What receptor fingerprints reveal about macaque cingulate cortex organization

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The cingulate region plays an important role in modulating complex cognitive and emotional behavior. Based on the integration of structural and functional data obtained from human and monkey studies, a subdivision of the cingulate gyrus into four distinct regions, namely the anterior (ACC), mid- (MCC) and posterior (PCC) cingulate cortex, as well as the retrosplenial cortex (RSC), has been proposed [1]. Each region is further subdivided, indicating subregional specializations. However, existing maps of the macaque cingulate cortex differ in the number and extent of identified areas [1-3].

Aim of the present study: characterize the receptor architecture of the macaque monkey cingulate cortex and provide a parcellation scheme in stereotaxic space

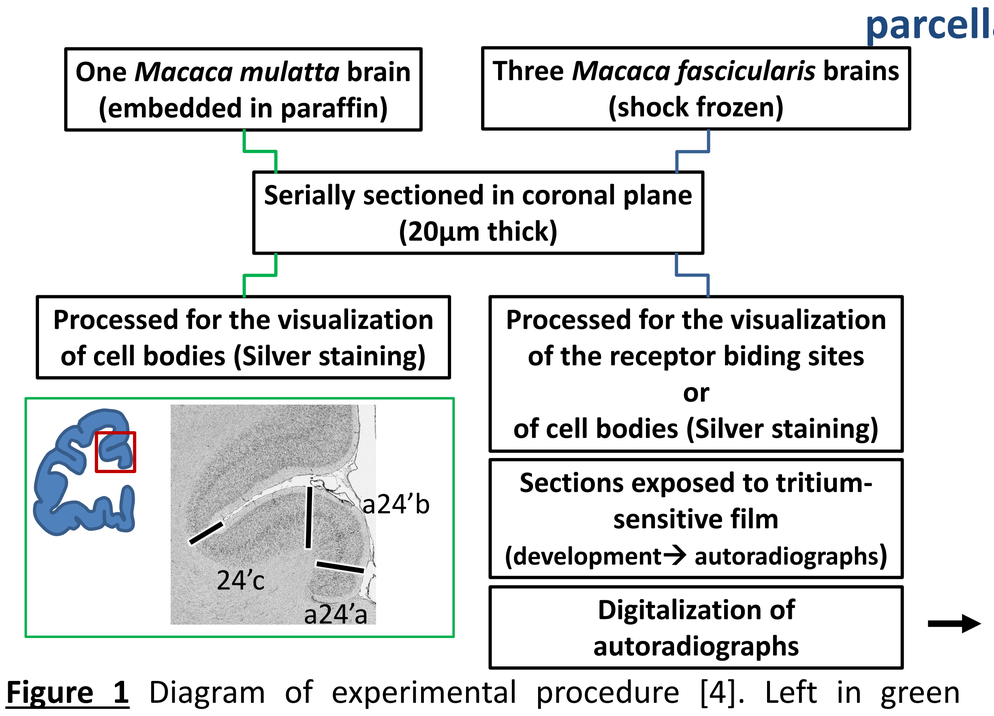

Figure 1 Diagram of experimental procedure [4]. Left in green square: Schematic drawing of a coronal section at the level of aMCC (24'c, a24'b and a24'a) and high resolution image of the silver stained section where cytoarchitectonic borders were quantified and confirmed by statistical analysis [4].

Distribution of transmitter receptor densities in cytoarchitectonically defined areas

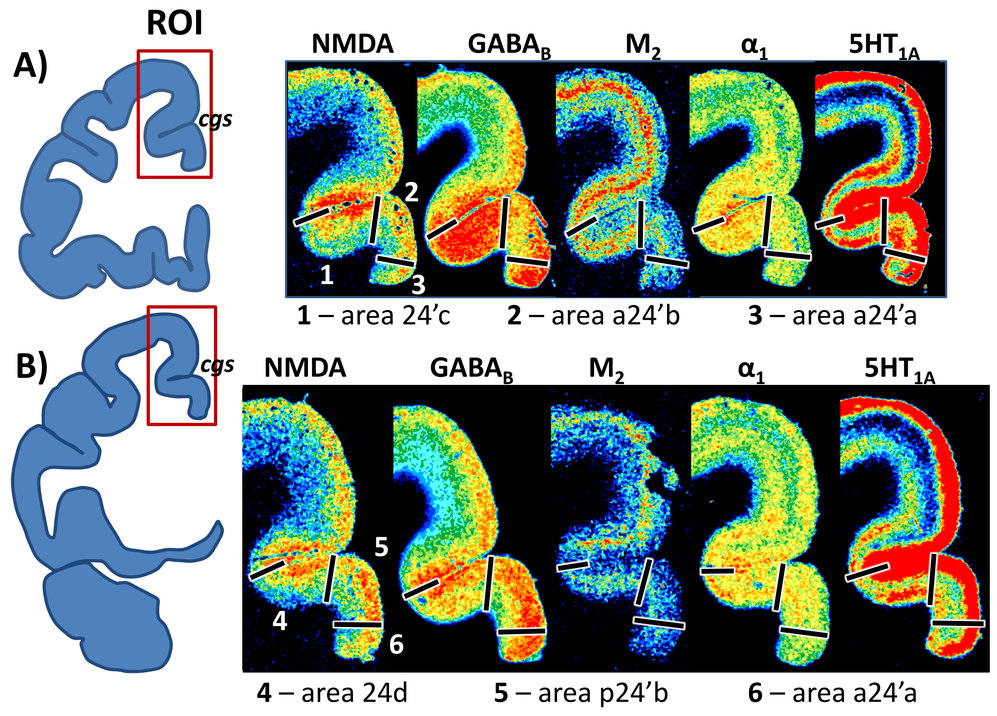

Figure 2 Exemplary distribution of NMDA, $GABA_B$, M_2, α_1 and $5HT_{1A}$ receptors in **A)** anterior (24'c, a24'b and a24'a) and **B)** posterior (24d, p24'b and p24'a) subdivisions of the MCC region.

Left: Schematic drawing of coronal sections at the level of **A)** the aMCC (24'c, a24'b and a24'a) and **B)** the pMCC (24d, p24'b and p24'a). Region of interest shown in the autoradiographs is marked by the red square.

Rostro-caudal differences between receptor fingerprints throughout the cingulate cortex

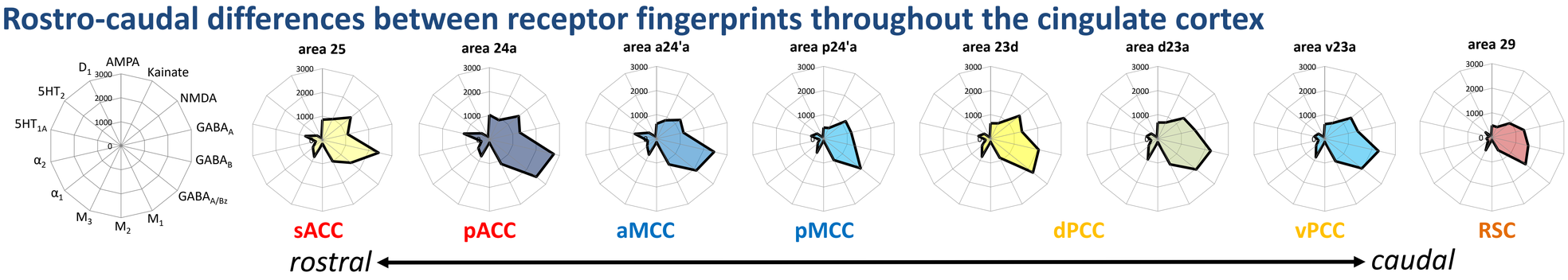

Figure 3 Example of distinct neurochemical balance (expressed as receptor fingerprint) between most ventral cingulate areas along the rostro-caudal axis (see Fig. 5).
Left: Schematic radial plot indicates 14 distinct receptor types examined in the present study.

Multivariate analyses of ensuing receptor fingerprints reveals clustering of cingulate areas based on their neurochemical organization

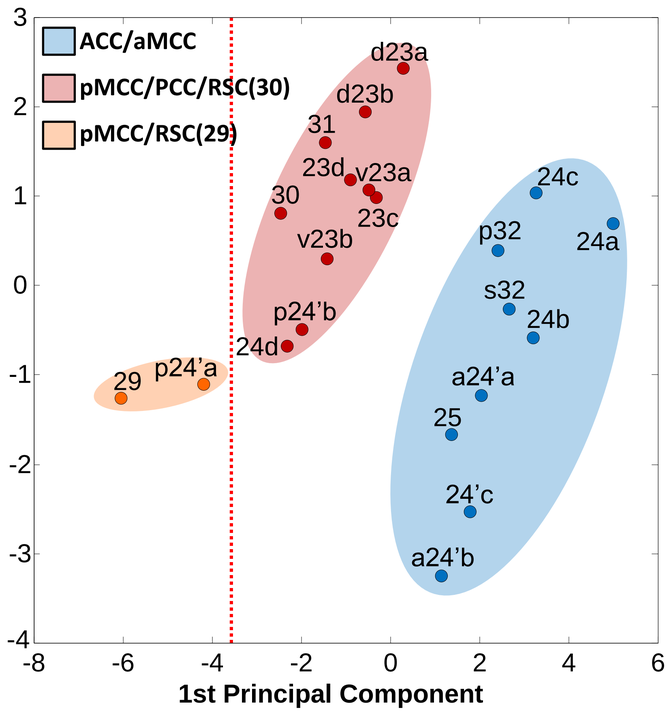

Figure 4 Principal component analysis of the receptor fingerprints extracted from macaque cingulate areas.
K-means clustering showed 3 as the optimal number of clusters. Red dashed line indicates fundamental segregation of areas 29 and p24'a into single cluster due to unique shape of their fingerprints (Fig.3).

In humans, hierarchical cluster analysis of receptor fingerprints clearly supports the concept of segregated ACC, MCC, PCC and RSC regions, as well as the existence of aMCC and pMCC subregions[5]. This is in contrast with present findings in macaque, where aMCC areas cluster with ACC areas and pMCC areas cluster PCC and RSC areas. Areas of aMCC had prominently different shape and size of the receptor fingerprint than pMCC areas (Fig.3). Conclusively, cyto- and receptor architectonic analyses in macaques segregate cingulate areas, as in humans, but do not support the four region model of cingulate organization.

Macaque cingulate areas in 3D stereotaxic space

Cingulate subregions
sACC, pACC: subgenual and pregenual ACC
aMCC, pMCC: anterior and posterior MCC
dPCC, vPCC: dorsal and ventral PCC
RSC: retrosplenial cortex

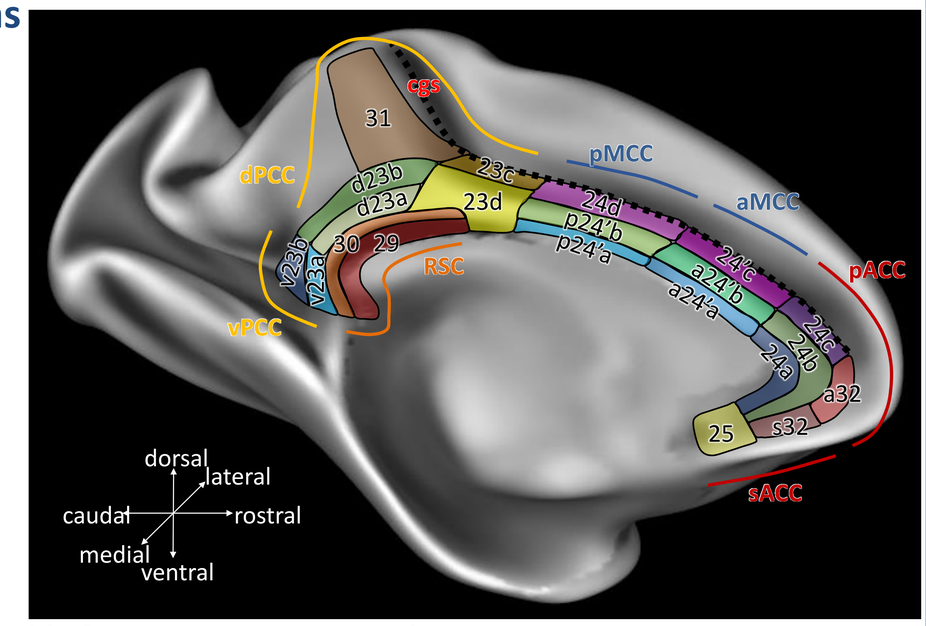

Figure 5 Location and extent of areas defined within the macaque cingulate cortex projected onto the Yerkes19 macaque template [6]. Assignment to cingulate regions as defined in the human brain [5,7] to enable future comparative analyses.

CONCLUSIONS:

- Heterogeneous distribution of transmitter receptors segregates cingulate cortical areas.
- We provide a 3D atlas of the entire cingulate region integrating cyto- and receptor (14 distinct receptor types) architectonic features of each defined area.
- Multivariate analysis resulted in 3 distinct cluster groups, where primary segregation revealed unique properties of areas 29 and p24'a from the rest of cingulate areas and regions.
- Cingulate regions (ACC, MCC, PCC and RSC) are neurochemically less distinct in macaque moneys than in humans [5], indicating an evolutionary specialization of the human cingulate cortex.

References

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