

## Study of the efferents projections from the prefrontal cortex to the dorsal raphe nucleus in the rat

Gonçalves, L., Tampelini, FS., Metzger, MA., Lagnado, SJS. and Nogueira, MI.

Instituto de Ciências Biomédicas, Universidade de São Paulo – USP

**Introduction:** Several studies had shown that the prefrontal cortex (PFC) can influence the activity of the dorsal raphe nucleus (DRN) via efferent projections. These projections may regulate behavioral and physiologic functions of the DRN, and also can regulate activity of PFC neurons via feedback mechanisms. Although some studies analyzed the projections from the PFC to the DRN, none presented a detailed description of the distribution of these projections. The present work injected the retrograde neuronal tracer CTb (cholera toxin b-subunit) in different parts of the DRN, and analyzed the distribution of CTb+ cells through the anterior-posterior axis of the PFC. **Methods and results:** In rats Wistar, CTb was injected by electrophoresis in the rostral, central and caudal parts of the DRN, and the animals were perfused after 7 days. The brains were removed from the skull and processed with immunohistochemical techniques against CTb. Injections placed in the rostral and central parts of the DR produced a robust retrograde labeling in the medial, orbital, and lateral divisions of the PFC. The largest number of retrogradely labeled neurons were observed in the frontal polar, prelimbic and infralimbic cortices. Retrograde labeling was also consistently found in the dorsal division of the anterior cingulate cortex, in the medial, ventrolateral, lateral and dorsolateral divisions of the orbital cortex as well as in the dorsal and ventral divisions of the agranular insular cortex. A conspicuous cluster of labeled neurons also surrounded the rostral pole of the accumbens. A similar, though much less dense retrograde labeling was produced by small injections in the caudal DR. The vast majority of prefrontal inputs to the DR arose from neurons in layer V. **Conclusion:** These results confirm the existence of a robust projection from the PFC to the DR, and underscore a substantial, hitherto undescribed, contribution of the frontal polar cortex.

**Keywords:** Prefrontal cortex, dorsal raphe nucleus, Immunohistochemistry, CTb, retrograde neuronal tracer.

**Financial support:** FAPESP and CAPES.