Predominance of excitatory-excitatory interactions between the anterior cingulate and orbitofrontal cortices associated with distinct aspects of emotions

M. Á. García-Cabezas and H. Barbas

Neural Systems Lab (www.bu.edu/neural/), Dept. Health Sciences
Boston University, Boston, MA 02215, USA
gcabezas@bu.edu, *barbas@bu.edu*

The anterior cingulate cortex (ACC) and posterior orbitofrontal cortex (pOFC) are limbic cortices distinguished by their connections and role in emotional process. The pOFC has connections with cortices associated with each and every sensory modality. In contrast, the ACC has sparse monosynaptic connections with sensory cortices with the exception of robust connections with auditory association cortices and the primary olfactory cortex. The ACC also has more connections with medial temporal cortices associated with memory and with central autonomic structures than the pOFC (Barbas 1993; reviewed in Barbas et al. 2011). Both cortices are strongly connected with the amygdala but the pOFC receives more input than it sends to the amygdala, whereas the opposite is true for the ACC (Ghashghaei et al. 2007). In previous studies we have suggested that ACC and pOFC appear to have complementary roles in emotional behavior and may work synergistically: the pOFC may be the cortical sensor for emotions while ACC is the motor effector for emotions.

The ACC and pOFC are strongly interconnected, but their synaptic interactions with excitatory and inhibitory neurons are unknown in primates. This information is prerequisite to investigating the unique involvement of these cortices in emotional processes. To study the connections between ACC and pOFC at the system and synaptic level we used axonal tracers to label pathways from area 32 of the ACC to pOFC in macaque monkeys. Labeled axon boutons from area 32 terminated in all sectors and layers of pOFC, and were arranged mostly in columns, consistent with their similar dysgranular structure. In spite of the columnar pattern of termination, more boutons from ACC axons were found in the middle-deep than in the superficial layers in pOFC. A significant proportion of ACC boutons were large suggesting high synaptic efficacy. At the level of the synapse, more than 90% of ACC boutons formed synapses with spines, a feature of excitatory neurons in the cerebral cortex. A minority of ACC boutons formed synapses with dendritic shafts, a morphological feature of synapses with cortical inhibitory neurons. In the superficial layers of pOFC, some of the dendritic shafts were labeled with calretinin, a marker for a subset of inhibitory neurons that are known to inhibit nearby inhibitory neurons and thus disinhibit excitatory neurons.

These features at the level of the system and synapse suggest that ACC pathways are poised to exert a powerful excitatory effect on pOFC. Our findings provide the structural framework to understand the synergistic roles that ACC and pOFC play in sequential processing and distinct aspects of emotional behavior.

Supported by: NIH grants (NINDS and NIMH) and NSF (CELEST). M. Á. García-Cabezas is the recipient of Grant for Research in Foreign Universities and Centers from Fundación Alfonso Martín Escudero (Spain) for 2011 and 2012.