VLCKD. Likewise, in the same model system, ROS production was not significantly influenced by dietary treatment. In conclusion, VLCKD exerts a positive effect on VAT decrease, ameliorating adiposity and blood chemistry parameters. Furthermore, short-term mild dietary ketosis does not appear to have a cytotoxic effect, nor does it represent a factor capable of increasing oxidative stress. Finally, to the best of our knowledge, this is the first study which shows an effect of VLCKD upon the orexinergic system, supporting the usefulness of such a therapeutic intervention in promoting reduction in the individual burden of disease.

Symposium 3

From whole-cell to single synapse engrams - Breaking the code for memory formation, storage and recall
Organizer: Marco Mainardi (Pisa, Italy)

Invited Oral Presentations

OP.69
Distinct granule cell populations are uniquely engaged in odor learning
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Olfaction is an important sensory modality driving fundamental behaviors. To determine whether an odor is good or bad, the brain essentially need to attribute a significance to this sensory stimulus. The allocation of a positive significance to an odorant usually depends on its association during learning with a reward outcome. Moreover, multiple forms of plasticity are involved when such odor-reward associations are formed. In the adult olfactory bulb, the continual production of newborn interneurons contributes to the functional plasticity of the system. We demonstrate that adult-born neurons, but not preexisting ones, contain information about learned positive significance. We also found that adult-born neuron activation heightens olfactory learning and enhances the ability to update the odor significance. Moreover, we reveal that adult-born cells are massively connected by higher brain regions and these contacts might be sensitive to odor experiences. In summary, our results show a specific involvement of adult-born neurons in boosting odor-reward association that is linked with a distinct connectivity within the olfactory system. These data unveil the relevance of encoding odor significance at early stages of sensory processing.

OP.70
Two-photon calcium imaging of memory engrams throughout the hippocampal formation in behaving mice
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Every day, we form memories about episodes of experiences that we make. The hippocampus is the cardinal brain structure for the formation of such episodic memories and cellular ensembles in this brain structure form representations or ‘engrams’ of each individual memory. To observe the formation and maintenance of such memory engrams, we repeatedly monitor the activity of thousands of hippocampal neurons using two-photon calcium imaging in head fixed mice. During our measurements, the mice perform memory tasks in a virtual environment, allowing us to monitor neuronal engram activity during encoding and recall of memories related to the virtual sceneries. Intriguingly, the coding properties of individual neurons differ vastly across the hippocampal formation. Pyramidal cells in the CA1 and CA3 areas show precise spatial tuning and remap rapidly between behavioural contexts, while granule cells of the dentate gyrus show a generalizing code. Furthermore, the firing fields of pyramidal cells are time-sensitive and remap as days pass, while those of granule cells are stable over many days. Our results suggest a multi-step process of memory assembly within the hippocampus with specific features being represented by the individual hippocampal subfields.

OP.71
Dendritic contributions to memory engrams: lessons from computational models
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Associative memories are believed to be stored in distributed neuronal assemblies through synaptic and intrinsic plasticity. The long-term plasticity of synapses involves the long-term potentiation/depression of
synaptic responses, spine growth/elimination, protein synthesis and capture, homeostatic plasticity etc [1-2]. Based on experimental evidence, we developed a simplified computational model of plasticity that examines the role of dendrites and synaptic turnover dynamics during associative learning [3]. We use multi-scale modeling to model synaptic processes which span different temporal and spatial scales, such as calcium influx, protein synthesis and delivery, synaptic tagging and homeostasis to assess how memories are encoded in a population of neurons. Using the model, we show that memory storage increases the sparsity of population firing and that local protein synthesis promotes dendritic synapse clustering [3]. Moreover, our model suggests that memories learnt in close temporal proximity are stored in overlapping neuronal and dendritic populations. This overlap serves as the main mechanism for linking memories across time. These neuronal and dendritic overlaps underlie memory linking even in the absence of dendritic spikes, albeit at a very high cost of increased afferent connections, indicating that active dendrites serve as a means for resource savings. Finally, we propose that the same mechanisms can bind together sequential memories, creating memory episodes [3]. Our model also predicts that increased synaptic turnover facilitates the formation of synapse clusters within active dendrites, which in turn improves learning and maximizes the storage capacity of newly learnt memories [4]. References: [1] Sutton, M.A. & Schuman, E.M., 2006. Cell, 127, 49–58 [2] Rogerson, T. et al., 2014. Nature Reviews Neuroscience, 15, 157–169. [3] Kastellakis G., Silva, A.J., Poirazi, P. Cell Reports. 2016 Nov. [4]. Frank A.C., Huang S., Zhou M., Gdalyahu A., Kastellakis G., Silva T.K., Lu E., Wen X., Poirazi P., Trachtenberg J.T., Silva A.J. Nat Commun. 2018 January

**Oral Presentations**

**OP 72**

**Responsibility of hippocampal asymmetry on the positive impact of predictable mild chronic stress on spatial memory in adolescent rats**

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Stress exposed during adolescence structurally and functionally affect the hippocampus, which is the critical brain region for spatial memory. Studies show that the impact of stress on cognitive functions is related to its predictability. In addition, hippocampal lateralization is suggested to be associated with optimal function and developing in adolescence. Investigating the effect of predictable chronic stress (PCS) exposed in adolescence on the asymmetry of memory related molecules and the correlation between memory performance and asymmetry was the aim of this study. We applied mild chronic stress (as PCS) during adolescence. Male rats were divided in two groups: control and PCS; n=11 for each. 15 min/day immobilization stress for 4 weeks was used as a PCS model. After 4 weeks spatial memory was tested in Morris Water Maze. The left and right hippocampus and frontal cortices were separated. Brain derived neurotrophic factor (BDNF) and oxidative markers malondialdehyde (MDA), protein carbonyl (PCO) and antioxidant superoxide dismutase (SOD) were measured by ELISA. Spatial memory of PCS group was improved compared to the control group (0.05). Hippocampal BDNF of the control group had left>right asymmetry while PCS group had right>left asymmetry (0.001). In the hippocampus of PCS group, MDA had right>left asymmetry (0.001). There was no difference between the left and right sides in terms of oxidative markers in the hippocampus of control group and frontal cortex of both groups. Our original findings suggest that asymmetric expression of BDNF and MDA (recently, it is reported that MDA may be a signal molecule for plasticity) in the right hippocampus, may strengthen spatial memory.

**OP 73**

**Oligomeric amyloid-beta at physiological concentrations rescues the impairment of hippocampal synaptic plasticity and memory in aged Amyloid Precursor Protein knockout mice**

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Amyloid precursor protein (APP) is a widely expressed transmembrane protein that is cleaved to generate different fragments, among which Amyloid-β (Aβ) peptide, a key actor in Alzheimer’s disease pathophysiology. Recent evidences indicate that the presence of APP is necessary for oligomeric Aβ and tau to exert a neurotoxic effect at the synapse, mediating their internalization into neurons. However, several studies have shown that APP and Aβ also play a role in physiological mechanisms underlying synaptic plasticity and memory. Here we have studied whether the genetic absence of APP affected different forms of synaptic plasticity and memory in APP knockout (APP
KO) mice. To this end, we performed in vitro electrophysiological recordings and behavioral studies to assess spatial learning, reference and fear memory in APP KO mice compared to WT animals. APP KO mice showed a significant impairment of CA3-CA1 hippocampal long-term potentiation (LTP) and different types of memory at 6 months of age, whereas an increase of paired-pulse facilitation (PPF), suggesting a decrease of neurotransmitter release, was found at 9 months of age. To study whether this impairment was due to the absence of endogenous Aβ, we treated APP KO mice with 200 pM oligomeric Aβ that was able to rescue the impairment of PPF, LTP and memory in APP KO animals. Taken together, these results show that APP is needed at the synapse and its absence determines an age-dependent impairment of synaptic function, which is rescued by low concentrations of oligomeric Aβ. This strengthens the importance of the physiological role of APP and Aβ in hippocampal plasticity and memory.

OP.75
Energy Metabolism of Reactive Astrocyte during Brain injury
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Impaired cerebral blood flow and extravagant increase of neuronal activities after brain injury deplete energy substrates in neurons and cause secondary neurodegeneration and poor network regeneration. Astrocytes are positioned between cerebral vasculature and neuronal network and play crucial roles in metabolism and delivery of energy substrates in the brain, however, astrocyte metabolic functions after brain injury are still largely elusive. Recent transcriptome analysis proposes multiple subpopulations of reactive astrocytes, thus astrocyte activation after brain injury likely impose complicated influences on energy metabolism. Accumulating publications suggest the upregulation of glycolysis in neurotoxic reactive astrocytes induced by pro-inflammatory cytokines, and the lactate produced by astrocytes may fuel neuron and/or accelerate inflammation. Meanwhile, neuroprotective scar-forming reactive astrocytes upregulate fatty acid oxidation, and likely produce ketone body for fueling neuron in addition to removing excessive fatty acid released from dead cells. These possibilities will be discussed by referring data we obtained in our originally-developed closed-head injury model, photo injury.