

A Computational Model of Stress Coping in Rats

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This work presents a computational neural-network model explaining the brain processes underlying stress coping in rats exposed to long lasting inescapable stress conditions, focussing on the three neuromodulators dopamine (DA), noradrenaline (NE) and serotonin (5-HT). The importance of the model relies on the fact that stress coping experiments are considered a good animal model of the mechanisms underlying human depression. Pascucci et al. (2007) used microdialysis to investigate the correlation existing between the presence of NE and DA in medial prefrontal cortex (mPFC) and the quantity of mesoaccumbens DA during a restraint test lasting 240 min. The comparison of the microdialysis results related to sham rats and rats with either NE or DA depletion in mPFC showed the role played by such neuromodulators on DA release in nucleus accumbens (NAcc) and the active/passive modality of stress coping.

In the model, the stressing stimulus initially activates a first group of neural systems devoted to active stress-coping and learning. The amygdala (Amg) activates the subsystems NAcc-shell/infralimbic-cortex (NAccS-IL) and NAcc-core/prelimbic-cortex (NAccC-PL). The latter subsystem is responsible for triggering actions that may terminate the stressing stimulus, whereas the former is responsible for (learning) the selected inhibition of those 'neural channels' of actions which are executed but fail to stop the stressing stimulus.

The ability of actively coping with stress (lasting about 120 min in experiments) and learning which actions have to be avoided as ineffective is modulated (either depressed or enhanced) by the presence of the three neuromodulators targeting the Amg-NAcc-mPFC systems. Amg activates the locus coeruleus (LC) which in turn produces NE, enhancing the activity of Amg, NAccS and mPFC. The activity in mPFC activates the mesoaccumbens module of the VTA which releases DA, enhancing the activity of NAcc. Passive stress coping, which follows active coping, is caused by both the release of 5-HT in the Amg-NAcc-mPFC systems and the VTA release of DA in mPFC. The cause of the shift from active to passive coping is assumed to be in the PL and its inhibitory control of the activity of the dorsal raphe (DR): when this inhibition terminates due to the IL inhibition of PL, the DR starts releasing 5-HT (Maier and Watkins, 2005), activating at the same time the mesocortical VTA via glutamatergic synapses.

The model has an architecture wholly constrained by the known brain anatomy and it reproduces rather in detail the micro-dialysis recordings of the slow dynamics (tonic) of DA and NE in mPFC and NAcc (e.g. see charts comparing microdialyses and simulations). On this basis, the model offers for the first time a coherent and detailed computational account of brain processes during stress coping.

References

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Conference: Bernstein Conference on Computational Neuroscience, Frankfurt am Main, Germany, 30 Sep - 2 Oct, 2009.

Presentation Type: Poster Presentation

Topic: Dynamical systems and recurrent networks

Citation: Fiore V, Mannella F, Mirolli M, Cabib S, Puglisi-Allegra S and Baldassarre G (2009). A Computational Model of Stress Coping in Rats. *Front. Comput. Neurosci. Conference Abstract: Bernstein Conference on Computational Neuroscience*. doi: 10.3389/conf.neuro.10.2009.14.050

Received: 26 Aug 2009; Published Online: 26 Aug 2009.

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