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ABSTRACTS OF THE TALKS

Denise Manahan-Vaughan

Ruhr University Bochum, Germany, Medical Faculty, Dept. Neurophysiology;

Title:

Subfield-specific encoding by the hippocampus of components of a spatial representation

Abstract:

Hippocampal synaptic plasticity is very likely to comprise the primary mechanism for long-term synaptic information storage and memory. Two forms exist that are known to endure for periods of days, weeks and in some cases months in rodents in vivo, and thus, may serve as physiological counterparts of long-term memory in mammals. Known as long-term potentiation (LTP) and long-term depression (LTD), together these forms of plasticity may shape the nature and content of spatial, and other forms of associative memories.

What is striking is that the triggering of LTP or LTD by a novel spatial learning event is tightly linked to specific aspects of a spatial experience, *and* that these processes are supported by sensory information transfer along the dorsal and ventral visual streams. A change in spatial environment, particularly when it is a global change, promotes synaptic encoding in the form of hippocampal LTP, by contrast spatial sensory experience and learning about spatial content triggers hippocampal LTD.

Different studies suggest that LTP may provide the initial template whereby new spatial and/or associative experiences are retained. By contrast, LTD may serve to shape and update this representation, such that the content details of the experience are integrated into the initial template to enable unique and differentiated representations of spatial experiences.

This work was supported by a German Research Foundation (DFG) grant to DM-V (SFB 874).

Martin J. Acerbo

Iowa State University, Ames, Iowa, USA; Department of Psychology

Title:

Relations and rewards: Hippocampal involvement in simple relational task and in inferential relational task

Abstract:

We studied hippocampal involvement in two relational tasks, transitive interference and transposition. A typical nonverbal transitive inference task (TI) consists of several overlapping discriminations (A+ B-, B+ C-, C+ D-, D+ E-, where letters indicate stimuli and the pluses and minuses denote reinforcement and nonreinforcement). A choice of stimulus B in a novel pair BD is interpreted as indicative of a TI (if B > C, and C > D, then B > D). In the first study, we investigated the effect of hippocampal lesion on TI in pigeons while controlling reinforcement history so that reliance on associative values would lead to a choice of a stimulus D in the pair BD instead of a choice of a choice of a stimulus B expected by inferential mechanisms. Prior to the lesion, some of the pigeons (relational group; n = 4) have selected B over D indicating TI, while other birds (associative group; n = 6) chose D over B suggesting reliance on associative values. Hippocampal lesion had no effect on post-lesion performance in associative group. In contrast, the relational group that preferred stimulus B in a pair BD prior to lesion showed a near-chance performance after the lesion. Our results demonstrate that

hippocampus may be involved in creating a representation of an ordered series of stimuli instead of maintaining reinforcement history of each stimulus. In the second study, we explored hippocampal involvement in a simple relational task, transposition, by using an immediate early gene expression approach. Unlike transitive inference, transposition does not require manipulating relation information; instead, animals are simply trained to learn the physical relation between the stimuli (eg., larger or smaller) and use the same relation when presented with novel pairs of stimuli. In this study, pigeons learned to discriminate two pairs of circles of different sizes, S1-S2 and S3-S4 (where S1 was the smallest circle and S4 was the largest circle). The relational group was trained to always select a smaller (or a larger) circle in each pair. The associative group was trained to select a smaller circle in one pair and a larger circle in another pair; in other words, these pigeons had to memorize exact stimulus instead of relying on their relationship. After all birds were trained, they were tested with two novel pairs, S2-S8 and S2-S3. The hippocampal area DLd revealed opposite lateralization patterns in the two groups: The ZENK expression was significantly higher in the right hemisphere of relational group, and in the left hemisphere of associative group. In addition, associative group showed significantly higher c-fos levels in the ventral nucleus accumbens of the right hemisphere, whereas c-fos levels in the nucl accumbens of relational group were low and non-lateralized. Together these results suggest hippocampal involvement in relational tasks that are not explicitly spatial in nature and that do not require inferential operations.

Vincent J. Coppola

Bowling Green State University, Bowling Green, Ohio, USA;
Department of Psychology

Title:

Hippocampal aging in homing pigeons: Recent data, speculations, and future directions

Abstract:
Much research has been conducted on aging of the mammalian hippocampus and its impact on cognition. By contrast, little research has been conducted on aging of the avian hippocampal formation (HF) and its cognitive impact. In 2012, I began a series of studies on neurocognitive aging in homing pigeons (*Columba livia*). I first documented spatial memory impairment in old pigeons, and then identified some age-related morphometric changes that occur to the pigeon HF. My current research, the focus of this talk, seeks to expand upon my previous findings by taking closer look at the relationship between HF aging and spatial cognition. Following a detailed presentation of recent data, I will offer some speculations and predictions that could potentially be useful in guiding future research on HF aging in birds.

Verner P. Bingman

Bowling Green State University, Bowling Green, Ohio, USA;
Department of Psychology

Title:
The Homing Pigeon Hippocampus: Past, Present and Future

Abstract:
The neuroethological investigation of the avian hippocampus began in the 1980s with studies taking advantage of the homing behavior of pigeons and food-storing members of the Paridae. Those seminal studies offered insights that would be confirmed by later experiments relying on vastly more sophisticated research methodologies. In homing pigeons, the later findings include the demonstration of failed corrective re-orientation following hippocampal lesions, a more "interesting" left hippocampus in the context of spatial cognition, neuronal response properties and functional connectivity, and even a possible role of the avian hippocampus in the *perception* of space. But what about the future? Certainly the most compelling question remains how the seemingly different neuronal organization of the avian hippocampus, compared to mammals, is able to implement perhaps informationally richer and more dynamic representations of space that can guide navigation and support memory.

Tom V. Smulders

Newcastle University, Newcastle upon Tyne, UK; School of Psychology

Title:

How similar are the avian and mammalian hippocampus? Exploring further functional features

Abstract:

There is a broad consensus that the avian and mammalian hippocampal formations are homologous to each other, and that the core function of this structure has been conserved through evolutionary time. Indeed, there is a lot of evidence that points to the involvement of both structures in spatial navigation and memory processing. However, we know a lot more about the mammalian than we do about the avian hippocampal formation. In a search for further functional similarities, we have explored two aspects in the avian hippocampus which are well known from its mammalian counterpart.

The first of these is the sensitivity to chronic stress: like in mammals, the avian hippocampal formation plays a role in down-regulating the activity of the HPA axis, and contains high concentrations of glucocorticoid and mineralocorticoid receptors. One of the consequences of this is that adult hippocampal neurogenesis in mammals is down-regulated by chronic stress. We investigate the same phenomenon in birds, and find that, indeed, adult

hippocampal neurogenesis is downregulated by chronic mild stress in chickens.

The second feature we investigate is the generation of gamma oscillations by the local hippocampal circuitry. In mammals, feedback loops between excitatory pyramidal neurons and inhibitory local interneurons set up oscillations in the gamma band, which can be elicited and measured in slice preparations. We show that in the avian hippocampal formation as well, gamma oscillations can be elicited in slice preparations. The pharmacological manipulations of different neurotransmitter systems suggest that a similar microcircuitry to that in mammals is responsible for this feature.

In summary, despite differences in cyto-architecture, the avian and mammalian hippocampal formations have conserved a wide range of functional similarities.

Olga Lazareva

Drake University, Des Moines, Iowa, USA; Dept. for Psychology and Neuroscience

Title:

Relational learning and space: A common ground?

Abstract:

An ability to respond to the relations between objects or events is a fundamental component of complex cognition. It has been long argued that a mental spatial representation underlies at least some of the aspects of deductive reasoning (De Soto, London, & Handel, 1965; Eichenbaum, 1999; Goodwin & Johnson-Laird, 2008). However, there has been very little direct experimental evidence supporting this spatial representation hypothesis in human cognition; the involvement of spatial representation in relational learning in non-human animals is even less clear. I will review three lines of research suggesting that (1) spatial representation underlies the formation of an ordered series during transitive inference task in both humans and non-human animals; (2) spatial representation is involved in learning a simple relational task, transposition, in both humans and non-human animals; and (3) non-human animals spatially organize numerosities even when the task does not require them to do so. Together, this evidence provides initial experimental support to the idea that the neural and cognitive mechanisms evolved for spatial cognition also provide the substrate for relational processing.

Nikolai Axmacher

Ruhr-University-Bochum, Bochum, Germany; Institute of Cognitive Neuroscience, Neuropsychology

Titel:

Engram patterns

Abstract:

Individual contents are represented by individual neurons in the brain. These neurons are embedded into larger networks, or assemblies, whose activity is characterized by synchronized oscillations at various frequencies as well as by asynchronous activity. The activity patterns of these networks differ significantly when different stimuli are presented. In my talk, I will present recent intracranial EEG data from epilepsy patients on how specific stimuli are represented in the human brain, and how such stimulus-specific “Engrams” are further processed during memory functions. These results provide important insights into meso-scale network representations of specific experiences.

Sen Cheng

Ruhr-University-Bochum, Bochum, Germany; Institute for Neural Computation

Title:

Episodic Memory and the Hippocampus

Abstract:

There appears to be no doubt that, in humans, the hippocampus plays a special role in episodic memory. However, the clarity ends here. We do not know 1. what episodic memory really is, 2. whether other animals have it, and 3. what function the hippocampus plays in episodic memory. In my opinion, the time-honored approach of divide-and-conquer, in which studies focus only on certain selected aspects of these questions, has not yielded significant progress towards a satisfactory resolution of these questions. I believe that instead an integrative approach is required, in which all major aspects of episodic memory and the function of the hippocampus are considered simultaneously. I will suggest that episodic memories are essentially sequential in nature, that the hippocampus is optimized to store neural sequences that represent episodic memories, and that it is highly likely that many species besides humans have a capacity for episodic memory.

Robert Naumann

Max Planck Institute for Brain Research, Frankfurt, Germany;

Title:

Evolution of the cerebral cortex: a view from the hippocampus of reptiles

Abstract:
Our ability to navigate through the world depends on the function of the hippocampus. This old cortical structure plays a critical role in spatial navigation in mammals, and in a variety of processes including declarative and episodic memory and social behavior. Intense research has revealed much about hippocampal anatomy, physiology and computation; yet even intensely studied phenomena such as the shaping of place cell activity or the function of hippocampal firing patterns during sleep remain incompletely understood. Interestingly, while the hippocampus may be a 'higher order' area linked to a complex cortical hierarchy in mammals, it is an old cortical structure in evolutionary terms. The reptilian cortex, structurally much simpler than the mammalian cortex and hippocampus, therefore presents a good alternative model for exploring hippocampal function. Here, I trace common designs in the evolution of the hippocampus of reptiles and mammals and ask which parts can be compared profitably to understand functional principles.

Asgeir Kobro-Flatmoen

Norwegian University of Science and Technology, Trondheim, Norway; Kavli Institute for Systems Neuroscience

Title:

The functional anatomy of the hippocampal region

Abstract:

The hippocampal region is a highly conserved part of the mammalian brain that enables what we humans perceive as conscious memory. Furthermore, studies on animals have convincingly shown that the hippocampal region is also heavily involved in navigation, while studies on Alzheimer's disease indicate that this region is amongst the first, if not the first, to show signs of pathology at pre-clinical stages. This talk will center on the basic functional anatomy of the hippocampal region by tracking the scientific progress in understanding this region, from the first mentioning of "the hippocampus", until the present-day concept.

ABSTRACTS OF THE BLITZ PRESENTATIONS

Noemi Rook

Title:

Intrinsic connectivity of the hippocampal formation of pigeons: an in vitro tracing study

Abstract:

Pigeons have incredible navigational abilities and are able to return to their home loft when being displaced at distances over thousands of kilometers. Ablation experiments have shown that an intact hippocampus (HC) is important for this capability. Similar to mammals, birds with damage to the HC are severely impaired on a variety of spatial tasks including navigation or retention of spatial information. However, the underlying mechanism as well as the comparability of the mammalian and avian HC is still a matter of intensive debate. The HC is a phylogenetically old structure and might have been present in the last common ancestor of birds and mammals. Nevertheless, 300 million years of independent evolution led to vastly different organizations of the avian and mammalian HC at macroscopic level. Given their similar role in spatial navigation, the question arises whether some characteristics of the avian and mammalian HC may be evolutionarily conserved.

In mammals, projections that interconnect the enthorinal cortex (EC) with Cornu Ammonis areas (CA1) and the subiculum, as well as projections from CA1 to the subiculum are organized in a topographic way. We hypothesize that topographic projections within the HC

constitute a crucial prerequisite for spatial navigation and will also be found in the HC of pigeons.

We combined in vivo with high resolution in vitro tracings in the HC of pigeons to address this issue. We found that input to the HC is distributed to all hippocampal regions via dorsolateral subdivisions (DL; predominantly via its ventral part). Our data suggests that a dorsomedial and ventrolateral zone can be distinguished within the HC. The former might process the thalamic input in intrinsic reverbatory circuits and then transfer it to the ventrolateral zone from which the hippocampal output is generated. Additionally, our in vivo tracing data indicates that projections from the area corticoidea dorsolateralis (CDL) are roughly topographic such that the more proximal part of CDL projects to more dorsal parts of the HC, whereas the distal part of CDL projects to more ventral parts of the HC.

Despite the large phylogenetic distance between birds and mammals, some features such as topographically organized intrinsic hippocampal connectivity are shared by those two taxa, and may be one explanation for the functional equivalence between the avian and mammalian HC in spatial navigation.

Martin Stacho

Title:

The circuitry of the avian forebrain and the evolution of the pallium

Abstract:

Up to the end of the 20th century, birds were thought to have limited cognitive abilities and their forebrain was mostly thought to be constituted by hypertrophied basal ganglia with only a minimal fraction of the forebrain recognized as pallium. These facts together with the knowledge about the basal ganglia function at that time resulted in the conclusion that birds were only capable of instinctive behavior. Nowadays, scientific evidence about the avian cognition and modern neuroanatomical studies unequivocally disproved this view and shed light on a radically different picture. Although birds do not possess a six-layered neocortex, detailed studies of the visual and auditory system in chicken uncovered columnar-like organization and canonical circuits akin to neocortical columns and canonical circuits in mammals. To confirm and further extend these results, we performed in-vitro tracing on the visual and trigeminal system as well as the somatosensory and visual hyperpallium (H) in pigeons. We found that the thalamo-recipient sensory areas Field L2 (auditory), entopallium (visual), and nucleus basalis (trigeminal) were directly interconnected with dorsal and ventral mesopallium. The intercalated nidopallium was reciprocally connected with both the primary sensory

areas and the mesopallium. The nido- and mesopallium were the sources of projections to arcopallium – the output region of the avian forebrain. Interestingly, the H showed a conspicuously different organization. In contrast to nido/mesopallial areas, the H (both visual and somatosensory components) did not display such a strict columnar organization and showed strong within-layer connections. Moreover, the interstitial part of the H apicale (IHA, the thalamo-recipient layer of H) directly projected to the apical part of H (HA), the output layer of the H, and did not project to mesopallium. The intercalated part of the H (HI) was reciprocally connected to IHA, HA and to adjacent densocellular part of the H (HD). HD further projected to HA and IHA, and together with HI and HA also to the mesopallium. In turn, the mesopallium projected to all layers of H. Despite profound differences between the H and the nidopallial circuit, some similarities in the connectivity can be pointed out. The canonical pathway from IHA to HA via HI with feedback connections at each level is similar to the organization centered around the nidopallium. Thus, the avian sensory forebrain seems to be characterized by a single canonical circuit that has some local variations. Future studies have to show how similar the avian canonical circuit is to its mammalian cortical counterpart.

Catrona Anderson

Title:

Magnetoreception, spatial memory, and the pigeon hippocampus

Abstract:

It is known that many animals are sensitive to the Earth's geomagnetic field, and can alter their behaviour accordingly in response to this sense. Pigeons in particular use this sense to orient themselves during homing and navigation. However, while a behavioural response to magnetic information can be observed, little is known physiologically and neurally about how this information is collected. There is some support for the existence of 'magnetoreceptors' within the retina and operculum of pigeons, but it is also theorised that there must a neuronal aspect: that is, the pigeon brain must process geomagnetic information at some level.

The pigeon hippocampus has been shown to be involved in homing, as lesions to this area cause impairments to their navigational abilities. Furthermore, the pigeon hippocampus appears to play a critical role in spatial processing and memory. Therefore, it seems likely that a neural correlate for magnetoreception would be found in the hippocampus. As a series of experiments, the Colombo lab has investigated whether several brain regions, including the hippocampus, display neural activity under the influence of an artificial magnetic field. We also sought to find whether magnetic stimulation to the hippocampus

would affect spatial memory during an analogue of the radial arm maze.

Martina Manns

Title:

Hemispheric-specific evaluation of interhemispheric associative memory in pigeons when confronted with a transitive inference task

Abstract:

The hippocampus is generally involved in forming representations of associative and hierarchical relations[1]. Accordingly, it participates in transitive inference, which is the ability to infer the relationship between items after learning to discriminate overlapping premise pairs that represent an ordered series of stimuli[5]. There is however, some debate in how far relational or associative strategies underlie transitive responding and hence, about hippocampal contributions[1,5]. Recent evidence from pigeon research supports a critical role for the hippocampus in creating a transitive line[2] but the hippocampus may also update associative values of training stimuli enabling the selection of stimuli with richer reinforcement history[1]. Since there is some evidence that the left and right hippocampus differentially contribute to transitive responding[6], it is conceivable that the hemispheres differ in their encoding strategies when confronted with a transitive inference problem. One strategy may dominate depending on the training and/ or test conditions[2]. We therefore explored hemispheric-specific transitive responding in pigeons[4] since they display profound left-right differences in the structural and functional organization of their brain[3]. Pigeons were trained in overlapping color discriminations in which each

hemisphere learned only half of the information that represented a linear hierarchy (i.e. one hemisphere learned A>B, B>C, the other one learnt C>D, D>E). When each hemisphere was then confronted with critical test pairs (like BD), interhemispheric memory about the relational values of the stimulus pairs had to be transferred and combined to establish the transitive line. Pigeons displayed transitive responding under binocular but not under monocular seeing conditions. These results suggest that pigeons do not integrate hemisphere-specific knowledge to adopt a transitive inference strategy when using only one hemisphere. But the hemispheres displayed intriguing differences in their response pattern. The right hemisphere adopted an associative strategy while ambiguous choices of the left hemisphere indicate interferences between intra- and interhemispheric information preventing relational computations. These data show that pigeons use flexible intra- and interhemispheric encoding strategies depending on the seeing conditions[4] and suggest a differential contribution of the left and right hippocampus in transitive responding that should be addressed in future studies.

Literature:

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[2]Lazareva et al. (2015) Hippocampal lesion and transitive inference: dissociation of inference-based and reinforcement-based strategies in pigeons. Hippocampus 25:219-226.

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Beate Knauer

Title:

Distribution of redox-active metals in the primate hippocampus

Abstract:

Redox-active metals play an important role in cell physiology. They are essential elements that are incorporated in an estimated 50% of your proteins, for example as cofactors with catalytic functions or as structural support elements. Especially iron and copper, are implicated in a number of neurodegenerative diseases with research focused on Parkinson's and Alzheimer's disease. Also epilepsy and mood disorders are being investigated and manganese appears to take notable part in these. Particularly in the hippocampus, zinc may be involved in a wealth of physiological and pathophysiological processes because it is enriched in zinc-containing neurons which are a subset of glutamatergic neurons.

We employed laser ablation - inductively coupled plasma - mass spectrometry (LA-ICP-MS)[1] to investigate essential elements in the cerebrum of common marmosets (Callithrix jacchus). The brains originated from a tissue archive established and maintained by David Reser with the kind support of Marcello Rosa's group. All in vivo procedures were approved by the Monash University Animal Ethics Committee and conformed to the Australian NHMRC Guide for Care and Use of Laboratory Animals. We sampled the content of phosphor(^{31}P), carbon(^{13}C),

manganese(^{55}Mn), iron(^{56}Fe), copper(^{63}Cu), and zinc(^{66}Zn) with a 100µm square laser pulse directed onto 40µm thick brain slices at inter-slice-intervals of 200µm. Adjacent sections were stained for Nissl, myelin and cytochrome oxidase to allow parcelation based on cytocarchitectonic and histochemical markers, and alignment of metal data with brain structures.

We recently reported the distribution of redox-active metals in the primate cortex showing that particularly Fe and Mn were enriched in primary sensory areas[2]. However, Fe and Mn did not co-localize in other areas of the brain, like the basal ganglia and the hippocampus. Preliminary data on the hippocampus will be presented showing that the distribution of Mn was more diffuse, whereas Fe and Zn distributions were more circumscribed. High relative concentrations of Mn were found in the dentate gyrus and CA3, with still moderate levels in CA1 and adjacent regions. In contrast, high relative concentrations of Fe and Zn seemed to co-localize in CA1 and the subiculum. Fe concentrations differed from those of Zn by a marked lack of Fe in the DG and CA3, whereas relative Zn levels in these regions were moderately low.

Quantitative and more detailed investigation of hippocampal essential element levels are underway. Preliminary conclusions are that hippocampal Fe and Mn are distributed in opposing trends. The divergence of Zn concentrations from the expected high values at CA3 synapses will be discussed.

Richard Görler

Title:

A parametric anatomical model of the pigeon hippocampal formation

Abstract:

Three-dimensional models of neuroanatomy are an important resource for knowledge documentation, experimental planning, and incorporating spatial constraints in computational simulations. Such resources are already available for several mammalian species such as the rat and mouse, e.g., the Allen Brain Explorer [1] and Waxholm Space atlases [2-4]. While a recent volumetric atlas has been released for the pigeon brain [5], the technological difficulties of accessing and using these data, e.g. for computational models, remained. I will present a first computational model of the 3-d structure of the pigeon hippocampal formation. The model was constructed using Parametric Anatomical Modeling [6], a technique that facilitates the translation of anatomical data into a computational description and that allows for the determination of connection patterns and connection lengths from the computational model. Our pigeon hippocampus model reflects, to the best of our knowledge, the current research regarding subdivisions and interconnections while allowing for the connection properties to be further parametrized. The model can be applied to visualize the 3-d structure of the pigeon hippocampus, to document the results of future anatomical studies, and to generate neural networks with realistic connection properties for computer simulations.

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Meng Gao

Title:

The neural circuit underlying extinction learning in pigeons - evidence from pharmacological studies

Abstract:

Extinction learning is an essential learning mechanism that enables constant adaptation to the ever changing environmental conditions. The underlying neural circuit was mostly studied with rodent models using fear conditioning tasks. In order to uncover the variant and the invariant neural properties of extinction learning, we adopted pigeons as an animal model in an appetitive sign-tracking paradigm. The animals firstly learned to respond to two stimuli in two different contexts (CS-1 in context A and CS-2 in context B) and then extinguished their conditioned responses to the corresponding stimulus in the opposite contexts (CS-1 in context B and CS-2 in context A). Finally, they were tested for both stimuli in both contexts. Before the extinction training, we locally injected the sodium-channel blocker tetrodotoxin (TTX) or the N-methyl-D-aspartate receptor (NMDAR) antagonist 2-Amino-5-phospho-novalerianacid (APV) in specific areas to investigate their involvement in the extinction learning process. With this within-subject renewal design, we discovered that the extinction learning does not only engage the neural circuit of the nidopallium caudolaterale (NCL; the avian equivalent structure to the mammalian PFC), hippocampus, and amygdala, but also involves arcopallium, the avian premotor area, and the nidopallium

frontolaterale (NFL), one of the avian higher visual-processing areas. Importantly, our findings suggested that the encoding of extinction memory requires the activation of NCL, amygdala, and NFL, seen from an impairment of extinction acquisition due to the pre-extinction inactivation of these areas. Whereas the consolidation and expression of extinction memory possibly involve NCL, hippocampus and arcopallium, indicated by an impaired spontaneous recovery during testing. In addition, the absence of a context-dependent renewal effect while the pre-extinction NFL inhibition reflects an involvement of the NFL in contextual encoding and context-dependent retrieval of extinction memory. This study provides new insights on the extinction network in the avian brain and its resemblance to the data obtained from various other species, which also indicates a shared neural mechanism underlying extinction learning shaped by evolution.

ABSTRACTS OF THE POSTER PRESENTATIONS

Mehdi Bayati

Title:

Generating sequences in recurrent neural networks for storing and retrieving episodic memories

Abstract:

It has been suggested that the reliable propagation and transformation of neural activity within and between different brain regions is crucial for neural information processing. Furthermore, temporal sequences of neural activation have recently been proposed to play an important role in the explanation of the function of hippocampal neural circuits in episodic memory, our memory of experienced events in our lives [1]. One central feature of CRISP is that hippocampal area CA3, because of its abundant recurrent connections, intrinsically produces temporal sequential activities. In this project, first we review the possible mechanisms by which a relatively fixed recurrent network structure (as a model of CA3) can generate neural activity sequences intrinsically. Next we implement the CA3 models in a complete framework of cortico-hippocampal circuits (We use EC-CA3-CA1-EA network), each subregion has certain function based on CRISP theory. During memory encoding, intrinsic CA3 sequences are hetero-associated with sequences that are driven by sensory inputs. Later on sequences in CA3 are hetero-associated with the sequence in CA1 and finally, the CA1 activities are hetero-associated with sensory inputs in the EC. During memory retrieval, intrinsic CA3 sequences have to be reactivated based on partial, noisy cues which is provided to EC. Finally, the retrieved

sequences in CA3 reactivate the initial input sequences in EC via CA1 layer. Memory performance is determined by the network's ability to perform sequence completion. If the network's output is more similar to the original sequence, then the network has done some amount of sequence recall. As a measure for similarity we use the Pearson correlation coefficient between the corresponding patterns of the originally stored and retrieved sequences in different layers. Overall, we find that the neural network mechanism in CA3 generating the sequences has to be robust to noise in the triggering cue. On the other hand less temporal-correlated patterns in CA3 give rise to more confidence in retrieving the sequence in a complete framework. To conclude, we find that using the right model in CA3, CRISP model surprisinglly retrieves almost correctly the stored sequences up to moderate noise levels.

Acknowledgements

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References

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Mehdi Behroozi

Title:

Funtional connectivity pattern of the internal hippocampal network in awake pigeons: a resting state fMRI study

Abstract:

In the last two decades, the avian hippocampus has been repeatedly studied with respect to its architecture, neurochemistry, and connectivity pattern. We review these insights and conclude that we unfortunately still lack proper knowledge on the interaction between the different hippocampal sub-regions. To fill this gap we need information on the functional connectivity pattern of the hippocampal network. These data could complement our structural connectivity knowledge. To this end we conducted a resting state fMRI experiment in awake pigeons in a 7T MR scanner. A voxelwise regression analysis of BOLD fluctuations in 6 distinct areas (dorsomedial (DM), dorsolateral (DL), triangular shaped (Tr), dorsolateral corticoid (CDL), temporo-parieto-occipital (TPO), lateral septum (SL)) was performed to establish a functional connectivity map of the avian hippocampal network. Our study reveals that the system of connectivities between CDL, DL, DM, and Tr is the functional backbone of the pigeon hippocampal system. Within this network DM is the central hub and is strongly coupled to BOLD-signal fluctuations of DL and CDL. DM is also the only hippocampal region to which large areas of Tr are functionally connected. In contrast to published tracing data, TPO and SL are only weakly integrated in this

network. In summary, our findings uncovered a structurally otherwise invisible architecture of the avian hippocampal formation by revealing the dynamic blueprints of this network.

Neslihan Edeş & **Patrick Anselme**

Title:
The long-term behavioral effects of sensitization to apomorphine in pigeons

Abstract:
When rodents are given a free choice between a variable option and a constant option, they may prefer variability. This preference is even sometimes increased following repeated administration of a dopamine agonist. The present study was the first to examine preference for variability under the systemic administration of a dopamine agonist, apomorphine (Apo), in birds. Experiment 1 examined the effects of Apo sensitization on delay preference, in comparison with previous control tests. Apo sensitization decreased the number of pecks at the constant option across the different experimental phases, but failed to induce a preference for the variable option. In Experiment 2, two groups of pigeons (Apo-sensitized and saline) were used in order to avoid inhomogeneity in treatments. They had to choose between a 50% probability option and a 5-s delay option. Conditioned pecking and the propensity to choose were higher in the Apo-sensitized pigeons, but, in each group, the pigeons showed indifference between the two options. This experiment also showed that long-term sensitization to Apo can occur independently of a conditioning process. These results suggest that Apo sensitization can enhance the attractiveness of conditioned cues, while having no effect on the development of a preference for variable-delay and probabilistic schedules of reinforcement.

Meng Gao

Title:

The neural circuit underlying extinction learning in pigeons - evidence from pharmacological studies

Abstract:

Extinction learning is an essential learning mechanism that enables constant adaptation to the ever changing environmental conditions. The underlying neural circuit was mostly studied with rodent models using fear conditioning tasks. In order to uncover the variant and the invariant neural properties of extinction learning, we adopted pigeons as an animal model in an appetitive sign-tracking paradigm. The animals firstly learned to respond to two stimuli in two different contexts (CS-1 in context A and CS-2 in context B) and then extinguished their conditioned responses to the corresponding stimulus in the opposite contexts (CS-1 in context B and CS-2 in context A). Finally, they were tested for both stimuli in both contexts. Before the extinction training, we locally injected the sodium-channel blocker tetrodotoxin (TTX) or the N-methyl-D-aspartate receptor (NMDAR) antagonist 2-Amino-5-phospho-novalerianacid (APV) in specific areas to investigate their involvement in the extinction learning process. With this within-subject renewal design, we discovered that the extinction learning does not only engage the neural circuit of the nidopallium caudolaterale (NCL; the avian equivalent structure to the mammalian PFC), hippocampus, and amygdala, but also involves arcopallium, the avian premotor area, and the nidopallium

frontolaterale (NFL), one of the avian higher visual-processing areas. Importantly, our findings suggested that the encoding of extinction memory requires the activation of NCL, amygdala, and NFL, seen from an impairment of extinction acquisition due to the pre-extinction inactivation of these areas. Whereas the consolidation and expression of extinction memory possibly involve NCL, hippocampus and arcopallium, indicated by an impaired spontaneous recovery during testing. In addition, the absence of a context-dependent renewal effect while the pre-extinction NFL inhibition reflects an involvement of the NFL in contextual encoding and context-dependent retrieval of extinction memory. This study provides new insights on the extinction network in the avian brain and its resemblance to the data obtained from various other species, which also indicates a shared neural mechanism underlying extinction learning shaped by evolution.

Richard Görler

Title:

Modeling semantic learning driven by episodic memory

Abstract:

Semantic memories, which are general facts about the world, and episodic memories, which are about personally experienced events, interact with each other [1]. In the serial-parallel-independent (SPI) model [2], Tulving hypothesized that encoding is serial, i.e., sensory information is passed through the semantic system before being encoded into episodic memory. The semantic representation is therefore crucial for episodic memory, but the SPI model does not allow for episodic memory to influence the learning of semantic representations. Experimental findings indeed show that semantic learning occurs without episodic memory [3]. However, since such learning is slow [4], episodic memory may facilitate the learning of semantic representations, which contradicts the idea of strictly serial encoding in the SPI model. We have recently developed a computational model to study the interrelation between the semantic and the episodic system. In that model, the semantic system compresses the high-dimensional sensory inputs to a lower dimensionality both in space and time via slow feature analysis [5]. Episodic memories are represented by an algorithmic sequence storage network that resembles properties of neural network models of memory storage. In this project, the computational model is extended to allow for memory-driven category learning. The model is used to explore whether such learning is more efficient than pure

sensory-driven learning. Such a finding would account for slower semantic learning in the absence of a functioning hippocampus.

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[3] Vargha-Khadem F, Gadian DG, Watkins KE, Connely A, Van Paesschen W, Mishkin M. *Differential effects of early hippocampal pathology on episodic and semantic memory*. Science 1997;277:376–380
[4] Levy DA, Bayley PJ, Squire LR (2004) *The anatomy of semantic knowledge: medial vs. lateral temporal lobe*. PNAS 101:6710–6715
[5] Wiskott, L and Sejnowski, T (2002). *Slow feature analysis: Unsupervised learning of invariances*. *Neural Computation* 14(4): 715-770

Beate Knauer

Title:

Distribution of redox-active metals in the primate hippocampus

Abstract:

Redox-active metals play an important role in cell physiology. They are essential elements that are incorporated in an estimated 50% of your proteins, for example as cofactors with catalytic functions or as structural support elements. Especially iron and copper, are implicated in a number of neurodegenerative diseases with research focused on Parkinson's and Alzheimer's disease. Also epilepsy and mood disorders are being investigated and manganese appears to take notable part in these. Particularly in the hippocampus, zinc may be involved in a wealth of physiological and pathophysiological processes because it is enriched in zinc-containing neurons which are a subset of glutamatergic neurons.

We employed laser ablation - inductively coupled plasma - mass spectrometry (LA-ICP-MS)[1] to investigate essential elements in the cerebrum of common marmosets (Callithrix jacchus). The brains originated from a tissue archive established and maintained by David Reser with the kind support of Marcello Rosa's group. All in vivo procedures were approved by the Monash University Animal Ethics Committee and conformed to the Australian NHMRC Guide for Care and Use of Laboratory Animals. We sampled the content of phosphor(^{31}P), carbon(^{13}C),

manganese(^{55}Mn), iron(^{56}Fe), copper(^{63}Cu), and zinc(^{66}Zn) with a 100µm square laser pulse directed onto 40µm thick brain slices at inter-slice-intervals of 200µm. Adjacent sections were stained for Nissl, myelin and cytochrome oxidase to allow parcelation based on cytocarchitectonic and histochemical markers, and alignment of metal data with brain structures.

We recently reported the distribution of redox-active metals in the primate cortex showing that particularly Fe and Mn were enriched in primary sensory areas[2]. However, Fe and Mn did not co-localize in other areas of the brain, like the basal ganglia and the hippocampus. Preliminary data on the hippocampus will be presented showing that the distribution of Mn was more diffuse, whereas Fe and Zn distributions were more circumscribed. High relative concentrations of Mn were found in the dentate gyrus and CA3, with still moderate levels in CA1 and adjacent regions. In contrast, high relative concentrations of Fe and Zn seemed to co-localize in CA1 and the subiculum. Fe concentrations differed from those of Zn by a marked lack of Fe in the DG and CA3, whereas relative Zn levels in these regions were moderately low.

Quantitative and more detailed investigation of hippocampal essential element levels are underway. Preliminary conclusions are that hippocampal Fe and Mn are distributed in opposing trends. The divergence of Zn concentrations from the expected high values at CA3 synapses will be discussed.

Noemi Rook

Title:

Intrinsic connectivity of the hippocampal formation of pigeons: an in vitro tracing study

Abstract:

Pigeons have incredible navigational abilities and are able to return to their home loft when being displaced at distances over thousands of kilometers. Ablation experiments have shown that an intact hippocampus (HC) is important for this capability. Similar to mammals, birds with damage to the HC are severely impaired on a variety of spatial tasks including navigation or retention of spatial information. However, the underlying mechanism as well as the comparability of the mammalian and avian HC is still a matter of intensive debate. The HC is a phylogenetically old structure and might have been present in the last common ancestor of birds and mammals. Nevertheless, 300 million years of independent evolution led to vastly different organizations of the avian and mammalian HC at macroscopic level. Given their similar role in spatial navigation, the question arises whether some characteristics of the avian and mammalian HC may be evolutionarily conserved.

In mammals, projections that interconnect the enthorinal cortex (EC) with Cornu Ammonis areas (CA1) and the subiculum, as well as projections from CA1 to the subiculum are organized in a topographic way. We hypothesize that topographic projections within the HC

constitute a crucial prerequisite for spatial navigation and will also be found in the HC of pigeons.

We combined in vivo with high resolution in vitro tracings in the HC of pigeons to address this issue. We found that input to the HC is distributed to all hippocampal regions via dorsolateral subdivisions (DL; predominantly via its ventral part). Our data suggests that a dorsomedial and ventrolateral zone can be distinguished within the HC. The former might process the thalamic input in intrinsic reverbatory circuits and then transfer it to the ventrolateral zone from which the hippocampal output is generated. Additionally, our in vivo tracing data indicates that projections from the area corticoidea dorsolateralis (CDL) are roughly topographic such that the more proximal part of CDL projects to more dorsal parts of the HC, whereas the distal part of CDL projects to more ventral parts of the HC.

Despite the large phylogenetic distance between birds and mammals, some features such as topographically organized intrinsic hippocampal connectivity are shared by those two taxa, and may be one explanation for the functional equivalence between the avian and mammalian HC in spatial navigation.

Marie Sanders

Title:

The Indusium Griseum: A new story of an old hippocampal outskirt

Abstract:

The Indusium griseum (IG) is a thin cortical structure lying dorsal to the corpus callosum and is often referred to as an extant hippocampal continuation. It is still discussed whether it resembles a remnant of the dentate gyrus (DG), the cornu ammonis (CA)or the subiculum or whether it should rather be considered a distinct hippocampal subregion. In order to elucidate the affiliation of the IG to hippocampal subareas we investigated the protein expression patterns of Prox1, Secretagogin, NECAB2 and Calbindin using peroxidase immunohistochemistry. We also performed Golgi-Cox staining to show neuronal cell characteristics.

Furthermore, we used a transgenic mouse that expresses eGFP exclusively in dentate granule cells, allowing to clearly distinguish the identity of IG neurons from dentate granule cells. In conclusion, our investigations reveal novel insights into the expression pattern in time and space of these proteins during postnatal development, and allow us to address the IG as a hippocampal subregion with its own particular identity.

Martin Stacho

Title:

The canonical circuit of the avian sensory forebrain

Abstract:

Up to the end of the 20th century, birds were thought to have limited cognitive abilities and their forebrain was mostly thought to be constituted by hypertrophied basal ganglia with only a minimal fraction of the forebrain recognized as pallium. These facts together with the knowledge about the basal ganglia function at that time resulted in the conclusion that birds were only capable of instinctive behavior. Nowadays, scientific evidence about the avian cognition and modern neuroanatomical studies unequivocally disproved this view and shed light on a radically different picture. Although birds do not possess a six-layered neocortex, detailed studies of the visual and auditory system in chicken uncovered columnar-like organization and canonical circuits akin to neocortical columns and canonical circuits in mammals. To confirm and further extend these results, we performed in-vitro tracing on the visual and trigeminal system as well as the somatosensory and visual hyperpallium (H) in pigeons. We found that the thalamo-recipient sensory areas Field L2 (auditory), entopallium (visual), and nucleus basalis (trigeminal) were directly interconnected with dorsal and ventral mesopallium. The intercalated nidopallium was reciprocally connected with both the primary sensory areas and the mesopallium. The nido- and mesopallium were the sources of projections to arcopallium – the output region of the avian forebrain. Interestingly, the H showed a

conspicuously different organization. In contrast to nido/mesopallial areas, the H (both visual and somatosensory components) did not display such a strict columnar organization and showed strong within-layer connections. Moreover, the interstitial part of the H apicale (IHA, the thalamo-recipient layer of H) directly projected to the apical part of H (HA), the output layer of the H, and did not project to mesopallium. The intercalated part of the H (HI) was reciprocally connected to IHA, HA and to adjacent densocellular part of the H (HD). HD further projected to HA and IHA, and together with HI and HA also to the mesopallium. In turn, the mesopallium projected to all layers of H. Despite profound differences between the H and the nidopallial circuit, some similarities in the connectivity can be pointed out. The canonical pathway from IHA to HA via HI with feedback connections at each level is similar to the organization centered around the nidopallium. Thus, the avian sensory forebrain seems to be characterized by a single canonical circuit that has some local variations. Future studies have to show how similar the avian canonical circuit is to its mammalian cortical counterpart.

Kaya von Eugen

Title:

Differences in location, trajectory, and size of the NCL in a variety of bird species.

Abstract:

Nearly a decade ago, Emery and Clayton (2004) reviewed how the cognitive capacities of birds equaled, and sometimes even exceeded, those of mammals. Particularly remarkable are the corvids (crows, jays, magpies), who have been shown to be capable of tool use, complex reasoning, and mirror self-recognition. The required underlying neural architecture giving rise to this range of behaviors is still poorly understood. Previous studies have shown a positive correlation between specific complex behaviors and forebrain-size. However, the 'forebrain' is still a highly heterogeneous area, giving rise to a multitude of behaviors. Thus, there is the need for a closer examination of structures within the forebrain that are crucial for higher cognition. In birds, the area of interest is the nidopallium caudolaterale (NCL), also known as the 'avian prefrontal cortex' because of similarities in function, connectivity, and cytoarchitecture (Güntürkün, 2005). Behaviorally, it has been coined the seat for executive functioning; an umbrella term for an array of complex capacities such as working memory. This area can be delineated with an immunohistochemical stain against tyrosine hydroxylase (TH). The NCL can be characterized by a higher density of TH-fibers in comparison to the surrounding nidopallium. However, the NCL has been delineated and mapped in pigeons only, and almost nothing

is known about its location and trajectory in other bird species, let alone its size. The main aim of this study is to 1) identify the location-, 2) map the trajectory throughout the brain-, and 3) determine the size of the NCL in different species of birds that are known to vary in their level of complex cognition. It is hypothesized that the location and trajectory of the NCL differs between species, and, moreover, that the more cognitively abled species, e.g. the corvids and jays, have a larger NCL compared to less cognitively able species, e.g. pigeons and chickens, in both absolute and relative terms.