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tal. Instituto de Fisiología y Biofísica Houssay, Facultad de Medicina, UBA-CONICET. (2) Instituto de Neurociencia Cognitiva y Traslacional, Favaloro - INECO – CONICET.

Living organisms inhabit environments that are being permanently modified, so adapting their behavior to such changes could determine their survival. The concept of "cognitive flexibility" refers to this ability and serotonin (5-HT) has been identified as an important player in decision making. So, it would be reasonable to assign the serotonergic system a major role in processes of cognitive flexibility. Pharmacological experiments support this statement. However, it is still questionable which are the receptors that mediate these processes.

One of the most important post-synaptic receptors of the serotonergic system is the type 2A (5-HT2aR). This receptor is highly expressed in the limbic system as well as frontal regions of the cortex and has been associated with various psychiatric disorders. The lack of specific antagonists makes complex the identification of its function. Then, we assessed the role of the 5-HT2aR using protocols of extinction and reversal learning as measures of cognitive flexibility in genetically modified mice. Our preliminary results indicate that WT mice extinguish a fear conditioned memory faster than 5-HT2a$^{-/-}$ mice (two-way ANOVA, $p<0.01$). This would indicate that 5HT2aR is necessary for cognitive flexibility.

Since cognitive rigidity is a common behavior symptom of many psychiatric disorders, it has clinical relevance to identify its underlying neurobiological substrate to generate new and specific pharmacological tools.

Palabras clave: cognition, behavior, serotonin.

(671) **UNDERSTANDING MEMORY LOSS: DEVELOPMENT OF A RETRIEVAL-INDUCED FORGETTING PARADIGM IN RODENTS**

Francisco Tomás Gallo, Juan Facundo Morici, Magdalena Miranda, Noelia Weisstaub, Pedro Bekinschtein
FAVALORO - CONICET - INECO

In the last two decades there´s been a growing human literature on a phenomenon called retrieval-induced forgetting (RIF). RIF has pointed to inhibitory control processes that resolve retrieval competition as a cause of adaptive forgetting. Using spontaneous recognition memory in rats, we have developed a rodent paradigm for RIF. We were able to show that forgetting of an item associated with a particular context happens under conditions that cause competition between memory traces for two items that share a particular retrieval cue. Under these conditions, forgetting is long lasting and independent of the selected retrieval cue. We used local pharmacological inactivation to show that this kind of forgetting requires the activity of the medial prefrontal cortex (mPFC). With pharmacological inactivation, we showed that the Ventral Tegmental Area (VTA) is necessary for the forgetting to occur and that the infusion of a D1/5 agonist in the mPFC is sufficient to rescue the expression of the RIF phenomenon impelled by the inactivation of the VTA. These results are consistent with the idea that the RIF occurs via a top-down inhibitory control mechanism exerted by the mPFC on structures linked by hypothesized memory traces. With the latter results, we bring new evidence supporting the role of dopamine in the resolution of interference via mPFC inhibitory control.

Keywords: mPFC – Memory - Forguetting

(1932) **SURVIVAL AND DIFFERENTIATION EFFECTS OF PIGMENT EPITHELIUM DERIVED FACTOR (PEDF) ON RETINA NEURONS**

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PEDF promotes survival of photoreceptor cells and in an R28 retinal progenitor cell line by binding to PEDF membrane receptors. However, the intracellular molecular effects of PEDF in retina neurons are still unknown. Here we investigated these effects using pure neuronal cultures of photoreceptors and amacrine neurons, prepared from newborn rat retina and grown in a chemically defined medium. Cultures were supplemented at day 2 with either recombinant human PEDF (10 nM); PEDF plus P1 (a PEDF receptor blocking peptide, 100nM); or vehicle (control). At day 5, cells were fixed and cell death and apoptosis were evaluated by DAPI staining, Propidium Iodide and TUNEL assays, respectively. Mitochondrial activity was assessed with Mitotracker and opsin expression and axonal outgrowth were determined by immunocytochemical methods.

PEDF decreased the percentages of Propidium Iodide and TUNEL-positive photoreceptors by 55% and 65%, respectively, with respect to controls without PEDF, and significantly prevented the loss of mitochondrial membrane potential. Pre-incubation with the blocking P1 peptide abolished PEDF effects. PEDF had no effect on opsin expression but promoted its apical localization in photoreceptors as occurs in mature retinas, in contrast to its diffuse distribution on the cell body in controls. PEDF also stimulated axon outgrowth in amacrine neurons, by 2-fold, in neurons treated with PEDF, compared to controls. These effects were blocked by the blocking P1 peptide pre-treatment.

In summary, this work shows that PEDF acts as a survival factor for photoreceptors, preserving their mitochondrial functionality, and induces the differentiation of amacrine and photoreceptor neurons during their development in vitro.

Keywords: PEDF, apoptosis prevention; retina photoreceptors; amacrine neurons

(1935) **SUPERIOR CERVICAL GANGLIECTOMY INDUCES DRY AGE-RELATED MACULAR DEGENERATION IN MICE: A NEW EXPERIMENTAL MODEL**

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Dry age-related macular degeneration, a prevalent cause of blindness, is a progressive and degenerative disease, characterized by alterations in Bruch´s membrane, retinal pigment epithelium, and photoreceptors exclusively localized in the macula. Despite there are experimental murine models, the vast majority take too long to develop retinal alterations, which in general are ubiquitous, many result from non-eye specific genetic manipulations, and most do not always reproduce the hallmarks of human age-related macular degeneration. Choroid vessels receive sympathetic innervation from the superior cervical ganglion, which together with the parasympathetic system, regulate the blood flow. Choroid blood flow changes have been involved in age-related macular degeneration development and progression. At present no experimental models take this factor into account. The aim of this work was to analyze the effect of superior cervical gangliectomy on the choroid, Bruch´s membrane, retinal pigment epithelium, and retina. Adult male C57BL/6J mice were submitted to unilateral superior cervical gangliectomy and a contralateral sham procedure. Although superior cervical gangliectomy induced ubiquitous choroid and choriocapillaris changes ($p<0.01$), it induced Bruch´s membrane thickening, retinal pigment epithelium melanin content and retinoid isomerohydrolase loss, drusen-like deposit occurrence, and retinal pigment epithelium and photoreceptors atrophy, exclusively localized in the temporal side ($p<0.01$). Moreover, superior cervical gangliectomy provoked a localized increase in retinal pigment epithelium and photoreceptors apoptosis ($p<0.01$), and photoreceptors electroretinographic function decline ($p<0.01$). Therefore, superior cervical gangliectomy recapitulated the main features of human dry age-related macular degeneration, and could become a new experimental model of dry age-related macular degeneration, and a useful platform for developing new therapies.

Keywords: age-related macular degeneration, superior cervical ganglion, choroid, retinal pigment epithelium, experimental model.