Supplemental Methods and Results of

Cortical chemoarchitecture shapes macroscale effective functional connectivity patterns in macaque cerebral cortex

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Supplementary Methods

Alternative Statistical analyses

For each cortical area the out- and in-strength of functional connectivity strength were re-examined, by excluding all connections of unknown strength from the matrix (i.e. all connections with X). Pearson's correlation was used to test the relation between regional receptor densities and functional connectivity (see Table S1 and Figure S1 for results), cross-correlating the 6 receptor density levels and the ExIn ratio with the nodal functional out- and in-strength values of the residual regions (n=6).

Supplementary Results

Alternative Statistical results

	Out-strength		**In-strength**	
	R	**p**	**R**	**p**
AMPA	0.2073	0.6935	-0.1899	0.5760
5-HT$_{2A}$	0.8286	0.0416	-0.2038	0.5479
Kainate	-0.7710	0.0727	-0.1602	0.6381
M$_1$	-0.8621	0.0272	-0.1557	0.6475
M$_2$	-0.7554	0.0824	0.1171	0.7318
GABA$_A$	-0.9094	0.0119	-0.1292	0.7050
ExIn ratio	0.5254	0.2844	-0.2297	0.4969

Supplemental Table S1. Correlations of regional receptor levels and functional outward connection strength. To validate our main findings we removed all (124) pathways with an unknown connection strength (i.e. depicted as an 'X' in the connectivity matrix). Fourteen relations were represented between all excitatory receptor levels, inhibitory receptors, ExIn ratio and the (out or in-) strength of the functional connections. Similar correlation coefficients were found using the complete dataset (as reported in main text), although we believe that due to the low power of the data (n=6) lower p-values are found when all unknown connection strengths are removed.

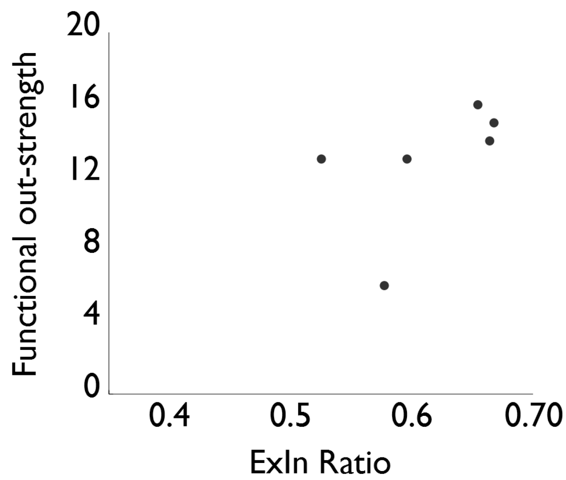
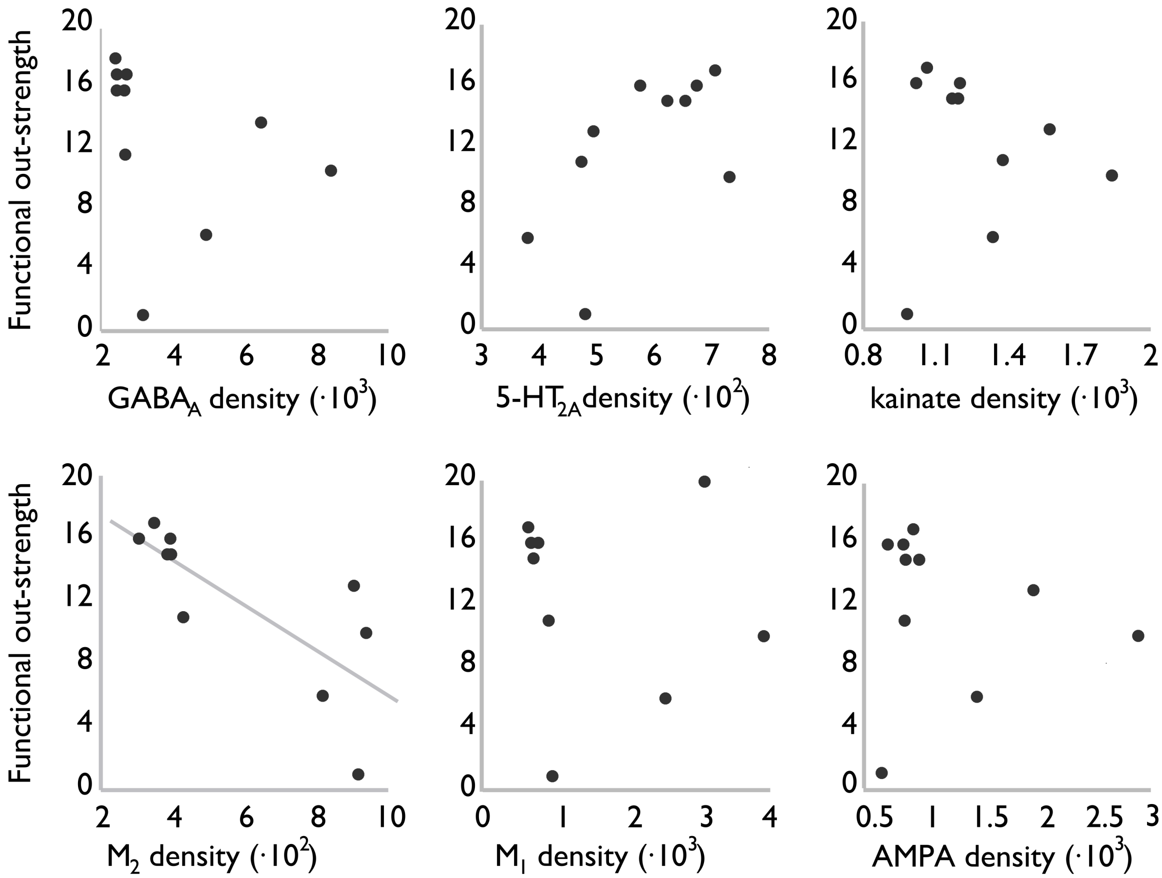


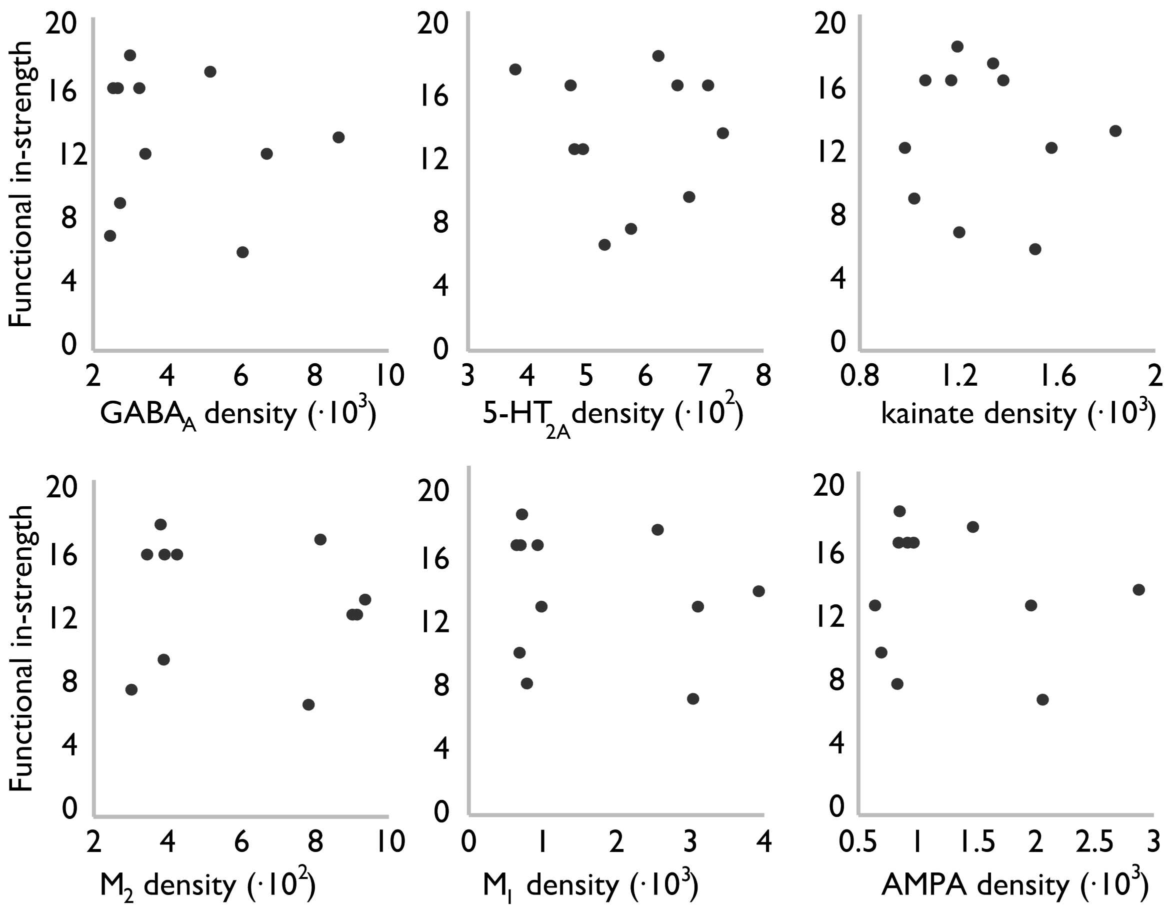
Figure S1. Interplay between receptor ExIn chemoarchitecture and macroscale functional out-strength connectivity. The graph shows a non-significant association between local chemoarchitecture ExIn ratio (x-axis) and the level of macroscale strychnine functional out-strength of cortical areas (y-axis, note that the out-strength is calculated without all unknown connections, n=6). Figure illustrates the re-examined main finding of our study of the local excitatory chemoarchitecture of cortical areas to be of positive influence on outgoing global interregional functional influence of cortical areas when all unknown connections strength were removed (i.e. depicted as an 'X' in the connectivity matrix).

	Out-strength		**In-strength**	
	R	**p**	**R**	**p**
AMPA	-0.1707	0.6372	0.0736	0.8298
5-HT$_{2A}$	0.5549	0.0959	-0.069	0.8403
Kainate	-0.2927	0.4118	-0.0782	0.8193
M$_1$	-0.7988	0.0056*	-0.2253	0.5054
M$_2$	-0.8659	0.0012*	-0.0598	0.8614
GABA$_A$	-0.7744	0.0085*	-0.2529	0.4531
ExIn ratio	0.7561	0.0114*	0.0966	0.7776

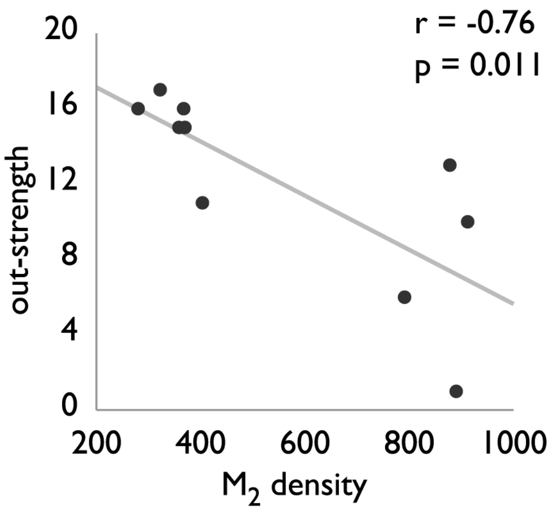
Supplemental Table S2. Spearman Rank Correlations of regional receptor levels and functional connection strength. Spearman Rank correlation coefficients (R) between neurotransmitter receptor level densities and out-strength or in-strength of the strychnine-induced functional regions are represented. Receptor levels are collated from the study of Kötter and colleagues {Kötter, 2001 #84}. Relations were calculated between all excitatory receptor levels (AMPA, $5HT_{2A}$, kainate and M_1), inhibitory receptors ($GABA_A$ and M_2), ExIn ratio and the (in or out) strength of the functional connections. Similar results were found using Pearson's correlations (as reported in main text), although we believe that due to the low power of the data (n=10) Spearman's tests overestimates the relations. * Effects reaching a partial Bonferroni corrected α of 0.0125.



Supplemental Figure S2. Overview of associations between receptor densities and out-strength. Figure shows the scatterplots of the 6 receptor densities (on x-axis, in fmol/mg·10^3 protein) and strychnine-induced functional out-strength (y-axis). Plots of inhibitory $GABA_A$ and M_2 receptors are shown on the left, and plots of excitatory 5-HT_{2A}, M_1, kainate and AMPA receptors are presented in the middle and right. Figure illustrates an exclusive correlation between M_2 receptor densities and functional out-strength ($R = -0.76$, $p = 0.0111$, see Figure S4).



Supplemental Figure S3. Overview of associations between receptor densities and in-strength. Figure shows the scatterplots of the 6 receptor densities (on x-axis, in fmol/mg·10^3 protein) and strychnine-induced functional in-strength (y-axis). Plots of inhibitory $GABA_A$ and M_2 receptors are shown on the left, and plots of excitatory 5-HT_{2A}, M_1, kainate and AMPA receptors are presented in the middle and on the right. As expected (see main text for description), correlations revealed no significant relationships.



Supplemental Figure S4. Association of M_2 receptor density and macroscale functional out-strength connectivity. Figure shows a negative correlation (r=-0.76, p=0.0111), between regional M_2 density (on x-axis) and the level of strychnine-induced functional out strength (on y-axis), illustrating the influence of inhibitory M_2 receptors on the strength of cortico-cortical activity.