
**Supplementary Figure S2 B – Effect sizes of medication-induced changes in LFP power of resting state recordings from right hemispheres.** For each of 49 hemispheres, effect sizes were calculated as Cohen's d (MED OFF > MED ON) for the full LFP spectrum as described in the methods and statistically tested with cluster-based permutation testing. White dots indicate frequency bins that are part of a significant cluster ($p < 0.05$). For visualisation, hemispheres were sorted based upon stimulation amplitude. No clear pattern for SEG (~62,5 Hz) effects was observed and alpha/low-beta effects were spread across stimulation amplitudes. Again, some hemispheres showed strong broadband effects in the high-beta/low-gamma band.


Medication effect during movement (Cohens d, ~ 1 minute, left sorted hemispheres)
Hemisphere
sub40 3.4mA
sub05 2.9mA
sub47 2.9mA
sub54 2.9mA
sub41 2.6mA
sub69 2.6mA
sub70 2.6mA
sub15 2.5mA
sub23 2.5mA
sub14 2.4mA
sub16 2.4mA
sub28 2.4mA
sub35 2.4mA
sub51 2.4mA
sub68 2.4mA
sub48 2.3mA
sub26 2.2mA
sub34 2.2mA
sub13 2.1mA
sub22 2.1mA
sub43 2.1mA
sub73 2.1mA
sub17 2.0mA
sub11 1.9mA
sub19 1.9mA
sub31 1.9mA
sub32 1.9mA
sub36 1.9mA
sub71 1.9mA
sub30 1.8mA
sub27 1.7mA
sub37 1.7mA
sub52 1.7mA
sub57 1.7mA
sub83 1.7mA
sub20 1.6mA
sub25 1.6mA
sub38 1.6mA
sub10 1.5mA
sub33 1.5mA
sub53 1.5mA
sub21 1.4mA
sub76 1.4mA
sub78 1.4mA
sub09 1.3mA
sub60 1.3mA
sub80 1.3mA
sub45 1.2mA
sub79 1.2mA
sub56 1.0mA
sub50 0.9mA
10
20
30
40
50
60
70
80
90
Frequency bin [Hz]
1.3
0.8
0.5
0.3
0
-0.3
-0.5
-0.8
-1.3

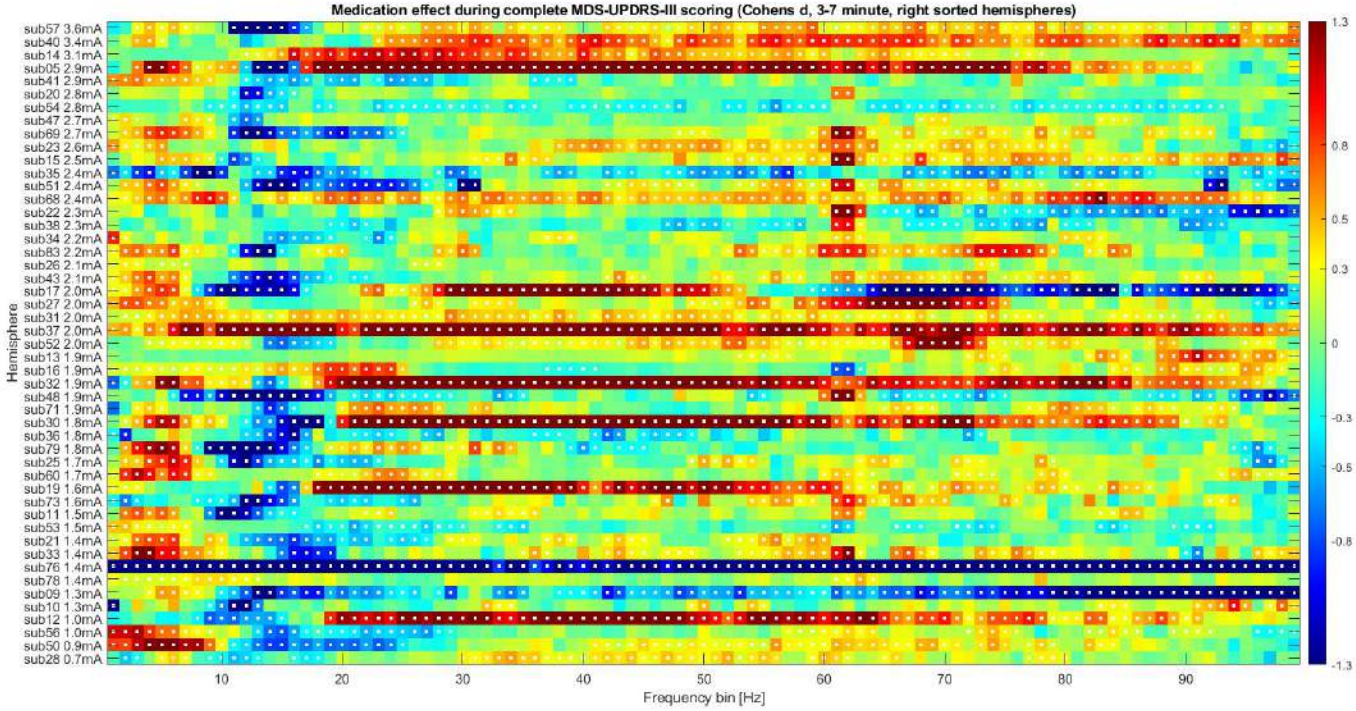
**Supplementary Figure S3 A – Effect sizes of medication-induced changes in LFP power of movement state recordings from left hemispheres.** For each of 51 hemispheres, effect sizes were calculated as Cohen's d (MED OFF > MED ON) for the full LFP spectrum as described in the methods and statistically tested with cluster-based permutation testing. White dots indicate frequency bins that are part of a significant cluster ($p < 0.05$). For visualisation, hemispheres were sorted based upon stimulation amplitude. No clear pattern was observed regarding the SEG (~62,5 Hz) effects, except their increased occurrence compared to the resting state, while alpha/low-beta (9-20 Hz) effects were spread across stimulation amplitudes. Some hemispheres showed strong broadband effects in the high beta/ low gamma band with only some showing modulation of low beta activity.


Medication effect during movement (Cohens d, ~ 1 minute, right sorted hemispheres)
Hemisphere
sub57 3.6mA
sub40 3.4mA
sub14 3.1mA
sub05 2.9mA
sub41 2.9mA
sub20 2.8mA
sub54 2.8mA
sub47 2.7mA
sub69 2.7mA
sub23 2.6mA
sub15 2.5mA
sub35 2.4mA
sub51 2.4mA
sub68 2.4mA
sub22 2.3mA
sub38 2.3mA
sub34 2.2mA
sub83 2.2mA
sub26 2.1mA
sub43 2.1mA
sub17 2.0mA
sub27 2.0mA
sub31 2.0mA
sub37 2.0mA
sub52 2.0mA
sub13 1.9mA
sub16 1.9mA
sub32 1.9mA
sub48 1.9mA
sub71 1.9mA
sub30 1.8mA
sub36 1.8mA
sub79 1.8mA
sub25 1.7mA
sub60 1.7mA
sub19 1.6mA
sub73 1.6mA
sub11 1.5mA
sub53 1.5mA
sub21 1.4mA
sub33 1.4mA
sub76 1.4mA
sub78 1.4mA
sub09 1.3mA
sub10 1.3mA
sub12 1.0mA
sub56 1.0mA
sub50 0.9mA
sub28 0.7mA
10
20
30
40
50
60
70
80
90
Frequency bin [Hz]
1.3
0.8
0.5
0.3
0
-0.3
-0.5
-0.8
-1.3

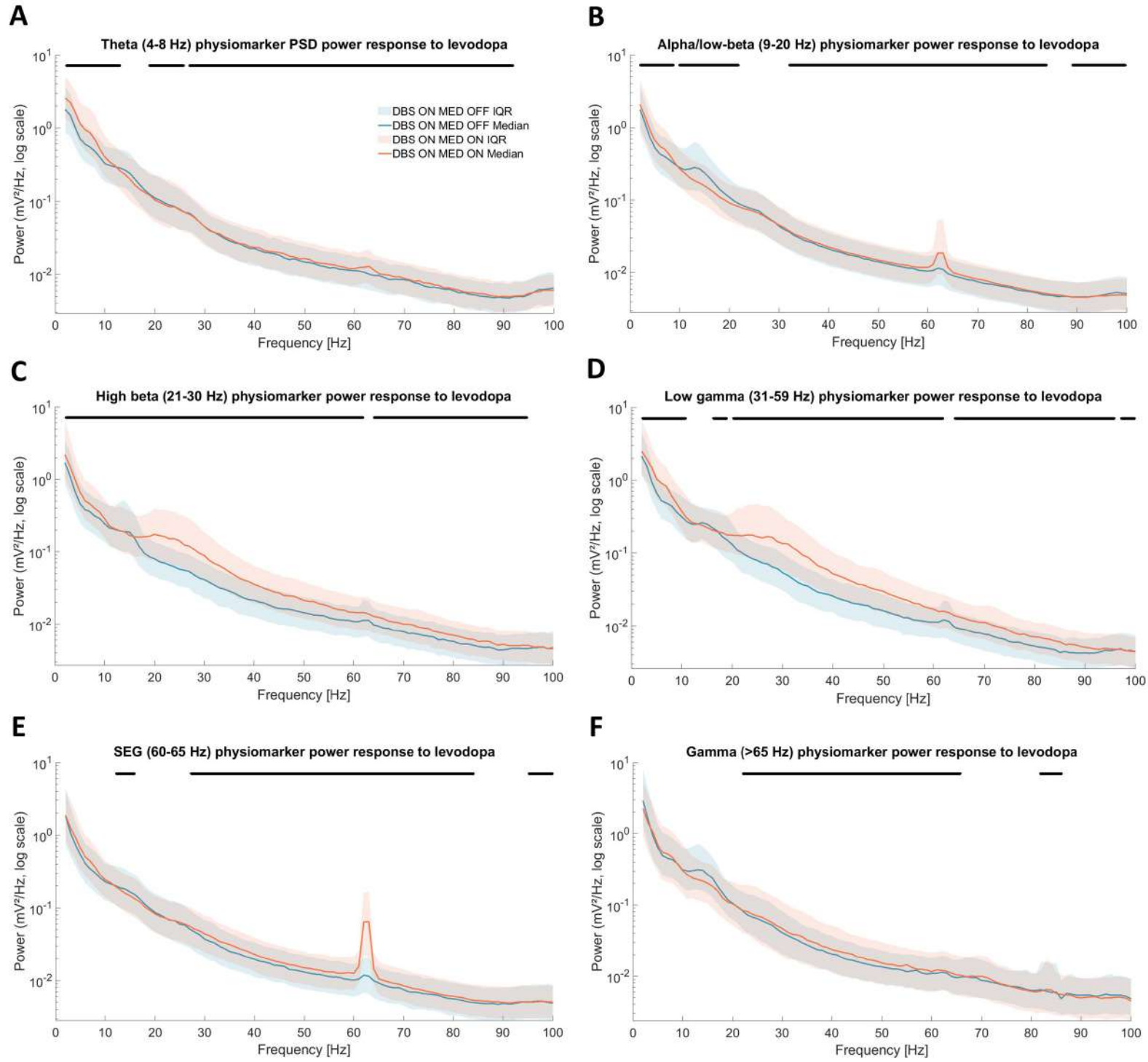
**Supplementary Figure S3 B – Effect sizes of medication-induced changes in LFP power of movement state recordings from right hemispheres.** For each of 49 hemispheres, effect sizes were calculated as Cohen's d (MED OFF > MED ON) for the full LFP spectrum as described in the methods and statistically tested with cluster-based permutation testing. White dots indicate frequency bins that are part of a significant cluster ($p < 0.05$). For visualisation, hemispheres were sorted based upon stimulation amplitude. No clear pattern was observed regarding the SEG effects (~62.5 Hz), except their increased occurrence compared to the resting state, while alpha/low-beta (9-20 Hz) effects were spread across stimulation amplitudes. Some hemispheres showed strong broadband effects in the high beta/ low gamma band.


Medication effect during complete MDS-UPDRS-III scoring (Cohens d, 3-7 minutes, left sorted hemispheres)
Hemisphere
sub40 3.4mA
sub05 2.9mA
sub47 2.9mA
sub54 2.9mA
sub41 2.6mA
sub69 2.6mA
sub70 2.6mA
sub15 2.5mA
sub23 2.5mA
sub14 2.4mA
sub16 2.4mA
sub28 2.4mA
sub35 2.4mA
sub51 2.4mA
sub68 2.4mA
sub48 2.3mA
sub26 2.2mA
sub34 2.2mA
sub13 2.1mA
sub22 2.1mA
sub43 2.1mA
sub73 2.1mA
sub17 2.0mA
sub11 1.9mA
sub19 1.9mA
sub31 1.9mA
sub32 1.9mA
sub36 1.9mA
sub71 1.9mA
sub30 1.8mA
sub27 1.7mA
sub37 1.7mA
sub52 1.7mA
sub57 1.7mA
sub83 1.7mA
sub20 1.6mA
sub25 1.6mA
sub38 1.6mA
sub10 1.5mA
sub33 1.5mA
sub53 1.5mA
sub21 1.4mA
sub76 1.4mA
sub78 1.4mA
sub09 1.3mA
sub60 1.3mA
sub80 1.3mA
sub45 1.2mA
sub79 1.2mA
sub56 1.0mA
sub50 0.9mA
10
20
30
40
50
60
70
80
90
Frequency bin [Hz]
1.3
0.8
0.5
0.3
0
-0.3
-0.5
-0.8
-1.3

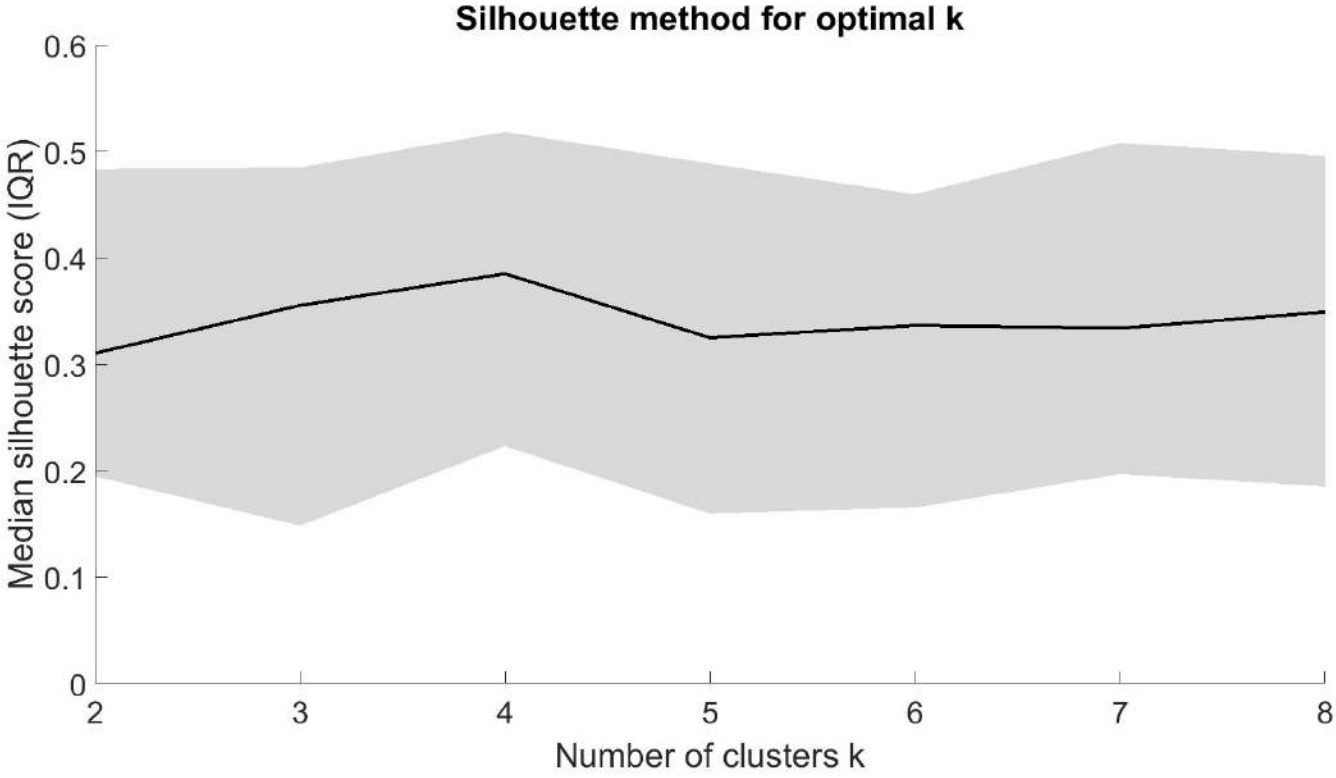
**Supplementary Figure S4 A – Effect sizes of medication-induced changes in LFP power of full MDS-UPDRS-III recordings from left hemispheres.** For each of 51 hemispheres, effect sizes were calculated as Cohen's d (MED OFF > MED ON) for the full LFP spectrum as described in the methods and statistically tested with cluster-based permutation testing. White dots indicate frequency bins that are part of a significant cluster ($p < 0.05$). For visualisation, hemispheres were sorted based upon stimulation amplitude. Alpha/low-beta and SEG physiomarkers appeared across stimulation amplitudes. Some hemispheres showed strong broadband effects in the high beta/ low gamma band with only some showing modulation of low beta activity. Finally, some hemispheres showed both SEG and alpha/low-beta modulation.


Medication effect during complete MDS-UPDRS-III scoring (Cohens d, 3-7 minute, right sorted hemispheres)
Hemisphere
sub57 3.6mA
sub40 3.4mA
sub14 3.1mA
sub05 2.9mA
sub41 2.9mA
sub20 2.8mA
sub54 2.8mA
sub47 2.7mA
sub69 2.7mA
sub23 2.6mA
sub15 2.5mA
sub35 2.4mA
sub51 2.4mA
sub68 2.4mA
sub22 2.3mA
sub38 2.3mA
sub34 2.2mA
sub83 2.2mA
sub26 2.1mA
sub43 2.1mA
sub17 2.0mA
sub27 2.0mA
sub31 2.0mA
sub37 2.0mA
sub52 2.0mA
sub13 1.9mA
sub16 1.9mA
sub32 1.9mA
sub48 1.9mA
sub71 1.9mA
sub30 1.8mA
sub36 1.8mA
sub79 1.8mA
sub25 1.7mA
sub60 1.7mA
sub19 1.6mA
sub73 1.6mA
sub11 1.5mA
sub53 1.5mA
sub21 1.4mA
sub33 1.4mA
sub76 1.4mA
sub78 1.4mA
sub09 1.3mA
sub10 1.3mA
sub12 1.0mA
sub56 1.0mA
sub50 0.9mA
sub28 0.7mA
10
20
30
40
50
60
70
80
90
Frequency bin [Hz]
1.3
0.8
0.5
0.3
0
-0.3
-0.5
-0.8
-1.3

**Supplementary Figure S4 B – Effect sizes of medication-induced changes in LFP power of full MDS-UPDRS-III recordings from right hemispheres.** For each of 49 hemispheres, effect sizes were calculated as Cohen's d (MED OFF > MED ON) for the full LFP spectrum as described in the methods and statistically tested with cluster-based permutation testing. White dots indicate frequency bins that are part of a significant cluster ($p < 0.05$). For visualisation, hemispheres were sorted based upon stimulation amplitude. Alpha/low-beta and SEG physiomarkers did not show a distinct pattern but appeared across stimulation amplitudes. Some hemispheres showed strong broadband effects in the high beta/ low gamma band with only some showing modulation of low beta activity. Finally, some hemispheres showed both SEG and alpha/low-beta modulation.


A
Theta (4-8 Hz) physiomarker PSD power response to levodopa
DBS ON MED OFF IQR
DBS ON MED OFF Median
DBS ON MED ON IQR
DBS ON MED ON Median
Power (mV²/Hz, log scale)
Frequency [Hz]
B
Alpha/low-beta (9-20 Hz) physiomarker power response to levodopa
Power (mV²/Hz, log scale)
Frequency [Hz]
C
High beta (21-30 Hz) physiomarker power response to levodopa
Power (mV²/Hz, log scale)
Frequency [Hz]
D
Low gamma (31-59 Hz) physiomarker power response to levodopa
Power (mV²/Hz, log scale)
Frequency [Hz]
E
SEG (60-65 Hz) physiomarker power response to levodopa
Power (mV²/Hz, log scale)
Frequency [Hz]
F
Gamma (>65 Hz) physiomarker power response to levodopa
Power (mV²/Hz, log scale)
Frequency [Hz]

**Supplementary Figure S5 – Medication-induced changes in LFP power for hemispheres with different physiomarker frequencies.** PSDs from individual hemsipheres were grouped based on the frequency band of the detected physiomarker: theta (4-8 Hz), alpha/low-beta (9-20 Hz), high beta (21-30 Hz), low gamma (31-59 Hz), SEG (60-65 Hz) and high gamma (66-100 Hz) band. Each panel presents the median and interquartile range of the PSD across hemispheres in the medication ON and OFF state. Differences in power between medication states were statistically tested with cluster-based permutation testing; significant clusters are marked with black lines at the top of each panel. **(A)** Hemispheres with a MED ON>MED OFF physiomarker in the theta band (number of hemispheres (n) = 8, number of PSDs ('PSDs') = 1865). **(B)** Hemispheres with a MED OFF>MED ON physiomarker in the alpha/low-beta band (n = 35, PSDs = 6821). **(C)** Hemispheres with a physiomarker in the high beta band in both directions (n = 9, PSDs = 1898) **(D)** Hemispheres with a physiomarker in the low gamma band in both directions (n = 9, PSDs = 1796). **(E)** Hemispheres with a MED ON>MED OFF physiomarker in the SEG band (n = 19, PSDs = 3493). **(F)** Hemispheres with a physiomarker in both directions in the high gamma band (n = 12, PSDs = 2482).


Silhouette method for optimal k
Median silhouette score (IQR)
0.6
0.5
0.4
0.3
0.2
0.1
0
2
3
4
5
6
7
8
Number of clusters k

**Supplementary Figure S6 – Silhouette score of clustering analysis.** Median (IQR is shaded) silhouette score as a function of the number of clusters used for the cluster analysis. Clustering was repeated 100 times per number of clusters (k). This metric is highest with four clusters, indicating the optimal number. The silhouette score with four clusters has a median of 0.38, indicating moderate structure of the clusters.