Supplementary material

Referring to respective parts in Methods

Clustering analysis: Silhouette measure

In order to determine the number of clusters *k* for the k-means clustering step, we additionally computed silhouette measures for k-means clustering solutions ranging from *k*=2 to *k*=8. The silhouette measure captures the within-cluster consistency of data and thus the goodness of a clustering process (Rousseeuw, 1987). It is computed as (*b*-*a*)/max(*a*, *b*) with the mean nearest-cluster distance *b* and the mean intra-cluster *a* for every sample and then averages over all samples. We here measured distance as Euclidean distance. Using this approach, the *k*=3 solution yielded the highest silhouette value, thereby confirming the results of the elbow-criterion analysis.

Referring to respective parts in Results

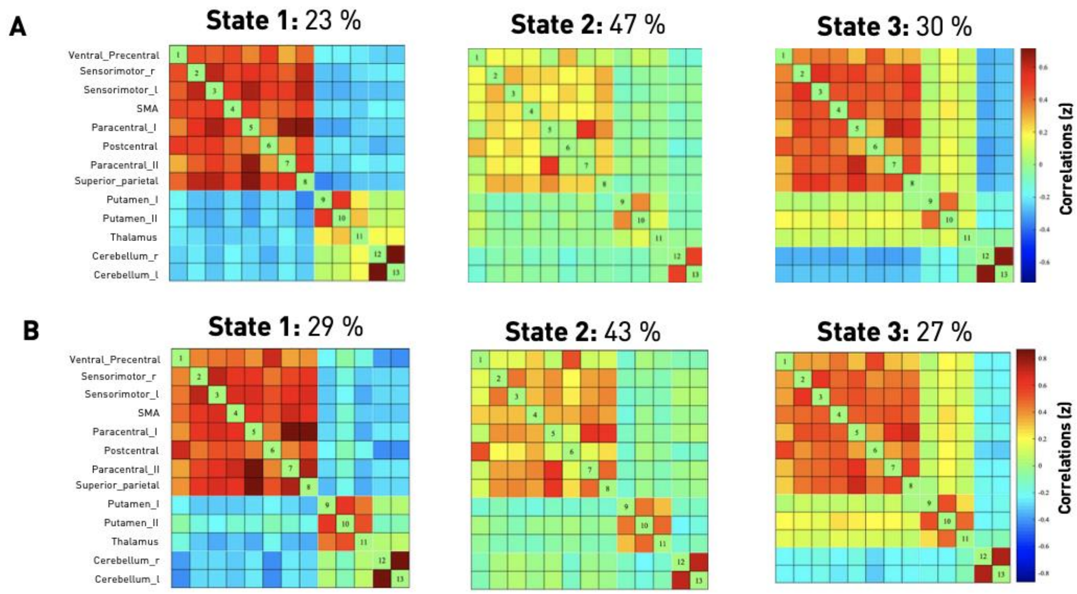
	Severely affected (n=13)	Moderately affected (n=18)	Healthy controls (n=17)	p-value
Age (in years)	70.0	67.0	65.4	Moderate-Controls: 0.65 Severe-Controls: 0.13
Sex (in % female)	61	22	12	Moderate-Controls: 0.66 Severe-Controls: 0.01*
Mean Framewise Displacement	0.29	0.27	0.27	Moderate-Controls: 0.99 Severe-Controls: 0.59
NIHSS	10	6	-	0.01*
ARAT *affected hand*	10	45	-	0.00*
Lesion volume (in ml, median)	13.0	13.0	-	0.61
CST overlap (in %, median)	9.2	4.8	-	0.68

Supplementary Table 1. Demographics and clinical characteristics of stroke patient subgroups and healthy controls. Cortico-spinal tract (CST) affection was computed based on lesion overlap with a CST template provided in the SPM Anatomy Toolbox (Eickhoff *et al.*, 2005).

Replication data set

We repeated the main dynamic functional connectivity analyses in an additional resting-state functional MRI data set of 24 acute ischemic stroke patients with motor symptoms and a control group comprising 30 acute ischemic stroke patients without motor symptoms (days post-stroke: 2.5 ± 1.5 days). A subset of the data was previously analyzed in regards to static connectivity in Rehme *et al.* (2014). While inclusion and exclusion criteria were comparable to those reported in the main manuscript, the replication data set differed in several aspects from that investigated in the main study: (i) resting-state fMRI scans were obtained during clinical routine and earlier (on average: 2.5 days) compared to the data set of the main study (7.2 days), (ii) a 1.5T scanner was used (Philips, Guildford, UK), (iii) scanning parameters differed (TR = 2100 ms, TE = 50 ms, FOV = 250 mm, 24 axial slices, voxel size: 3.9 × 3.9 × 3.9 mm^3, 182 volumes), and (iv) the comparison group consisted of stroke patients without motor symptoms. Motor impairment was quantified using the Motricity Index of the affected hand (MI; Demeurisse *et al.*, 1980), which uses a rating scale to describe the level of motor impairment concerning whether a movement can be performed against gravity or resistance. A score of 33 indicated normal power.

Intrinsic connectivity networks and dynamic functional connectivity measures were computed using the same procedures as employed for the main data set. Once again, we chose a sliding window length of 20 TRs (42 sec), resulting in 159 windows per subject. These were finally assigned to one of three connectivity states via k-means clustering (Supplementary Figure 4).



Supplementary Figure 4. Dynamic connectivity states across subjects and data sets. A. Connectivity states obtained in the replication data set and their frequencies across all 54 included ischemic stroke patients. **B.** Connectivity states and their frequencies of the original data set presented in the main body of the paper. In summary, the combination of the sliding window approach and k-means clustering resulted in very similar connectivity states and frequencies.

Statistical analysis & Results

As in the main analysis, the group of stroke patients with motor impairments was subdivided into two subgroups according to their MI score. Here, moderately affected patients (n = 19) were defined to have an MI of the affected hand between 22-32, while severely affected patients presented with an MI of lower than 22 (n = 5). This criterion ensured that in the severely affected group, patients were not able to hold a small 2.5 x 2.5 cm cube against gravity, indicating a severe hand motor deficit. Control patients had no motor deficit (MI = 33, normal motor function). Subsequently, we tested for between-group differences in the following dynamic measures: dwell and fraction times, as well as differences in inter-domain segregation (t-tests between the three different groups: level of significance: $p<0.05$).

Moderately affected patients dwelled significantly longer in State 2 than healthy controls (t-test: $p< 0.05$), and thus once again preferred a state with low system segregation and particularly weak intra-domain connectivity. This preference also became evident in the evaluation of segregation, computed based on the formula given in Chan et al. (2014) and described in further detail in the main manuscript (c.f., Methods: Domain-wide segregation). Moderately affected patients presented with a significantly reduced level of segregation in comparison to both stroke patients without motor symptoms and those with severe symptoms. On the other hand, severely affected patients once again had a significantly increased level of segregation in line with reports in the main manuscript (t-tests: $p<0.05$).

References

Eickhoff SB, Stephan KE, Mohlberg H, Grefkes C, Fink GR, Amunts K, et al. A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. Neuroimage 2005; 25: 1325–1335.

Rehme AK, Volz LJ, Feis D-L, Bomilcar-Focke I, Liebig T, Eickhoff SB, et al. Identifying neuroimaging markers of motor disability in acute stroke by machine learning techniques. Cerebral cortex 2014; 25: 3046–3056.

Rousseeuw PJ. Silhouettes: a graphical aid to the interpretation and validation of cluster analysis. Journal of computational and applied mathematics 1987; 20: 53–65.