POSTER SESSION

C1. The link between creative thinking and psychoticism

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Much evidence has demonstrated that top-down processing, which refers to the influence of past experience and expectations on the processing of incoming stimuli, is relatively impaired in some psychotic populations. While a range of cognitive deficits associated with this disparity are well-established, little attention has been directed towards the possible advantages that may result from this skewed processing. The present study endeavours to illustrate such an advantage in the process of conceptual expansion by investigating two groups of healthy participants who differ in the degree of psychotic characteristics they possess. The ability to expand or widen conceptual structures, particularly when developing novel ideas, is a vital creative process which would be considerably hindered by the influence of prior knowledge in the form of existing concepts. Following this rationale, the hypothesis that participants with a high degree of "psychoticism" traits, and consequently diminished top-down processing, would perform better on a task of conceptual expansion relative to their low psychoticism counterparts was strongly confirmed.

C2. Dynamics of rapid scene categorisation: backward masking and RSVP studies

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Human observers are very good at deciding whether a briefly flashed natural scene contains or not an animal and previous work has shown that the underlying visual processing can be performed in 150 ms (Fabre-Thorpe et al. 1998, Thorpe et al. 1996). We used a masking paradigm to determine how information accumulates over time by presenting a strong pattern mask after the picture. We analysed the disruption effects by varying the Stimulus Onset Asynchrony (SOA). With an SOA of only 12 ms, categorisation accuracy was already above chance level and increased rapidly to reach a plateau at around 40-60 ms. These results suggest that processing at each stage of the visual system is remarkably rapid, with information supported by continuous feedforward mechanisms. In a second series of experiments, we used a Rapid Serial Visual Presentation paradigm in which sequences of 20 natural scenes were flashed at different rates, with a fixed display time but varying the delay between the pictures (SOA). As we did in the masking experiment, half of the sequences contained an animal. Nevertheless, accuracy was much lower for similar SOA, and at least 100 milliseconds were necessary to reach the same optimal performance level. Experiments are underway to determine whether this impaired performance is due to forward masking from the previous image in the sequence or to some form of attentional blink induced by the strong semantic impact of certain distractor images.

C3. Attention-dependent, beta-frequency coupling between local field potentials recorded in the cat's lateral geniculate nucleus and primary visual cortex

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We have previously proposed that enhanced beta (16-24 Hz) local field potential (LFP) activity, recorded from the primary visual cortex (VCx) and lateral geniculate nucleus (LGN) of cats required to switch their attention from auditory to visual modality, may be an electrophysiological correlate of the attentional mechanism that increases the gain of afferent information in the thalamic nuclei. In this study we checked attention-dependent coupling within cortico--thalamic system in other frequency bands. The correlation between amplitude envelopes of band-pass filtered LFP signals recorded simultaneously in the LGN and VCx was calculated during visual and auditory attentive situations. The analysis was done for theta (3-8 Hz), alpha (8-13 Hz), beta (16-24 Hz) and gamma (30-45 Hz) frequency bands. The attention-related difference of correlation was found only between envelopes of LGN and VCx beta signals registered from representations of the central visual field. For such centrally aligned recording sites the correlations calculated during visual trials were on average two times higher than those obtained during the auditory attentive task. We conclude that beta activity appears to be specifically important for cortico-thalamic coupling during visually attentive processing.

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C4. Visual scanning in normal and dyslexic readers

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It is well known that reading process – based on Western alphabetic system –involves a systematic left-to-right visual scanning (VS). To which extent the scanning direction is an acquired variable or depends on some neural inborn mechanisms it is an open question. If VS direction and systematicity is affected by reading ability, the left-to-right bias should be less systematic in pre-school children. Our work investigated the development of VS passing from pre-school to school age in normal readers and in dyslexic children. Subjects. 150 (75 females) normal readers (four age-groups: mean age of 4.6, 5.6, 6.3, and 17.8 years, respectively) and 10 dyslexic children (age: 7-13 years) were tested. Method. 18 geometrical figures were presented on a computer screen along the horizontal axis. The target (triangle) appeared randomly on 7 positions: 3 on the left, 3 on the right, and 1 on the middle of the screen. The subject has to push the space bar in response to the target. RTs were collected. Results. RTs changed as function of age-group and target position on the screen. Although on the whole normal readers showed a left-side advantage in response speed (suggesting an early scanning direction bias toward the left side), this difference between the two sides increased with age (suggesting a reading practice effect on VS development). Dyslexics showed generally slower RTs and the absence of the left-side advantage.

C5. Behavioural and fMRI investigations of mental images constructed from visual experience and from the processing of verbal descriptions

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The present series of experiments were motivated by two questions. First, are the spatial properties of representations constructed from route information similar to those derived from survey experience? Second, are the properties of mental images resulting from visual experience similar to those derived from listening corresponding verbal descriptions? Participants memorized a circular garden surrounded by six objects marking six locations. In behavioural experiments, four learning conditions were compared: (1) viewing a video presentation of a travel around the garden, (2) listening to a verbal description of that travel, and, as reference conditions, (3) viewing a map of the garden and (4) listening to a description of the map. Spatial representations constructed from a route perspective (conditions 1 and 2) showed the same metric properties as the mental images memorised from a survey perspective (conditions 3 and 4), although to a lesser extent due to the cognitive cost of the mental transformation of the spatial information in route perspective into survey-type mental images. In addition, visual acquisition lead globally to higher performance than verbal acquisition. Brain imaging experiments (involving conditions 1 and 3) are currently being processed in order to compare the neural structures respectively activated in route (parahippocampal gyrus) *versus* survey (right hippocampus) acquisition of spatial information.

C6. An fMRI investigation of dissociation between spatial and object recognition and memory

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By using a reaction-to-change paradigm that implies participants to refer to an initial situation that may have been modified during the tests, the present fMRI experiment aimed at investigating further the brain structures involved in object and configuration processing, respectively. Two test conditions were used. In the first time, the two stimuli to compare were simultaneously presented whereas in the second, they were successively displayed (memory condition). Either the specific attributes (shape, colour) of the objects, or the configuration they defined had to be processed. The questions at issue were: are these two types of processing subserved by different brain areas? Do these brain areas differ according to the condition of presentation (with or without memory)? Eleven adult participants were instructed to remember the locations and features of 7 objects arranged within a room. Then, the objects were either presented in alignment, or 7 similar new objects defined the arrangement. The task was to indicate whether a change had been brought about to the nature of the objects or to the initial configuration. Results showed that during object recognition, medial temporal activity seemed to be confined to the inferior temporal gyrus, and extended to the rhinal cortex in the memory condition. The recognition of spatial configurations activated the parahippocampal gyrus whereas the middle part of the hippocampus was involved during recall. The present data confirm that different brain areas process recognition and memory of objects and configurations. In addition, they show that the hippocampus is not only involved in navigation (as evidenced by various studies) but also in the memory of spatial configurations.

C7. Lateralization of primary and secondary imprinting in the domestic chick

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Monocular chicks' preferences following primary and secondary imprinting were investigated using stimuli of different shape. Newly-hatched chicks (n = 120) were exposed in their own cage, in binocular conditions, on day 1 to a primary imprinting object, on day 2 to a secondary imprinting object of a different shape; on day 3 chicks were exposed to both objects simultaneously. The objects employed were a ball and a cylinder made of the same plastic material and colour (red) and of similar size. On day 4, each chick underwent a 6-min simultaneous free choice test in monocular conditions (with either their left or their right eye temporary patched; a separate group of chicks was tested in binocular conditions as a control). At test, chicks with only their right eye in use preferred the cylinder, no matter whether this constituted their primary or secondary imprinting object; on the other hand, chicks with only their left eye in use showed an overall preference for the ball. Binocular chicks behaved similarly to the left-eyed chicks. Results confirm previous data revealing lateralized mechanisms for the processing of primary and secondary imprinting object in the chick's brain (Vallortigara et al. 2000).

C8. Electrophysiological indexes of auditory distraction: MMN-P3a-RON

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Attention switching triggered by changes in the environment can lead to distraction and, therefore, deterioration of concomitant task performance. To simulate this situation of involuntary attention switching, distraction and reorienting of attention back towards the main task, event-related potential (ERPs) and behavioural measures were recorded in 11 healthy subjects during a task of auditory discrimination. The subjects were trained to respond to short tones (200 ms) and long tones (400 ms), with equal probability of appearance. All the tones began with a frequency of 1,000 Hz and, sometimes (P=0.12) changed to 1,100 Hz at 50 ms (condition 50), or at 150 ms (condition 150) from stimulus onset; in the remaining occasions (P=0.88) the frequency was kept constant until stimulus offset. The deviant tones caused distraction, in comparison to the constant tones, as shown a decrease of task performance (reaction time: $F(2,22)=57.01$, $P<0.01$; hit rate: $F(2,22)=16.93$, $P<0.01$). Brain activity, obtained by the analysis of difference waves from the ERPs, showed clearly the MMN-P3a-RON complex underlying behavioural distraction. The Mismatch Negativity (MMN) was time-locked with the time-moment of change in each condition (50 and 150), P3a was larger for early change (condition 50) ($F1,11=4.70$, P=0.05) and RON (reorienting negativity) did not differ statistically significantly in latency between conditions ($F(1,11)=3.54$, P=0.09; at Fz).

C9. Common prefrontal activations in a working memory task, a task switching paradigm and the Stroop task

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To investigate prefrontal brain regions involved in cognitive control, 20 subjects performed three tasks in counterbalanced order during one fMRI session: a verbal n-back task, a task switching paradigm and a manual Stroop task. After computing contrasts for the individual tasks, the resulting maps were overlaid to identify prefrontal areas commonly activated by these tasks. Overlapping activations were found at the junction of the inferior frontal sulcus and the precentral sulcus (the inferior frontal junction area, IFJ), in the preSMA extending into medial BA 8, in the middle frontal gyrus bordering the inferior frontal sulcus and in the anterior insula. These results indicate the existence of a network of prefrontal regions mediating cognitive control in working memory tasks, task switching paradigms and the Stroop task. Our results also provide further evidence for our assumption that the IFJ is functionally separable from mid-dorsolateral and mid-ventrolateral prefrontal cortex and subserves a function that we describe as "implementation of task rules".

C10. ERD changes in different frequency bands during the performance of an intelligence task

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In a series of studies Klimesch et al. (1997, 1998, 1999) have shown that distinct cognitive processes are reflected in different frequency bands of the human EEG. While episodic memory demands are predominantly reflected by changes of event-related band power in the theta frequency, semantic processes are represented in the upper alpha and aspects of attention in the lower alpha range. Investigating the influence of intelligence on these frequency bands Neubauer et al. (1995, 1999, 2002) reported differences in the amount and the topographical distribution of alpha ERD percent between high and low intelligent subjects. In the present study EEG was recorded while subjects had to perform a combination of the Ravens Standard and Progressive Matrices. A single trial consisted of a warning signal followed by a set of matrices, presented on a computer monitor. Subjects had to indicate the correct answers by verbal response after pressing a response key. Event-related and longer lasting band power changes have been calculated according to the ERD percent procedure (Pfurtscheller and Aranibar 1977) for IAF-adjusted frequency bands with individually adjusted band widths (Doppelmayr et al. 1998) ranging from 0.5 Hz to 18 Hz. Differences between high an low intelligent subjects will be reported with respect do the complexity of the respective task. For example the results for the upper alpha ERD show several significant main effects for IQ indicating a stronger desynchronization for the higher intelligent subjects.

C11. Attention capture by significant stimuli: semantic analysis follows attention switching

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Evoked potentials (EPs) were recorded from the human scalp to resolve an old controversy in auditory attention research, namely, when the "breakthrough of the unattended" takes place in the human brain. Nine subjects classified visual stimuli occurring after task-irrelevant standard tones (P=0.8) or "novel" environmental sounds (P=0.2) into odd/even categories. After the recordings, subjects scored the novel sounds as to whether they had any particular meaning to them (identifiable) or were perceived just as a short burst of noise (non-identifiable), and performance and EPs were analysed according to this classification. Results yielded identical N1 activity for the two types of novel sounds, indicating that attention switching was similarly triggered after these two types of unexpected sounds. However, there was a larger orienting of attention towards identifiable novels, as indicated both by larger behavioural distraction and novelty-P3. Moreover, this larger orienting of attention was due to the sounds being contingent with the visual stimuli, as no increase in novelty-P3 to identifiable novels was observed in a control condition, in which the sounds occurred non-contingently with the task-relevant visual stimuli. Therefore, the present results show that involuntary orienting of attention towards significant stimuli, such as our own name, occurs only after a transitory attention switch towards the eliciting stimuli.

C12. Endogenous control in task-switching: an investigation with fMRI

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It is widely acknowledged that the prefrontal cortex plays a major role in the coordination of goal-directed behaviour. In doing so, endogenous control is required regarding when and how to initiate a certain task or to switch from one task to another. The aim of the present study was to explicitly investigate the neural substrates of endogenous control in task-switching. Therefore we manipulated the degree of required endogenous control by introducing two different cue types. While "task cues" are explicitly associated with the upcoming task identity, "transition cues" provide information about repeating or switching the task but not about the task identity. The contrast of both cue types revealed significantly stronger activations for the transition cues in the left middle frontal gyrus along the left inferior frontal sulcus and the intraparietal sulcus bilaterally. We argue that this activation pattern reflects the coordination of updating and retrieval processes in order to implement the relevant task set. An additional activation focus was found in the posterior frontomedian wall (BA 8m) revealing the internal control effort while no explicit external cue was directly associated with the upcoming task. Taken together, we suggest that the internal activation of the relevant task set relies on coordination processes within working memory. Finally, we take this as evidence for a higher demand of endogenous control.

C13. Lateralized effect of emotional information processing: a visual evoked potentials study

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Particular qualities of pictures may elicit an emotional response that varies according to valence and arousing properties of the stimuli. Moreover, emotional arousal produced by certain situations can promote memory storage. Our aim was to investigate modifications of visual evoked potentials (VEPs) and assessing their relationship to hemispheric asymmetry during the presentation of standardized emotional pictures; to evaluate affective memory, free recall test was performed. We investigated VEPs to emotional slides selected from the International Affective Picture System according to the valence dimension. VEPs were recorded from Oz, Pz, Fz, P3, P4, and Cz locations. A high level of accordance among the subjects was shown in the evaluation of the emotional valence. The analysis of peak amplitude and latency of P300 revealed a significant valence effect. Compared to pleasant (P) and neutral (N), when unpleasant (U) slides were presented, larger amplitudes were revealed; the higher peak latency in P3 electrode site, compared to P4, showed a stronger activation of the right hemisphere, compared to the left one. The free recall showed the influence of emotional content on memory performance, which was better for U and P stimuli compared to N. Our data indicate a lateralized effect of affective picture processing. Both U and P slides, compared to N, induced higher amplitude of P300 and better recall.

C14. Attentional beta activity during visual processing

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We have previously demonstrated that experimental situations requiring attentive visual behavior are accompanied by enhanced power of local field potentials (LFP) in beta frequency range (16-24 Hz) as recorded in visual thalamic and cortical sites. This beta activity appeared after presentation of preparatory flash stimulus, which signalled the delayed visual cue. Here we analyzed in detail the dynamic of these attention-related signals. The flash preparatory stimulus elevated the LFP power spectrum in wide frequency range from 10 to 30 Hz, with strong peak in the beta range, during 200-1,000 ms period after the stimulus offset. This strong initial burst was followed by secondary oscillatory events at the beta range which appeared repetitively with the average rate of 0.2-0.3 Hz and gradually ceased in amplitude throughout the 10 s interstimuli period. These bursts were most evident in visual cortical area 18, but appeared also in area 17, lateral geniculate nucleus and lateral-posterior pulvinar complex. During relearning with new stimuli the beta activity peak shifted to 2-4 s after the preparatory stimuli offset. The following bursts were less frequent, when the animal reached the 100% level of performance. These bursts were correlated with the typical LFP events representing eye movements. Such correlation suggests that attention bursts of beta activity may be important for gaining the visual processing with each new fixation blink.

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C15. Audiotactile links in the perception of intensity: the importance of temporal and spatial correspondence for cross-modal perceptual enhancement

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This presentation puts forward novel evidence for cross-modal links between audition and touch in the perception of intensity. Stein, London, Wilkinson and Price (1996) found that coincident auditory stimuli enhance visual intensity judgements. They report that the effect was most pronounced at the lowest visual intensities, and was evident regardless of the location of the auditory cue. Our study extends Stein et al.'s findings to the audiotactile domain and also reveals a dependence on spatial coincidence that was not obtained in Stein et al.'s research. In our study 67 Hz buzzes of a duration of 210 ms and of 7 different intensities were presented auditorily *via* one of two different speakers, sometimes accompanied by 67 Hz vibrations of the same duration to the index finger of one hand. Participants were required to attend to these tones and to make a 9-alternative forced choice judgement on the intensity of each tone, while ignoring the concurrent tactile vibrations. In Experiment 1 we found that judgements of tone intensity were significantly higher in the presence than in the absence of a tactile vibration. This was especially so for the lower intensities. Furthermore, and in contrast to Stein et al.'s findings, the enhancement was dependent on the relative spatial locations of tones and vibrations. When tones and vibrations occurred in the same location, enhancements of intensity judgements were larger than when they occurred in different locations. In Experiment 2 additional tactile vibrations were introduced which stimulated the hand for 420 ms before the onset of the tone and again for 420 ms after the offset of the tone. These gap vibrations resulted in tone intensity judgements that were identical to judgements made in the absence of any tactile vibrations. In contrast, concurrent vibrations produced enhancements of intensity judgements as seen in Experiment 1. Thus the enhancement seems to be due to true audiotactile cross-modal interactions based on temporal concurrence, rather than to an alerting function served by the tactile stimulus. Experiment 3 established further evidence for the dependence of the enhancement effect on congruent spatial locations between tones and vibrations by introducing tones originating from a location behind the perceiver's back that was an unlikely source for vibrations to the hand. Results are discussed within a framework proposing audiotactile cross-modal interactions mediated by a mechanism that is both temporally and spatially defined.

C16. Direct behavioral and electrophysiological comparison of two forms of orienting of spatial attention

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Visual spatial attention modulates activity in extrastriate visual cortex, as shown by its effects on the early components (P1 and N1) of the event-related potential (ERP). Observers can orient their visual attention either voluntarily (following an instruction) or automatically (following an abrupt visual stimulus). These two forms of spatial attention were combined in this study to assess their neurophysiological correlates. Observers were required to manually respond to visual stimuli presented in one of three positions along the horizontal meridian either in the left or the right visual field or in a central position. In one condition ("blocked") the stimuli were presented on a given block of trials in one and the same position and therefore were attended to vol-

untarily. In the other condition ("random") the stimuli appeared randomly on any of the seven positions and therefore triggered an automatic attentional shift. We compared reaction time and ERPs elicited by the same physical stimuli under blocked vs. random conditions. Observers responded faster in the former than in the latter conditions. In keeping with this, the amplitude of both the P1 and the N1 components was larger in the blocked than in the random condition. These results show that voluntary orienting of attention exerts its effects at early levels of cortical visual processing.

C17. Simultaneity of EEG power reduction and CNV during expectancy periods

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The contingent negative variation (CNV) and the event-related desynchronisation (ERD) occur during expectancy periods. The possibility of an overall change in EEG oscillatory activity during expectancy periods has not been directly addressed. The present report shows the simultaneity of the contingent negative variation (CNV) and the modulation of the background EEG oscillatory activity by a warning signal. Scalp voltage and Source Current Density (SCD) maps of the CNV showed that the early phase was focused on frontal midline sites. The late phase had two foci, one overlying the primary motor cortex and one over occipital sites. During the same expectancy period, the temporal spectral dynamics (TSE) between 0 and 45 Hz ľ including theta, alpha, beta and gamma ľ and the power spectral density (PSD) decreased with respect to baseline. These results suggest that during expectancy periods there is a (1) CNV component with a topography that suggest the activation of the visual and the motor areas needed for processing the subsequent task, and (2) a generalised decrease in the EEG oscillatory activity. That reduction of the EEG power would facilitate the phasic and oscillatory neural activities triggered by the next target stimulus.

C18. Selective attention to change/no-change in color and shape

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To investigate the selection processing of stimulus change/no-change, event-related brain potentials (ERPs) were recorded while participants selectively attended to change or no-change in the two visual feature dimensions (color and shape). Each trial was consisted of sequentially presented stimulus pair (S1-S2) in which S2 was either (1) the same as S1, (2) different from S1 only in color (i.e., color change), (3) different only in shape (shape change), (4) or different in both color and shape (color and shape change). These 4 types of trial were presented in random order with equal probability, and participants were required to respond only one of these trials. By subtracting the ERPs to the unattended value from those to the attended value in each dimension, two main components were extracted; lateral occipito--temporal negativity initiating at about 150 ms post-stimulus (selection negativity, SN) and parietal positivity peaking at about 400 ms (P300). SN was elicited by the attended value in each dimension, and not affected by values of the other dimension. Whereas, P300 was elicited only by target stimulus (i.e., stimulus having attended values in both dimensions). These results suggest that independent selection of change/no-change in each dimension is followed by the integration processing between two dimensions, and these results are considered to be the electrophysiological evidence of feature specific change detection mechanism.

C19. Involvement of the hippocampus in contextual processing: three in one

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Lesion studies have emphasized the role of the hippocampus in contextual fear conditioning. But a debate still exists about the central role of this structure according to the complexity of contextual processing, ranging from acting as a simple conditioned stimulus to a more complex, occasion-setting like function. The present study investigates in a single task the hippocampal contribution to three different contextual functions. Rats received ibotenate lesions of the whole hippocampus or sham lesions. They were then daily exposed for 13 consecutive days to two different contexts. In the "target" context, an electrical footshock was delivered 90 seconds after the offset of a tone, whereas in the "neutral" context the same tone was presented alone. Hippocampal rats exhibited normal contextual conditioning and discrimination, evaluated by freezing behaviour, but did not modulate their response to the tone according to the context. This confirms that integrity of the hippocampus is not needed for basic contextual processing (conditioning or discrimination), but that it is critical for more complex functions (occasion-setting). This is consistent with the view that only complex, configural processing requires the hippocampus, whereas elemental contextual processing can be relayed by extra-hippocampal structures.

C20. Category-level hierarchy: what comes first in vision?

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Using priming with words, object recognition has been shown to be faster at the basic level when compared to the superordinate level (Jolicoeur 1984, Rosch 1976) Previous experiments (Fabre-Thorpe 2001, Thorpe 1996) using a go – no go task, showed that humans and monkeys can categorise natural scenes very rapidly and accurately at the superordinate level (animal/non-animal). Here, we used the same task to assess whether categorisation speed differs when the decision is taken at the basic level. Two separate basic categories were used: dogs and birds. In both cases, half the distractors were other animals. In the superordinate level control tasks, half the targets belonged to the corresponding basic level. Compared to the superordinate level, accuracy at the basic level was slightly lower for humans (1.5%) and significantly lower for the monkey (11.5%); but surprisingly, in both cases there were substantial increases in reaction time. For humans, we observed a 40-70 ms shift of the RT histogram towards longer latencies (bird: mean RT 433 vs. 394 ms; dog: 452 vs. 383 ms) when compared to the animal task. For the monkey the shift was 30 ms. The results imply that, for both humans and monkeys, the category level first accessed through vision is at the most abstract level (i.e., the superordinate level) using a coarse to fine analysis. The generally accepted view that basic level information is extracted first may reflect the use of lexical rather than visual representations in earlier studies.

C21. Electrical brain activity following confirmed or unconfirmed predicted outcomes

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Meaningful behavior requires experience, anticipation and the integration of outcomes. We studied the temporal dynamics when experience-based anticipations were confirmed or negated. High-density event-related potentials were recorded from 11 healthy subjects while they had to predict behind which of two rectangles an object drawing was hidden. The electrical scalp topography differed after confirmed and negated anticipations between 190-300 ms and 380-600 ms. Distributed linear inverse solutions located the electrical scalp configuration after negated anticipations during the early time period in the left prefrontal lobe and the electric scalp configuration after confirmed anticipations during the late time period bilaterally in temporo-occipital areas. The early specific topography after negated anticipations might indicate that early "automatic" frontal brain processes are at work to actively deactivate currently irrelevant anticipations; and the absence of a late temporo-occipital topography after negated anticipations might suggest an influence of early decision processes upon subsequent "conscious" stimulus treatment.

C22. Monkey prefrontal cortex neuronal activity correlates with categorical decisions

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The prefrontal cortex is known to play a role in decision making or response selection. To study this processes we used a discrimination task that requires memorizing the orientation of a line (reference) followed by a comparison of the remembered orientation with the orientation of another line. The monkey has to decide if the test is oriented to one side or another of the reference, and to signal the decision by pressing one of two buttons (Vazquez et al. 2000) We recorded the extracellular unitary activity in the prefrontal cortex, in front of the sulcus arcuatus in *Macaca mulatta* monkeys. Eye movements were recorded with the magnetic eye search coil technique. Sixty two neurons change their activity during the presentation of the test stimulus. The firing rate is higher and slope steeper depending on the decision the monkey makes – method of logistic binary regression (Wald=189.199; $P<0.001$). Furthermore, the firing rate is higher and slope steeper when the monkey has to decide the orientation of test stimuli closer to the reference; i.e., those more difficult. When the decision is incorrect the temporal evolution of the firing rate is different from when the decisions are correct. These changes might reflect categorical decisions based on sensory information. PB99-002 MCYT to C.A., BFM2002-03213 MCYT to C.C.S., V.N. and S.F.O. - FPI-MCYT.

C23. Does handedness recognition depend on body coordinates?

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The aim of this work is to investigate how handedness (the left or right nature of a hand) is recognized, that is, whether it is recognized *per se* or it depends on a matching between the observer body coordinates and the ones inferred from the hand. In Experiment 1 (E1), we presented a left and a right hand, with a colored circle in the middle, by both back and palm views in the center of the screen. The back view seemed to belong to the subjects and the palm view to somebody in front of the subjects (Ss). Ss were asked to response depending on the colors with two keys (a modified Simon Paradigm). According to the correspondence between handedness and response hand, a Simon effect (SE) emerged for back views and a reverse SE for palm views. This suggests that the observer can code the hypothetical owner of the hand and can recognize handedness based on such information. In E2, upside-down back hands were presented in the same way as in E1. These seemed to belong to somebody facing the observer. We observed a reversed SE, that seemed to be related to the body centered representation of the presented hand. In E3, the same stimuli as in E1 were presented on the right or the left side of the screen. The results revealed a SE for position, a SE for to handedness, and no significant interaction between position and handedness. This suggests that the effect of spatial correspondence and effect of handedness are additive and that they are computed by different mechanisms.

C24. Evidence for entorhinal and parietal cortices involvement in path integration in the rat

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Rodents are able to rely on self-motion cues and return to a reference place by path integration. In the present study, we examined the respective roles of the parietal and entorhinal cortices in path integration. Rats with either parietal cortex or entorhinal cortex lesions were trained in a homing task on a circular platform containing food cups and surrounded by curtains: they had to leave their nest, find a hidden piece of food and carry it back directly to the nest. Four successive phases were conducted. In phase 1, rats were trained in the procedural aspects of the task with each cup containing a food pellet. In phase 2 and 3, there was only one food pellet available, always located in the central cup or placed in a different cup on each trial, respectively. In phase 4, rats were tested in darkness with one food pellet placed in a randomly chosen cup on each trials. The results show that, in phase 2 and 3, although all groups had similar outward paths, parietal- and entorhinal-lesioned rats exhibited more inaccurate returns to the nest than control rats. In phase 4, entorhinal--lesioned rats had poorer path integration performance than both parietal and control rats. These results suggest that both the parietal and the entorhinal cortices are part of a neural network mediating path integration.

C25. Transient brain dynamic patterns, a nonlinear dynamical systems approach to neural function

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Brain activity can be conceptualised as a set of spatiotemporal patterns of neuronal activity, reflected as brain rhythms or oscillations in electrophysiological recordings. We propose that the investigation of the sources that generate and maintain these dynamic patterns, as well as the general laws that describe and capture their essential properties, will provide insight into brain cognitive processes. Building on the concept that large-scale transient dynamical patterns may be captured in simple mathematical models that explain essential phenomena of the complex dynamics, we attempt to determine dynamical regimes in brain activity using nonlinear dynamical systems theory. As an example of our approach, we present the study of dynamical bifurcations and specific dynamical regimes that describe the pathological neuronal synchronization patterns in epileptic phenomena. Considering the information derived from the mathematical description, it is feasible to use the system's own dynamics to perturb the activity of neuronal networks, at least *in vitro*, by stabilizing possible unstable steady states that represent desired patterns of activity. Hence, we conclude that the characterisation of the collective mechanisms involved in the transition between neuronal rhythms, in terms of global mathematical models, may help to map the substrates of cognitive function at different levels of description, from large ensembles to microcircuits.

C26. Double dissociations of the core and shell subterritories of the nucleus accumbens in selective attention and behavioural inhibition in rats

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The nucleus accumbens can be subdivided into "core", "medial-shell", and "rostral-shell" subterritories on anatomical grounds. The functional significance of this distinction has been an interest of our laboratory. In a continual effort towards this characterization, we examined the effects of bilaterally NMDA-induced cytotoxic lesions restricted to one of the three subterritories on selective attention and behavioural inhibition (as opposed to impulsive responding). Selective lesions of the medial-shell, but not of the core or the rostral-shell, disrupted a form of acquired inattention – latent inhibition, as evaluated on a two-way active avoidance paradigm. Core, but not medial-shell, lesions impaired performance on a DRL (differential reinforcement for low rates of response) task requiring a minimal delay of 18 s between successive lever-presses to gain reward. Rostral-shell lesions affected behaviour in neither tests. The double dissociations demonstrated here strength the view of a functional segregation within the nucleus accumbens delineated along distinct anatomical subregions. This is further discussed with respect to the differential input patterns from the hippocampal and parahippocampal regions to the distinct accumbens subterritories.

C27. Executive control and response conflict: an rTMS study on sequence-dependent modulations of stimulus-response correspondence effects

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Usually, responses are faster and less error-prone in case stimulus (S) and response (R) features correspond to one another. Such S-R correspondence (SRC) effects are accounted for by cognitive dual route models of response preparation. Recent findings point to sequential modulations of SRC effects, that is, after a non-corresponding predecessor the SRC effect is absent, it only shows up after a corresponding predecessor. We account for these sequential dependencies by executive control that suppresses direct route priming after a response conflict. To test this, repetitive transcranial stimulation (rTMS) was applied to the left and right dorsolateral prefrontal cortex (DLPFC), known to be involved in executive control of response conflicts. Moreover, we tested the role of the dorsal premotor cortex (PMd) in executive control. Thirdly, rTMS was applied to the caudal part of the intraparietal sulcus (cIPS), to interfere with visual processing. Our data show that with right DLPFC stimulation the SRC effect was present after both a corresponding and a non-corresponding predecessor. In contrast, stimulating the left DLPFC did not alter the SRC effect. We conclude that executive control of response conflict located in the right DLPFC are crucially involved in suppression of direct route priming. Missing effects of PMd and cIPS stimulation will be discussed.

C28. Newly-hatched naive chicks (*Gallus gallus*) prefer biological motion patterns

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In human subjects, it is difficult to test if sensitivity to biological motion has, in vertebrates, an innate base (Johansson 1973). We investigated spontaneous preferences for biological vs. non biological motion displays in overall over 500 few-hour-old, dark-hatched chicks. It is known that chicks can discriminate between point light displays depicting a walking hen or the movement of a rigid object (Regolin et al. 2000). Chicks, placed in a runway in between two computer-presented motion displays, underwent a 6-min simultaneous free-choice preference test, observing which animation the chick preferentially approached. Stimuli (all made of 13 point-lights) depicted either a walking hen or a scrambled hen ("biological" motion patterns); and a rotating solid object or a random dot motion ("non biological" motion patterns). Results showed that chicks approach preferentially the biological motion displays, they did not show any preference between the walking hen and its scrambled version, which were both preferred to the solid motion and to the random dot motion. In conclusion, naive chicks seem to exhibit a spontaneous preference for biological motion displays, such preference seems to rely on local rather than global motion cues. This is to the best of our knowledge the very first evidence of an innate preference for biological motion patterns in a vertebrate species.

C29. Event-related potentials during response inhibition in normal absentmindedness and traumatic brain injury

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The ability to inhibit the execution of a motor behaviour in response to a stimulus is termed response inhibition (RI). This capacity reflects our ability to exert dynamic control over our actions, seems to be closely related to attentional performance and may be mediated by a cortical network involving right prefrontal and parietal cortices, as well as the anterior cingulate region. Unlike imaging, event-related brain potentials (ERPs) offer a means through which the temporal dynamics of regional brain activation may be investigated. Here we report two experiments in which ERPs were recorded from humans while they performed a go – no go response inhibition task. In Experiment 1, we show that the success of an attempt to inhibit may depend on the timely activation of common brain areas, rather than the activation of different areas. ERPs also discriminated levels of absentmindedness in this normal group. Experiment 2 reports dramatically altered ERP waveforms for a group of traumatic brain injured (TBI) participants compared to normal controls during RI. These waveform abnormalities were accompanied by poorer task performance among the TBIs. These results compliment to imaging literature on RI, and further our understanding of the temporal dynamic involved in successful RI performance.

C30. Gender differences in emotional prosody

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Conventional wisdom suggests that women are more "emotional" than men. Does this mean that women express their emotions more fully than men? Or, do women experience more or stronger emotion than men? Substantial body of research has demonstrated that women are able to better understand emotional expression from face and gestures. Little is known whether similar sex differences exist in the ability to understand emotional expression in language (prosody). Prosodic cues communicate to the listener, among others, the affective disposition of the speaker (e.g., whether the speaker is angry or happy). There is now a growing number of studies, which suggests a dominant role of the right hemisphere in decoding affective prosody. The present study addressed two questions. First, we examined whether women were better than men in comprehension of emotional cues in voice. Second, we studied if lesions to different parts of the right hemisphere may differentially affect the prosody processing. Fifty two patients with damage to frontal, temporo-parietal or subcortical parts of the right hemisphere (RH) and 26 normal controls (C) made identification of emotions expressed by intonation in natural and pseudo sentences. The results showed that RH damaged subjects had decreased comprehension of emotional prosody. We also found that frontal RH damaged women had more impaired comprehension than frontal RH damaged men. However, subcortical (basalganglia) lesions led to stronger impairment in men. This study revealed sex differences in brain organization of prosodic functions. The results provide further evidence for the notions that women are more sensitive to emotional signals than are men.

C31. Effect of parietal cortex lesions on hippocampal place cell firing

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Evidence indicates that the hippocampus and the parietal cortex both contribute to spatial memory. However, the nature of their interaction remains unknown. To address this issue, we investigated the effects of parietal cortex lesions on hippocampal place cell firing in rats. Following cortical lesions and electrode implantation, place cells were recorded as the rats performed a pellet-chasing task in a circular arena containing 3 cue-objects. Five successive sessions were conducted to examine: 1) place cell firing under stable conditions (S1 and S2); 2) the control exerted by the cue-objects (rotated 90°) over place fields (S3); 3) the stability of place fields after removal of the cue-objects (S4). A last session (S5) similar to S1 was made. The results show that place fields in parietal-lesioned rats remained stable in constant conditions and were usually controlled by the objects, i.e., they rotated 90°. However, when the objects were removed from the arena, place fields were found to return to their initial position (as during S1) whereas they remained stable or disappeared in control rats, suggesting a switch from an object-based frame of reference to a room-based frame of reference. This hypothesis was confirmed by a second experiment. Overall, these results demonstrate that the parietal cortex cooperates with the hippocampus for spatial cognition and suggest that this area is involved in the processing of proximal cues.

C32. Preferential left and right eye-use in fish: concordance between different methods

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We measured the time spent in monocular viewing during inspection of their own mirror images in females of three species of fishes (*Xenotoca eiseni*, *Gambusia holbrooki* and *Xenopoecilus sarasinorum*), using a rectangular-shaped tank in which animals could observe their own reflection in two mirrors positioned along the major walls, and in females of five species of fishes (*Xenotoca eiseni, Gambusia holbrooki, Xenopoecilus sarasinorum, Danio rerio* and *Gnatonemus petersii*), using a quasi-circular tank in which the animals could rotate clockwise or anticlockwise and observe their own reflection in a mirror positioned along the outer wall. Results revealed a consistent left-eye preference during initial sustained fixation in all species irrespective of the apparatus, though in the quasi-circular tank fish showed more variability of response. The asymmetry was apparent during the first 5 minutes of observation and tended to fade thereafter, probably as a result of habituation. These findings add to current evidence for a quite invariant pattern in the direction of lateralization in similar tasks in a variety of vertebrate species, with a preferential involvement of structures located to the right side of the brain in response to the viewing of images of conspecifics.

C33. Cortical modulation of thalamic local field potentials evoked by the vibrissa stimulation in the rat

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It is widely agreed that the projection from deep layers of the cerebral cortex to the thalamus is crucial for thalamic information processing. Cortico-thalamo-cortical loop has been proposed to be involved in the mechanisms underlying phenomena of habituation, sensitization and attention. In order to identify the dynamics within the loop we studied cortical modulation of the local field potentials evoked (EP) in thalamic somatosensory nuclei (POm and VPM) by vibrissa stimulation in rats anaesthetized with urethane. We manipulated a level of the barrel cortex activation by means of electrical stimulation of the deep cortical layers and surface cooling or xylocaine (Xyl) application. The shortest latency negative wave of thalamic EP was insensitive to cortical manipulations. The longer latency components, followed by oscillations in the alpha frequency range, were enhanced when the moderate inactivation disinhibited the deep cortical layers, and were attenuated during cortical blockade. The stimulation of the cortex produced thalamic EP that matched those long latency components of vibrissa-evoked response that were modulated by surface cooling and Xyl. All effects, especially putative inhibitory ones, were more pronounced in VPM than in POm. We conclude that the earliest thalamic EP component represents peripheral input and the later ones correspond to the activity of cortico-thalamic and cortico-reticulo-thalamic projections.

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C34. Song learning-related immediate early gene expression restricted to lateral parts of the caudomedial neostriatum (NCM) in zebra finch males

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Songbirds, such as zebra finches, learn their song from a tutor when they are young. Forebrain nuclei in the "song system" are important for the acquisition and production of song. Brain regions outside the song system (NCM and caudo-medial hyperstriatum ventrale, CMHV) show increased expression of the immediate early gene ZENK when a zebra finch male is exposed to song. We have shown previously that the strength of the ZENK response in the NCM to tutor song is significantly positively correlated with the strength of song learning (i.e., the number of copied elements). Here, we exposed live-tutored adult zebra finch males to either taped tutor song, their own song, or unfamiliar song. Immunocytochemical analysis was performed on the expression of the Zenk protein. As in our previous studies, we found a significant positive correlation between Zenk expression in the NCM (but not in CMHV or hippocampus) when males were exposed to tutor song, but not when they were exposed to their own song, or to unfamiliar song. The correlation holds for lateral aspects of the NCM (0.7-1 mm from the midline), not for medial aspects (0.25-0.4 mm). These results show that the correlation between ZENK expression and strength of song learning is specific to the lateral part of the NCM, and that it is not a result of non-specific arousal or attention effects.

C35. Power and coherence of spectrum EEG mapping during perfection of stability of posture by visual feedback

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The actual problem of neuroscience is how nervous system allows individuals to adapt to stimulus spatial orientation. The present study revealed power and coherence EEG mapping during motor learning perfection of standing posture. The motor task was to train the maintenance of posture with special computer game by visual feed-back on the stabiloanalyzer. EEG (0.5-120 Hz) were recorded from 15 cortical areas according to 10-20 system. EMG (0.5-1,000 Hz) of m. soleus was used for indication of movement. Power (Asum), maximum frequency (Fmax), interhemispheric coherence (ICoh) of spectrum EEG and coherence (Coh) EEG-EMG were analyzed by program "Conan" in ranges 5-7, 7-9, 9-12, 12-18, 18-29, 30-40, 40-50, 50-60 Hz. The comparison of Z-estimates topographic maps of spectrum EEG before and after learning revealed that level of brain activation was significantly increased. High differences of Asum EEG were observed mainly in 7-12 Hz in the right primary motor area, in 12-18 Hz -in both parietal and occipital lobes, in 30-60 Hz – in premotor, parietal areas and right temporal lobe. Fmax EEG increased predominantly in 5-12 Hz in frontal lobes, in 30-60 Hz – in premotor and primary motor areas. Discriminant analysis showed that ICoh significantly changed between somatosensory and temporal areas after learning. Effect of motor learning on Coh EMG-EEG was detected in the both primary motor areas, right somatosensory area, frontal, parietal, and occipital lobes in the left hemisphere cortex.

C36. Of rubber hands and rubber fingers

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We report three experiments on the Rubber Hand Illusion (RHI). Watching a rubber hand being stroked synchronously with one's own unseen hand causes the rubber hand to be attributed to one's own body, to "feel like it's my hand". Attribution can be measured behaviorally as a drift of the perceived position of one's own stroked hand towards the rubber hand. In experiment 1, we investigated whether the attribution would occur if the identity of the seen and felt hand did not match. Participants were stroked on their left hand (knuckle of middle finger), but they watched a left or a right rubber hand. The results suggest that there is a local perceptual process of attribution, since the drifts were significantly bigger only for the stimulated finger. Furthermore, felt and seen identities of the hands should match in order for the RHI to be induced. To further investigate the local effect of attribution, we performed 2 experiments. In experiment 2, only one finger was stimulated per block (index/little), and subjects had to judge the position of both fingers in separate blocks. In experiment 3, both fingers were stimulated in each block. The results showed that only the perceived position of the synchronously stimulated finger drifted significantly. Taken together, the results suggest that at the level of the process underlying the built-up of the illusion, the mechanism might be local, whereas at the level of the effect, the illusion is modulated by top-down influences, possibly originating from body-schema representations.

C37. Integration of disparity and texture gradient signals for the representation of 3D surface orientation in parietal area CIP

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David Marr postulated that the detection of surface orientation is an important intermediate stage towards the representation of three-dimensional (3D) structure of objects, which is the main goal of visual processing. Recently we found a group of neurons that respond selectively to a 3D orientation of a flat surface in the caudal part of the lateral bank of intraparietal sulcus (area CIP). We examined the responses of these neurons with i) random-dot stereograms in which the surface orientation was defined only by disparity gradients and ii) texture patterns in which the surface orientation was defined only by texture gradients. We found three types of surface orientation selective neurons: those which were sensitive to disparity gradients alone ("D neurons"), those which were sensitive to texture gradients alone ("T neurons"), and those which were sensitive to both disparity and texture gradients ("DT neurons"). Among three types, the most prominent in number was DT neurons. In DT neurons, preferred orientation was the same between the surface orientation defined by disparity gradients and that defined by texture gradients. The result suggests that different kinds of gradient signals are integrated in CIP in order to construct a general representation of 3D surface orientation which is independent from specific depth cues.

C38. Top-down and bottom-up processing of binocular information

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The ability of the brain to process positional differences in the retinal images falling on the retinas of the two eyes (retinal disparity) forms the basis for binocular vision and stereopsis. A crucial stage in processing binocular visual information is to correlate the two images using disparity and motion information. The initial steps of binocular information processing takes place in primary visual cortex, but further processing leading to the perception of depth of our 3D world that is invariant for eye movements and self-motion occurs in extrastriate areas. Although monocular or eye-of-origin information is irrelevant for our perception of the binocular visual world, it is crucial for maintaining binocular vision. Movements of the two eyes can be different, as both amplitude and direction of the retinal image motion in the two eyes can vary independently. These movements jeopardise the correlation between the two retinal images and cause false disparity signals. Appropriate compensatory eye movements that can minimize independent motion of the two eyes, can only be generated when eye-of-origin information about stimulus motion is present. To investigate which mechanisms the human brain employs to solve this dual task, we used visual stimuli that were presented under dichoptic viewing conditions The stimuli consisted of two random dot patterns (1,000 dots each) forming correlated and anti-correlated stereograms, which oscillated in orthogonal directions. Eye movements were recorded using the scleral search coil technique. Our data show that humans use eye-of-origin information and are capable to generate independent eye movements. We suggest that the possibility to generate independent movements of the two eyes depends on bottom-up top binocular information from V1 to extra-striate areas and back again.

C39. Language experience determines functional organization of prefrontal language areas

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A current issue in multilingualism research is the significance of age of language acquisition for the cortical language representation. In our study, we provide evidence for the part of the prefrontal language network in the context of early language acquisition in multilingual subjects. We confirm a critical early period in which exposure to one or to two languages determines permanently the participation of prefrontal areas in language processing: subjects which were exposed to two languages early in life show an increased response of the prefrontal language related network during processing of an early acquired language. In the same subjects, this activation is not observable for later acquired languages. This different activation of different acquired languages in a group with early exposure to two languages is attributable to the specialization of the prefrontal cortex. As to include learning circumstances, the outstanding function of this area in cognitive control is established: thus, the prefrontal cortex is known to have a rule dependent activity and needs the "knowledge about a given situation to select the appropriate goal". In our contribution we have found that this holds true for language processing as well.

C40. Association between sleep and cognitive disturbances in aging: involvement of the PPT

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Objectives: Comorbidity between sleep disorders – which are prevalent in the elderly – and cognitive disorders has been observed. However, little is known about the etiology of this relationship. Using aged rodents, our objectives were to 1) demonstrate comorbidity between the deficits in sleep circadian rhythms and spatial memory, 2) study the link between these disorders and 3) evaluate the implication of cholinergic (ACh) neurons of the pedunculopontine (PPT) nucleus – which is a key regulator of the sleep/wake rhythm – in the severity of these deficits. Methods: Spatial memory of male rats (22-24 months) was tested in the Morris water maze. Circadian rhythm of sleep was estimated by locomotor activity and polygraphic recordings (EEG/EMG). Morphology of PPT ACh neurons was studied by optical microscopy, using ChAT immunohistochemistry. Results: In these aged animals, a sub-population presented: 1) a deficit of spatial memory associated with a reduction in the amplitude of the circadian rhythm of sleep, 2) a fragmentation of slow waves sleep and 3) a change in the structure of the PPT with a decrease in the number of large neurons (150-400 μm) and an increase in the number of small ones (0-100 μm). Conclusion: We demonstrate in aged rats that the severity of sleep disorders is correlated with the severity of cognitive disorders and that these alterations are also correlated with morphological changes of the PPT ACh neurons. Thus, the PPT seems to be crucial in the genesis of these disorders.

C41. Individual vulnerability in the effects of noise on sleep and their consequences on cognitive processes

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Noise disturbs human sleep, a factor that may lead to impairment of cognitive performances. Little is known concerning the consequences of long-term exposure to noise on sleep structure and their subsequent effects on cognitive processes. Furthermore, the individual vulnerability to these effects has never been considered. The effects of noise on sleep were evaluated using electroencephalographic recordings in rats. In a separate experiment, the after-effect of 9 days of noise was evaluated on cognitive processes using a spatial memory test (place recognition test). Emotional locomotor reactivity to novelty was evaluated using a circular corridor and whereby rats were divided into high or low responders (HR or LR). Noise induces a decrease of both slow wave sleep (D1 $P<0.05$; D6 to D9 $P<0.05$) and paradoxical sleep (all the days except D2). Moreover, rats showed impairments in long term memory processes as shown by worsened scores in the place recognition task. Finally, HR rats accumulated a more sleep debt than LR rats during the 9 days and there was a negative correlation between memory performances and locomotor response to novelty. All these results tend toward to the hypothesis that long-term exposure to noise is deleterious to sleep and consequently to cognitive processes and that these effects could be modulated by the emotional profile of the individuals.

C42. Individual differences in the information processing speed and brain organization in preschool children

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The aim of this study was to examine a possible relation between the speed of information processing and individual differences in brain organization in preschool children. The speed of information processing was measured in 34 children at 6-7 years with the computerized technique, developed by the author (Kiselev S., Lupandin V. Computerized Technique for investigation of temporal Characteristics of Sensorimotor Reactions in Preschool and First-Grade Schoolchildren (2001) Journal of high nervous activity Vol. 2). The individual differences in brain organization were investigated with the neuropsychological technique for children, developed by T.V. Ahutina in Moscow State University. This technique allows to establish the primary development of left- or right-hemisphere function in children. We used the U test Mann-Whitney. Children with the primary development of right-hemisphere and left-hemisphere function had the differences in level of performance of some sensorimotor reactions. In particularly, the "right-hemisphere" children were more successful in performance of the differential reactions on stimulus, which differed only on orientation. At the same time the "left-hemisphere" children were more successful in performance of the differential reactions on stimulus, which differed only on color. We have not found out the distinctions between these groups concerning of simple reaction.

C43. Hemispheric laterality and dissociation in normal subjects: changes in emotional processing

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Some evidence indicates that dissociative patients exhibit changes in patterns of hemispheric laterality suggesting that disturbances in laterality mechanisms are involved in pathological dissociation. However, the general relationship between dissociation and hemispheric laterality in normals has not yet been studied. We addressed this subject by comparing laterality patterns in normal high dissociators with those of normal low dissociators, evaluated by the Dissociative Experiences Scale (Bernstein and Putnam 1986), in a dichotic listening task on discrimination of both verbal and emotional stimuli. Low dissociators exhibited the expected right ear advantage (REA effect) and left ear advantage (LEA effect) for verbal and emotional stimuli, respectively. High dissociators exhibited atypical laterality patterns, characterized by: a) an attenuated REA effect for verbal processing; and b) no significant differences in performance between left and right hemispheres for emotional processing (no LEA effect). These results support the hypothesis that, within the range of normality, dissociative tendencies are related to changes in patterns of hemispheric laterality.

C44. Preferential eye use during mirror image inspection: a simple behavioural test to measure lateralization at different stages of development in zebrafish

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An aspect of lateralization in non-mammal species is the presence of systematic preferences in eye use. This is particularly clear in birds, fishes and reptiles, which have laterally placed eyes and complete decussation at the optic chiasma. A simple behavioural test, the mirror test, has been devised to measure eye preferences during inspection of their own mirror images. Fish are placed in a rectangular tank with two mirrors positioned along the major walls and the time spent in monocular viewing is measured. Recently this test has been employed to measure laterality in the adults of several teleost species and with some modification in the tadpoles of five anuran Amphibians. We adapted the mirror test to allow measurement of laterality in zebrafish at different stages of development: 15, 30, 60 days old larvae in two different zebrafish strains (GT and TL). Previously, using adult fish of both strains, we found a significant left-eye preference in GT and right-eye preference in TL. The results obtained with the larvae show the same preferential differences in eye use at all three different stages of development. Furthermore, because we tested some individuals three times with the same experimental set-up, our results also provide a measure of mirror test reliability.

D1. Skill learning and long term retrieval in multiple sclerosis

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Many studies have demonstrated a poor performance on cognitively demanding memory tasks, but not in less demanding-automatic memory tasks, in subjects with Multiple Sclerosis (MS). Recently, some studies have found evidence of impairment on motor implicit learning performance in MS patients using the non-dominant hand and on perceptual implicit memory in primary progressive MS patients. However, different types of skill learning have not been fully examined. The current study examines the performance in 63 MS patients and 28 healthy controls (C) on explicit learning and cognitive and sensorimotor skill learning tasks, as well as on long term retrieval. Explicit learning and long term retrieval was evaluated using the Selective Reminding Test. Cognitive and sensorimotor skill learning were examined by 5 consecutive trials of the Tower of Hanoi, Mirror Star and Porteus Maze Test. Long term retrieval was assessed by the execution of the tasks one week later. MS patients exhibited normal skill learning on the three tasks and deficits on explicit learning and long term retrieval as well as impairment on the long term retrieval of the Tower of Hanoi compared with C. These results indicate that long term retrieval of cognitive skill is impaired in MS patients and that cognitive skills can be dissociated from sensorimotor skills.

D2. Effects of right or left substantia nigra pars compacta lesion on the working memory and motor behavior of rats

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Many cognitive deficits, including spatial working memory deficits are reported to affect Parkinson's disease (PD) patients. Rats with bilateral lesion of the substantia nigra pars compacta (SNpc) proved to be a good model of this PD-related deficit when tested in the working memory version of the Morris Water Maze. The objective of the present study was to test if unilateral lesion of the SNpc is sufficient to induce working memory deficits in rats and if this deficit is more prominent for the right or left SNpc. Adult male Wistar rats received a unilateral left (UL) or right (UR) or a bilateral (BIL) injection of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) (1 mmol/side) into the SNc. Three weeks after surgery the BIL group presented the worst memory scores and increased locomotor scores in the open field test compared to the other groups. The UL and UR groups presented less severe but significant working memory impairment compared to the sham-operated group. When challenged with 1 mg/kg apomorphine, both the UR and UL groups presented a significantly increased turning behaviour with rotations ipsilateral to the SNpc lesion side compared to the BIL and sham-operated groups. The results suggest that unilateral lesion of the SNpc causes higher motor disabilities while an additive effect is observed for the working memory deficits in relation to the right and left SNpc lesion.

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D3. Visual and spatial working memory in patients with dementia of Alzheimer type

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Alzheimer's patients (AD) show impaired performance in short-term memory tasks such as verbal span (Orsini et al.1988), Brown-Peterson paradigm (Sullivan et al.1986) and in visuo-spatial working memory tasks (Grossi et al. 1993). There are very few studies on visual and spatial recall. We evaluated the performances of two groups of 11 and 14 AD patients and two groups of age-matched normal controls (NC) on a serial recall task for sequences of similar and dissimilar abstract pictures and for spatial positions at 0, 5, 10 and 20 s delay. A preliminary visual and spatial span tasks were used to assess the general capacity of short-term memory and to decide the length of the sequences to be used for the single individual in the experimental task. AD patients showed reduced visual and spatial spans. AD and NCs performed similarly at 0 s delay in the dissimilar abstract pictures and in spatial positions recall. AD showed greater forgetting in visual but not in spatial recall. In the visual task, AD patients showed greater performance decrement in the recall of similar respect to dissimilar abstract pictures (P<001). In conclusion, AD seems to have reduced buffer capacities for both visual and spatial data. In visual recall there is an additional difficulty at encoding perceptually similar stimuli and at rehearsing the stored items for preventing decay. In spatial recall AD patients seems to have a normal rehearsal processes.

D4. Visual and olfactory place learning deficit in rats with low glutathione during development: a behaviour model with relevance to schizophrenia

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Glutathione (GSH) has been shown to be decreased in prefrontal cortex and cerebrospinal fluid of patients with schizophrenia. Because GSH is an important endogenous anti-oxidant that protects cell from damage, its diminution could lead to synaptic changes resulting in abnormal neuronal connectivity. In our animal model, rats were treated with L-buthionine-(S,-R)-sulfoximine (BSO), an inhibitor of GSH synthesis, from P5-P16. Cognitive function was evaluated in the homing board task (Rossier et al. 2003) at age 260–400 days. Cognitive behaviour was assessed by the animal's capacity to perform visual and olfactory place learning. We found that in BSO-treated animals, place learning was impaired with only distant visual cues. Place learning was not impaired in condition where only one olfactory cue was present (trained arena). However, the performance was impaired in BSO-treated animals on the same homing table when five new different controlled olfactory cues (one olfactory for each arena) were used. Our data suggests that these deficits are not attributable to sensory impairments but rather problems arising at the level of integration. The olfactory deficit observed in the proposed animal model is consistent with the reported olfactory recognition impairment in schizophrenia.

D5. Deficits in learning-dependent cortical plasticity and sensory discrimination learning in presymptomatic Huntington's disease mice

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Huntington's disease (HD) is an autosomal dominant genetically transmitted neurodegenerative disorder, characterized by cognitive and motor disorders. The neuropathology of HD involves selective neuronal cell death in several brain regions, including both corpus striatum and cerebral cortex. Although changes in synaptic plasticity have been described in hippocampus and striatum of HD transgenic mice, as well as related deficits in several forms of learning and memory, no studies have considered cortical synaptic plasticity and cortex-dependent learning. We investigated the effect of classical conditioning on the cortical representation of single vibrissae in presymptomatic R6/1 HD mice, using 2-deoxyglucose (2DG) brain mapping. The training consisted of row B of vibrissae stimulation paired with sweet-taste reward. We also studied performance in a sensory discrimination task. Presymptomatic HD mice were trained to distinguish between two discriminanda (two different metal gratings) with their vibrissae and to indicate their choice by jumping from the start platform to one of two reward platforms. R6/1 HD transgenic mice showed deficits in learning-dependent plasticity of sensory cortex as well as severe impairment in the discrimination learning that is dependent on the cortex.

D6. Learning and memory effects following bilateral intrahippocampal injections of aggregated non-beta amyloid component (NAC 61-95)

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In the current study, male Sprague-Dawley rats were trained in two-lever operant test chambers under an alternating lever cyclic ratio (ALCR) schedule of reinforcement. When responding showed no trends, subjects were divided into three groups. Two groups were injected bilaterally with 5 microliters of aggregated non-beta amyloid component (NAC 61-95), which is derived from alpha-synuclein precursor protein, into the CA3 area of the dorsal hippocampus; the other groups were injected bilaterally with 5 microliters of sterile water. Subgroups were treated twice daily either 0.1 ml (40 mg/kg) ibuprofen orally or an equivalent volume of 10% sucrose vehicle. Bilateral injection of aggregated NAC 61- 95 produced a decline in behavioural performance on two parameters of the ALCR schedule. The chronic administration of ibuprofen alleviated behavioural deficits following aggregated NAC 61-95 injections. Aggregated NAC 61-95 induced reactive astrocytes and microglia. These results suggest that induced inflammatory processes may play a role in Parkinson's disease dementia and that ibuprofen may have a protective effect.

D7. Long-term estrogn replacement in ovariectomized rats failed to protect the substantia nigra pars compacta from lesion induced by 6-hydroxydopamine

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Parkinson's disease (DP) results from the degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNpc), affecting more males than females. Possibly the high estrogen levels observed in females can protect dopaminergic cells from degeneration. The aim of the present investigation was to study the effect of estrogen replacement on the survival of dopaminergic mesencephalic cells insulted with 6-hydroxydopamine (6-OHDA) in ovariectomized rats. The ovaries of adult female Wistar rats were bilaterally removed and 400 mg of 17-b-estradiol or oil capsules were implanted subcutaneously. Plasma estradiol concentration was monitored from 10 to 52 days after capsule implantation. Intranigral infusion of 6 mg/side 6-OHDA in ovariectomized female rats caused a significant decrease in the optical density of tyrosine hydroxylase (TH)-immunostaining in the SNpc. However, 52 days of estrogen replacement did not prevent TH-immunoreactive cell loss in the SNpc of 6-OHDA-lesioned rats. This result suggests that the neuroprotective effect of dopaminergic mesencephalic cells is not observed with long-term estrogen replacement.

D8. Hypoactivation in parahippocampal areas during an "encoding" task reflects general memory disturbances: a study comparing AD and MCI patients

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Previous studies have revealed that patients with Alzheimer's disease (AD) show a reduced activation in some parahippocampal areas during visual encoding/ retrieval tasks. To evaluate if this fact is a characteristic of AD or rather reflects a more general memory disturbance, we have investigated using fMRI brain areas involved in encoding in patients with AD or Mild Cognitive Impairment (MCI). Four patients with AD, 4 with MCI and 5 aged matched healthy subjects participated in the present study. All three groups were instructed to carefully look at a series of pictures which recognition was assessed later. In agreement with previous research, a bilateral activation of the parahippocampal, fusiform and lingual gyri was observed during the encoding phase in the control group. On the other hand, when comparing the different groups, both AD and MCI patients presented a decreased activation of the left parahippocampal gyrus and a bilateral decrease in the fusiform and lingual gyrus. When comparing both patient groups, the MCI group showed a lower activation in the temporo-occipital cortex than the AD group. The present study suggests that the hypoactivation in parahippocampal areas is not an exclusive feature of AD patients but a more general index of memory disturbances. In this regard, the differences in the temporo-occipital cortex activation could be a more specific diagnostic strategy to distinguish between MCI and AD patients.

D9. Spatial neglect: offset from normal resting position

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The characteristic deficit of patients with spatial neglect is a bias of their exploratory movements towards the right. When searching for targets, copying, or reading, the patients direct their eye and hand movements towards the ipsilesional side, leading to neglect of the contralesional side. How elementary is this disorder? Is it linked with active behaviour (such as drawing or exploring) or is it inherently obvious without any specific requirements? To address this issue we investigated the patients' spontaneous resting position while sitting in the wheelchair, just waiting and "doing nothing". Using magnetic search coil technique, we recorded spontaneous gaze, eye-in-head, and head orientation of 10 right hemispheric neglect patients while they were "waiting for an experiment". In a subsequent condition, patients were instructed "to look exactly straight ahead". In comparison to controls, neglect patients showed a marked rightward deviation of about 20 degrees in both conditions. Their spontaneous resting position thus corresponded with the subjective "straight ahead" orientation. Spatial neglect seems to be associated with a very elementary disturbance of spatial information processing which might be understood as a re-adjustment of the normal resting position to a new, more rightward located origin.

D10. Auditory sensory gating in chronic alcoholism

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Measurement of evoked potentials has shown that repetitive auditory stimulation activates some neuronal inhibitory processes referred as sensory gating. It can be assessed by the amplitude reduction of the P50 event-related potential to the second stimulus of a double-click paradigm. Disturbed P50 suppression has been found in multiple psychiatric disorders as schizophrenia, bipolar disorder or Alzheimer's disease and also in some drug abusers. Acute alcohol ingestion reduces auditory sensory gating but there's no understanding of the effects in chronic alcoholism. We investigated whether alcoholics display disturbed sensory gating expressed by a deficit in P50 suppression. Repetitive tones were presented, and EEG was recorded from patients and control subjects. Low Resolution Tomography (LORETA) was performed on data to obtain sources of activation. Alcoholics presented reduced P50 gating compared to control group.

D11. Implication of the serotonergic system in cognitive and non-cognitive disturbances associated to Alzheimer's disease

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In addition to the widely accepted cholinergic deficit in Alzheimer's disease (AD), it has been suggested that an imbalance of different neurotransmitters plays an important role in the pathophysiology of the illness. To investigate this hypothesis, cholinergic and serotonergic function were assessed in *post mortem* cortical tissue (BA10 and BA20) from AD patients who had been prospectively assessed with the Mini-Mental State Examination (MMSE) for cognitive impairment and with Present Behavioral Examination (PBE) for non-cognitive disturbances. Cholinergic deficits were significantly correlated with last MMSE score, as well as with aggressive factor, supporting a dual role for the cholinergic system in cognitive and non-cognitive disturbances. On the other hand 5-HT depletions showed a marked correlation with overactivity and psychosis. Among the different serotonergic receptors, 5-HT1B/1D receptors are of special interest as they appear to regulate cholinergic neurotransmission. In the present study we found a significant correlation between lowered 5-HT1B/1D receptor densities in frontal cortex and MMSE. Moreover the ratio 5-HT1B/1D/AChE was also correlated to last MMSE score, supporting the implication of this receptor in memory impairment.

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D12. Absence of visual feedback of arm movements enhances the magnitude of the effect of prism adaptation in normal subjects

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Prism adaptation can improve left unilateral spatial neglect, even though it induces only a small left-like bias in normal individuals. The question why prism adaptation induces larger effects in left neglect patients is still unsolved. Recent data from our laboratory show that when neurologically unimpaired subjects are requested to perform a visuo-manual line bisection task, with no visual feedback of their right arm movements, their performance is biased rightwards. This deviation is directionally similar to the error made by left neglect patients, suggesting that the availability of the visual control of the action may play a role in at least some components of unilateral left neglect patients' behaviour. If this is true, then it may be possible to predict that the effects due to prism adaptation in normal subjects should be larger when the visual feedback of arm movements is prevented rather than when it is not. To this aim two groups of normal subjects were requested to perform a visuo-manual line bisection task before, immediately after, and 15 minutes later prism adaptation. Group 1 performed the task with visual feedback, Group 2 without it. As predicted, the effect of prism adaptation was larger in Group 1 than in Group 2. Results are discussed in terms of the possible role played by the availability of the visual control of the action in left neglect and its relationship with prism adaptation.

D13. Prednisone induces cognitive dysfunction, neuronal degeneration and reactive gliosis in rat brain

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Background: High glucocorticoids serum levels and prednisone (PDN) therapy have been associated with depression, post-traumatic stress disorder and some cognitive dysfunctions in humans. Objective. To assess whether chronic administration (90 days) of PDN produces disturbances on learning and memory retention associated with neuronal degeneration and cerebral glial changes. Methods: Male Wistar rats were studied. Controls orally received 0.1 ml distilled water vehicle. Prednisone group was treated orally with PDN 5 mg/kg per day, which is the equivalent to moderate doses employed in clinical settings. Learning and memory retention were assessed using the Morris water-maze. The index of degenerated neurons, the number and cytoplasmic transformation of astrocytes and microglia cells were evaluated at prefrontal cortex and CA1 hippocampus. Results: PDN-treated rats showed a significant delay of 20% in learning and memory retention as compared with controls. In addition, the neuronal degeneration index was two times higher of the PDN group at cortex and around ten times higher at hippocampus when compared with controls. The number and cytoplasmic transformation of astrocytes were also significantly higher in the PDN group. Isolectin-B4-labeled microglia cells were higher at prefrontal cortex, but not in hippocampus, in the PDN-treated group. Conclusions: These data suggest that chronic exposure to PDN produces learning and memory impairment, reduces neural viability and increases glial reactivity in cerebral regions implicated with these cognitive functions.

D14. Beneficial effects of alpha-lipoic acid plus vitamin E on neurological deficit, infarct volume and neuronal remodeling in penumbra of the ischemic rat brain

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Background: During a cerebral ischemia, oxygen-derived species are involved in the initiation and progression of neural damage. Alpha-lipoic acid (ALA) and vitamin E (VE) combination have synergistic beneficial effects. Objective. To analyze possible beneficial effects of ALA-VE combination in focal ischemia. Methods: Using male Wistar rats (350-400 g), four groups were assembled (n = 10 per group): ischemic, vehicle (0.1 ml sesame oil, p.o. for 30 days, pre-ischemia), intensive (100 mg/kg ALA plus 140 mg/kg VE p.o. post-ischemia), and prophylactic (20 mg/kg ALA plus 50 mg/kg VE p.o. for 30 days pre-ischemia). All groups underwent ischemia by arterial thromboembolism. The variables evaluated were functional recovery, infarction volume and neuronal remodeling (GAP 43 and synaptophysin over-expression) at 1, 3, 7 and 14 days. Results: The prophylactic group obtained lower scores in the neurological deficit scale than the other groups (P=0.001, Mann-Whitney U test). Infarction volume in pre-ischemic-treated animals was twice lower than in the other groups (P=0.036, ANOVA-Bonferroni). Over-expression of synaptophysin and GAP 43 in both antioxidant-treated groups was higher (~20-25% and 40-45%, respectively), as compared with controls (P<0.05, ANOVA-Bonferroni). Conclusions: Pre-ischemia treatment with ALA and VE improves functional recovery, reduces infarction volume, and increases neuronal remodeling. Post-ischemia treatment increases neuronal remodeling, but does not modify functional recovery and infarction volume.

D15. Memory profiles and executive function in schizophrenia

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Schizophrenia is defined as a heterogeneous disorder that has been characterized in terms of various forms of cognitive dysfunction. Verbal learning, memory and executive functions are especially compromised. This study examined memory and executive performance in schizophrenia to determine whether groups conforming to fronto-temporal and subcortical memory patterns could be identified and, if these patterns have a relationship with executive functions. Were included 77 schizophrenic patients. Episodic memory was explored by California Verbal Learning Test (CVLT) and executive function by Wisconsin Card Sorting Test (WCST). Cluster analysis of CVLT classified patients into 3 groups: group 1 (n = 10) was characterized by good learning, delayed memory and recognition (unimpaired group); group 2 (n = 32) by poor learning, delayed memory and partially impaired recognition (fronto-temporal group); and group 3 (n = 35) by partially impaired learning and delayed memory and good recognition (subcortical group). With regard to group's discriminability to WCST variables was found differences in perseverative errors (groups 1-2) and total errors (groups 1-2, 1-3). This study shows that different severity and type of memory performance discriminates between different performance in executive function. Impaired memory (fronto-temporal or subcortical patterns) discriminates a general difficulty in WCST and fronto-temporal discriminates perseveration.

D16. Impaired perception of body orientation despite intact visual-vestibular processing

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Some stroke patients show a disorder of spatial orientation termed „pusher syndrome". They actively push themselves from the non-paretic side until they loose stability and fall over to the paretic side. In these patients, Karnath et al. (Neurology 2000) found normal perception of the visual vertical indicating undisturbed visual-vestibular processing. The patients rather showed a marked tilt of the subjective postural vertical (SPV) towards the ipsilesional side. The finding suggested that the SPV relies on a graviceptive system distinct from the visual-vestibular system. Here, we investigated a sample of patients with pusher syndrome on a tilt chair while letting them view the surroundings *via* a head-mounted display fitted by a video camera. Unbeknown to the subjects, the camera was oriented either in line with the vertical body axis (0°), or was tilted 20° clockwise or anti-clockwise. We measured the patients' SPV in relation to the optical tilt of the visual surroundings. The patients showed a contraversive tilt of the SPV under both conditions of optical tilt (+20° and -20°), while the SPV was upright under non-tilted visual field conditions (0°). This paradoxic behaviour can not be accounted for by current theories of visual-vestibular and somatosensory integration. We tentatively interprete the finding as evidence for an inability to suppress the induced visuo-vestibular conflict while determining upright body orientation.

D17. Dopamine transporter in the nigrostriatal system of adolescents with ADHD and neurocognitive performance

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Dysfunction of the dopamine has been suggested as the underlying pathophysiological mechanism in Attention Deficit/Hyperactivity Disorder (ADHD). The aims of the present Positron emission tomography (PET)-study were to examine the nigrostriatal system of adolescents with ADHD and to search for relationship between dopamine markers and clinical symptoms. Twelve adolescents with ADHD (DSM-IV criteria) and 10 young adults participated in the study. The radioligands [11C]PE2I and [11C]raclopride were used to determine regional binding potentials for dopamine transporter (DAT) and the dopamine D2 receptors, respectively. ADHD adolescents performed visuospatial working memory, continuous performance tasks and their movement activity was measured using a motion analysis system. DAT binding potential in the midbrain was significantly lower in the group of adolescents with ADHD ($P<0.03$). Dopamine markers in the striatum did not differ between the groups, but were lower in ADHD after correction for age. There was a significant positive relationship between DAT binding in the striatum and movement range whereas negative relationships were found for neurocognitive performance. The findings suggest that adolescents with ADHD may have altered dopamine function in the midbrain and the striatum.

D18. Turning behaviour in rats with unilateral lesion of the substantia nigra pars compacta induced by MPTP

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Turning behaviour in rats with unilateral lesion of the substantia nigra pars compacta (SNpc) induced by 6-hydroxydopamine (6-OHDA) is an extensively used model of motor disability related to Parkinson's disease (PD). Although the SNpc of rats is more resistant to the neurodegeneration induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) compared to 6-0HDA, rats with bilateral SNpc lesion induced by MPTP have being successfully used to study memory disabilities related to PD. The aim of this investigation was to test if rats with unilateral MPTP-induced SNpc-lesion also present turning behaviour when challenged with s.c. injection of direct or indirect dopamine agonists. Adult male Wistar rats received a unilateral right injection of 1 mM MPTP into the SNpc. Fourteen days after surgery, the rats received 0.25, 0.5, 1.0 or 2.0 mg/kg apomorphine, 1.0, 5.0, 7.5 or 10 mg/kg amphetamine, 0.1, 0.25 or 0.5 mg/kg nicotine, 25/12.5, 50/12.5 or 100/25 mg/kg levodopa/benserazide or saline. Apomorphine and amphetamine caused a dose-effect increase in the number of ipsilateral turns in relation to the lesioned side. On the other hand, the number of turns induced by nicotine and levodopa was not significantly different from that observed in the saline group. These results suggest that, like unilaterally 6-OHDA-lesioned rats, MPTP-lesioned rats also present turning behaviour when challenged with dopaminergic drugs, although some differences are observed between these two models of PD.

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D19. Attention during EXG paradigm in patients with chronic schizophrenia

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Contingent negative variation and the postimperative negative variation are electrophysiological correlates of the attention processes. These potentials were measured in 30 chronic schizophrenia patients and 30 healthy subjects, using the electroexpectogram (EXG) paradigm, which is an expanded (100 trials) and modified version of the classical CNV paradigm. Based on a biofeedback design, the occurrence of S2 tone in the EXG paradigm depends on the amplitude of the CNV potential. If CNV reaches a predefined threshold level, the S2 tone turns off, which causes an extinction of the CNV potential. The computer recognizes this and S2 tone turns on again. As a result an electrophysiological oscillatory process occurs in subjects mind, graphically presented by a curve named electroexpectogram. In every separate attempt of the EXG paradigm PINV was measured and analyzed through mean amplitude, occurrence and extinction during 100 trials. The amplitude of the late CNV within the EXG curve was 10.7 ± 3.98 to 5 ± 6.1 microvolts in patients and 13.5 ± 2.6 to 0.9 ± 3.3 microvolts in healthy subjects ($P<0.05$). PINV occurred in 80% of the patients and in 36.6% healthy controls, and was present during the whole EXG paradigm (from 22.5 ± 28 trial to 77.8 ± 21.3 trial), in patients. It started in 20.7 ± 23.4 trial and lasted until 41.5 ± 30.11 trial, in healthy controls. These results point out that patients with chronic schizophrenia show disturbance in adjustment of their attention during the EXG paradigm.

D20. Neurodegeneration profile in a mouse model overexpressing Dyrk1A

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There is a consistent phenotypic relationship between the neuropathology of Down's syndrome (DS) and that of Alzheimer's disease, but its pathogenesis is unknown. We have analysed the neurodegenerative profile in transgenic mice that overexpress Dyrk1A (TgDyrk1A), a candidate gene for DS. TgDyrk1A present motor alterations and cognitive deficits similar to those of DS. To determine the possible implication of overexpression of Dyrk1A in the DS neurodegenerative processes, we have used aged (22-25 months old) compared to adult (12 months old) wild-type and TgDyrk1A mice. Behavioral studies showed a different pattern of age-associated cognitive/behavioral decline in TgDyrk1A. Using Fluoro-Jade B staining to mark cells in process of neurodegeneration, we observed that aged TgDyrk1A present a significantly lower number of stained cells, suggesting a neuroprotective role for Dyrk1A overexpression. Thus, other possible mechanisms to explain the age-associated cognitive changes present in TgDyrk1A were explored by immunocytochemical analysis of noradrenergic and cholinergic systems. The identification of neuropathological alterations and cognition decline pattern in aged TgDyrk1A mice may have important consequences for the understanding of the age-associated changes observed in DS patients.

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D21. Unilateral visuospatial neglect in children with tuberous sclerosis complex (TSC)

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Tuberous sclerosis is a multisystem disorder caused by a mutation in either the TSC1 gene on 9q34 or the TSC2 gene on 16p13.3. Loss of tuberin (TSC2) or hamartin (TSC1) expression during embryological development leads to multisystem aberrations. In the CNS, widely distributed cortical tubers, subependymal nodules and other white and grey matter deficits are seen. Even in individuals with TSC who are of normal intelligence, there is evidence of specific cognitive deficits, particularly of sustained attention. Unilateral neglect is seen following right hemisphere lesions, and is associated with non-lateralised attention deficits, notably of sustained attention. We hypothesized that in children with TSC with cortical tubers in the right hemisphere and sustained attention deficits, unilateral visuospatial neglect would also be present. Eight children with TSC of normal intelligence and 7 matched controls without TSC were tested. All the children with TSC had one or more cortical tubers in the right hemisphere. Eye-tracking during visual search tasks of varying complexity revealed that, as the task became more demanding, the search patterns became more chaotic and predominated on the right side of the display, thus manifesting as left neglect. Left neglect was not predicted by the presence of right-sided tubers or a history of epilepsy. Taken together, the findings suggest that TSC genes may be involved in hemispheric specialisation and that genetic aberrations may lead to lateralised and non-lateralised attention deficits.

D22. Electrophysiological correlates of ipsilesional hyperattention in neglect patients

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In speeded light detection tasks patients with neglect react paradoxically faster to mid-periphery than to more central stimuli in the ipsilesional field thus showing a tendency of exaggeratedly attending toward the ipsilesional hemispace (Smania et al. 1998). In order to explore the possible neural mechanism by which such an ipsilesional hyperattention modulates the processing of visuo-spatial information in neglect, we recorded event-related potentials (ERPs) from four patients in response to stimulation with checkerboards tachistoscopically displayed along the horizontal meridian of the visual field. Stimuli were randomly presented in one of four positions from 0° up to 12° either to the left or to the right of the fixation point within distinct blocks of trials. We also recorded simple reaction time (RT) in response to the same stimuli, by requiring the patients to press a button as quickly as possible when a stimulus appeared. As expected, neglect patients showed a delay in RT to central as compared to peripheral stimuli in the ipsilesional field. Such a delay was associated with an abnormally increased latency of the P1 component of the ERP response to central as compared to peripheral stimuli. Given that P1 represents an index of early attentional effects, these results strongly support the possibility that the abnormal distribution of speed of RT in the ipsilesional field of neglect patients reflects the alteration of neural, attentional mechanisms in early stages of visual processing. These mechanisms, which we refer to as hyperattention, would act by speeding up transmission of more peripheral rather than central signals from the ipsilesional field.

D23. Cognitive functions in nigerians with newly diagnosed epilepsy

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This study evaluated the pattern of cognitive disturbances in Nigerian Africans with newly diagnosed epilepsy, prior to drug therapy. A total of 60 consecutive patients (mean age 31.6 ± 17.4, range 14-55 years) presenting with a clinical diagnosis of epilepsy were recruited for the study. Sixty healthy volunteers without history of epilepsy matched for age, sex and level of education with the epileptic subjects served as controls. The administration of cognitive tests was done with the FePsy computerized neuropsychological test battery. The tests administered were visual and auditory reaction times, continuous performance test and recognition memory test to assess the mental speed, attention and memory, respectively. The means of the epileptic patients and controls were statistically compared. Epileptic patients performed worse than controls across the spectrum of cognitive tasks assessed (P=0.00001; P<0.025), with the exception of the response bias of the vigilance test (P=0.488; P>0.025). The results of this study will be useful in counseling of patients about their educational, social and vocational needs.

D24. Antipsychotics in the treatment of Alzheimer's disease

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Background: Toxicity and calcium-channel activity of beta-amyloid peptide, derived from the ubiquitously expressed amyloid-precursor-protein, both in the central nervous system and in the peripheral tissues have been considered to play a crucial role in Alzheimer's pathology. Several investigators have reported a low frequency of Alzheimer's disease in patients with schizophrenia, and it has been proposed that antipsychotic medications may be responsible. Haloperidol, one of the most frequently prescribed neuroleptics, has also been recently described as a calcium and calmodulin antagonist; however, no study has ever evaluated haloperidol for its effects on beta-amyloid-induced imbalance of the basal intracellular calcium concentration of cells. Moreover, despite of the widespread use of antipsychotic medication among the elderly, little information is available on the effect of haloperidol on the metabolism of amyloid precursor protein. Therefore we evaluated haloperidol for its effects on beta-amyloid-induced calcium-imbalance and on the metabolism of the amyloid-precursor-protein. Methods: Basal intracellular calcium-levels were measured *in vitro* in Fura-2AM-loaded human fibroblasts by dual wavelength spectrofluorimetry. Cortical amyloid-precursor-protein levels were estimated *in vivo* in male Sprague-Dawley rats using western immunonoblot technique. Results: *In vivo*: Alzheimer cells exhibited lower calcium-levels as compared to the control cultures. Exposure of fibroblasts to beta-amyloid peptide resulted in increased calcium concentration of the con-

trol cells, but not of Alzheimer fibroblasts. Preincubation of control cultures with haloperidol blocked the beta-amyloid-induced elevation of calcium. *In vitro*: Acute therapeutic and toxic haloperidol treatment increases cortical amyloid-precursor-protein levels in 24-96 hours and 12-24 hours, respectively. Chronic (1-4 weeks) haloperidol administration had no significant effect on amyloid-precursor-levels neither in therapeutic, nor in toxic doses. Discussion: Our findings indicate that haloperidol efficiently attenuates beta-amyloid-induced calcium imbalance. Our results also demonstrate that acute administration of haloperidol has a beneficial effect, whereas chronic haloperidol treatment could be considered as relatively safe regarding amyloid-precursor-protein metabolism. Conclusion: These findings suggest that haloperidol may serve as a potential agent in alleviating toxic effects of beta-amyloid peptide; also, it may be a useful lead in the development of an effective Alzheimer therapeutic agent.

D25. Size judgements in patients with spatial neglect

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Many patients with hemispatial neglect underestimate the horizontal size of 2-D stimuli presented on the left side relative to the right side. However it has been difficult to replicate this result using two solid objects as stimuli, with the finger and thumb being used to indicate a size estimate of the leftward or rightward of the two. In the present study, we tried to overcome this problem by placing objects close together in order to maximize their mutual influence in determining size judgements. Two patients with neglect, and a group of healthy controls, were tested on a task in which a central rectangular block was paired with a distractor block (of greater, smaller or equal size) on the left or right side. In control trials, the central object was presented alone, in order to assess whether the size distortion effect observed was due to an underestimation of leftward objects, overestimation of rightward objects, or both. In addition to the judgement task, we tested the subjects in a second version of the task in which they had to reach out and grasp the central object on each trial – a task in which we have previously found no evidence of size distortion in neglect patients. In both tasks, the separation between finger and thumb was monitored continuously using a magnetic recording system. The data are interpreted within a theoretical model that attributes neglect to an interference with a perceptual representation system fed from the ventral visual stream.

We are grateful to the Medical Research Council for supporting this research.

D26. Grey matter atrophy in Parkinson's disease with and without dementia. A voxel-based morphometry study

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Dementia in Parkinson's disease may result from neuropathological changes in cortical o subcortical regions. The objective of this study was to investigate, the gray matter loss in patients with IPD (Idiopathic Parkinson's disease) with and without dementia at 1.5 year follow-up. The PDD (Dementia in Parkinson's disease) group included 9 patients and the IPD group included 12 patients. Subjects in all 2 groups were matched for gender, age and years of education. MRI was obtained in all subjects using a 1.5 T GE. We used the voxel based morphometry technique (VBM) that allows whole brain examination. Mental Status decreased in PDD patients. Significant grey matter loss was observed in both groups at the corrected $P<0,05$ level. In the PDD group the grey matter loss was localized in bilateral cerebellum, left hippocampus, middle and superior frontal gyrus. In the IPD group the grey matter atrophy was seen in cerebellum, posterior cingulated gyrus and temporal bilaterally. In addition, we observed basal ganglia increases in both groups. Hippocampal atrophy seems to be a crucial region in the evolution of dementia in Parkinson's disease.

D27. Sound recognition, sound localization and sound motion perception: patterns of recovery following unilateral focal lesions

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Evidence from human activation and lesion studies suggests that sound recognition and localization are processed in distinct cortical networks. We now report on recovery patterns of initial deficits in sound recognition and/or spatial processing. Eighteen patients (aged 23 to 68 years) who sustained a first unilateral hemispheric lesion (documented by MRI and/or CT scan) have been tested for sound recognition (SR), sound localization (SL) and sound motion perception (SMP) in acute (1-9 days; 3 cases), subacute (13 days - 1 month; 7 cases), or early chronic stages (7 weeks - 5 months; 8 cases) and then 8 to 52 months later. At the first testing, 3 patients had a selective deficit in SL; 7 patients a combined deficit in SL and SMP; 1 patient a combined deficit in SR and SMP; and 6 patients a combined deficit in SL, SR and SMP. Twelve of 17 patients with a selective or combined deficit in the auditory spatial domain recovered completely (7) or partially (5); 4 remained stationary and 1 worsened. Complete recovery was observed for patients tested in either stage. Three patients with partial recovery, i.e., recovery of one or two but not all functions, normalized their performance in SL; 1 in SMP; and 1 in SR. Anatomo-clinical correlations suggest that recovery relies on reorganization of specialized networks for sound recognition and sound localization.

D28. Taking account of peripheral visual stimuli in optic ataxia

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We have tested two patients with bilateral optic ataxia following parietal lesions, on two tasks using the same experimental arrangement. The subject either had to (a) reach between two objects whose location varied from trial to trial, or (b) bisect the space between the two objects under similarly varying conditions. Both tasks were performed in open loop. In a previous study using similar tasks (McIntosh R.D., McClements K.I., Dijkerman H.C. and Milner A.D. (submitted) "Preserved obstacle avoidance in patients with left visual neglect"), we found that most neglect patients failed to take much account of the varying locations of the leftward object when making bisection responses, but took good account of both objects when performing the reaching task. We argued that this reflected a

functionally intact dorsal stream in the neglect patients. A strong form of this argument would predict the opposite outcome in optic ataxia: due to their dorsal stream damage, these patients should take full account of both objects in the bisection task, but little or no account of them in the reaching task. We present data showing that this prediction was unambiguously confirmed. We are grateful to the Leverhulme Trust and Medical Research Council for supporting this research.

D29. Water maze extinction as a model of depression in aged and young rats: interaction of extinction-induced despair with learning ability

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Lack of reinforcement during extinction in the water maze due to the absence of a platform, was hypothesized to induce a negative state, including the development of immobility, held to reflect a state of "despair" when measured in the Porsolt test. Aged (n = 27) and young (n = 8) animals were tested in the water maze during 9 days with a platform hidden, followed by 7 days of extinction with the platform absent and one trial of 2 min administered on each day. Both age groups developed significant amounts of immobility over extinction trials, with the aged showing more than the young. To examine whether the age difference was related to differences in learning ability, the aged were subdivided into superior, intermediate and inferior learners (n = 9 per group) on the basis of overall times to platform during acquisition, and compared with each other and the young. The aged inferior learners displayed most immobility in comparison with the other groups, and differed significantly from the young. Conversely, groups that were determined as superior, intermediate and inferior on the basis of the times spent in the former platform quadrant during extinction, did not differ significantly from each other in amounts of immobility. The data indicate that multiple extinction trials can induce "behavioral despair" in the water maze, and that inferior learning ability may present a vulnerability factor in the degree of its expression.

D30. Poorer cognitive performance in MCI subjects carrying the Asp variant of the Glu/Asp NOS3 polymorphism

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Introduction. The well-established category of Mild Cognitive Impairment (MCI) refers to a transitional state between normal aging and Alzheimer's disease and is a high-risk condition for dementia. The endothelial nitric oxide synthase (NOS3) gene encodes endothelial NOS (eNOS), an enzyme that regulates the production of the vasodilatory nitric oxide (NO) associated with the cerebral small vessels pathology observed in early Alzheimer's disease. Objectives. In the present study we aimed to determine whether Glu/Asp NOS3 polymorphism in MCI is associated to neuropsychological performance. Methods. A sample of 62 MCI and 136 controls were genotyped for the NOS3 G894T substitution. Results. The Odds Ratio calculation indicated a lack of association between NOS3 variants and the condition of MCI. Nevertheless, within this group, those subjects carrying the Asp variant (T carriers) performed worse in the Mini-Mental State Examination (MMSE) (t=2.042, P<0.046). The WMS-R long term visual memory test (t=2.442, P<0.018), and the phonetic verbal fluency test (FAS) (t=2.641, P<0.011) were also significantly associated to MCI T carriers. Conclusions. Our results suggested that the presence of the NOS3 T allele in MCI subjects is a vulnerability genetic factor for cognitive impairment in elderly.

D31. Age effects on the structural alterations in obsessive-compulsive disorder

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Volume changes in the fronto-striatal system and anatomically connected structures have been observed in obsessive-compulsive disorder (OCD). Some of these alterations may be related to different rates of gray matter loss, as an interaction between group differences and age has been appreciated. The aim of the present study was to assess this age effect by studying two independent samples of young and adult OCD patients. Gray matter segments from three-dimensional MRI of 37 young (0-22 years, SD = 3.4) and 35 adult (0-38 years, SD = 8.8) OCD patients were compared with those of 37 young and 35 adult sex-and-age-matched controls using statistical parametrical mapping. Compared to controls, absolute decreases in the gray matter of young patients were observed in the gyrus frontalis medialis and the left perisylvian region. In adult patients, gray matter loss was located in the ventromedial prefrontal cortex. Relative increases in gray matter volume were appreciated bilaterally in the ventral part of the striatum and in the anterior cerebellum only in adult patients. The present results show that the pattern of structural alterations seen in OCD changes throughout lifetime. As the adult pattern is consistent with functional studies, we suggest that some structural alterations in OCD may be the consequence of prolonged hyperactivity in the fronto-striatal system.

D32. Effects of pleasant and unpleasant olfactory stimuli in anorexia nervosa as revealed by spectral EEG changes

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The question if the perception of olfactory stimuli is altered anorexia nervosa is still an open issue. The aim of the present study was to investigate these mechanisms by the analysis of the electroencephalogram (EEG) recorded in control (n = 18) and anorexic subjects (n = 9), exposed to different olfactory stimuli. The subjects were exposed for two minutes to unpleasant (polymethylacrylate) and pleasant (orange, vanilla) olfactory stimuli. Power spectrum analysis was performed on the EEG recorded according to the 10-20 system. It was found that with respect to resting baseline conditions both types of olfactory stimuli changed the spectral characteristics of the EEG in all subjects and mostly in the beta1 and beta2 frequency bands. In the baseline condition, both the beta1 and beta2 bands were found to be lower in AN patients than in the controls. With respect to baseline, in anorexic patients the different odors elicited an increase of the power of the beta1 range, which was higher in the left side after expose to orange and polymethylacrylate. Exposure to vanilla in-

creased the beta1 band in the right side. The power of the beta2 frequency band was lower in the patients compared to the control group both after orange and polymethylacrylate exposure. Our findings indicate a decreased level of fast (beta1 and beta2) frequency band in AN. According to the electrophysiological indices studied the olfactory sensitivity of An patients differs from that of the control subjects.

D33. Functional analysis of the serotoninergic system in murine models of prion diseases

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Although structural and molecular studies have provided much insight into prion diseases, the pathophysiological mechanisms are still largely unknown. In the CNS, the role of the neuronal phenotype, neurotransmitters and receptors in the susceptibility to infection remains to be elucidated. Several lines of evidence suggest that the serotoninergic system might be a candidate target for prion infection. The aim of the present work was to study the development of the pathophysiology in mice using non-invasive methods i.e. brain imaging (MRI, 7 tesla) and *in vivo* spectroscopy together with behavioural tests designed to evaluate serotoninergic functions: light/dark boxes (anxiety), hot plate test (pain), activity boxes (circadian rhythm). Mice infected intracerebrally with a scrapie (C506M3) or ESB strain (6BP1) showed behavioral abnormalities i.e. anxiolytic-like behavior and hyperalgesia preceding clinical signs by 15/20 days. Changes in circadian activity were observed concomitantly with clinical motor symptoms. Direct inoculation into the Raphe nuclei reduced the incubation period and survival time. MRI images showed early signal abnormalities especially in brainstem regions. These results suggest that the serotoninergic system may play an important role in the propagation and accumulation of the prion agents in the CNS.

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D34. Acute hypobaric hypoxia influences on brain bioamine levels and behaviour in newborn rats: peptidergic correction

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Different postnatal diseases can be induced by acute prenatal hypoxia. Therefore, methods to correct antenatal hypoxia can have very important consequences. One of the correction methods is the use of regulatory peptides such as Semax (ACTH4-7 - PGP) and b-casomorphin-7. Semax is a well known antihypoxic and nootropic agent and b-casomorphin-7 is an anxiolytic agent. We exposed pregnant rats to acute hypobaric hypoxia at the 4-5th day gestation. Brain bioamine levels were determined in newborn rat pups using fluorescent method on the 15, 22, 36 and 57th day of postnatal period. Other experiment were carried out to evaluate the delayed effects of acute hypobaric hypoxia on behavior and on anxiety levels of newborn albino rats using classical behavioral tests. Prenatal stress led to low birth weights and could have an influence on the developing brain. Changes of bioamine levels showed phasic age-dependant characteristics: A significant increase of NE, DA and 5-HT levels in the brain was observed on the 15th and 36th day of postnatal period, a marked decrease of the same bioamine levels was shown on the 22nd postnatal day, and an increase of 5-HT levels in the brain on the 57th postnatal day of males, but not of females. In all cases the observed biochemical changes correlated with behavioral characteristics. The 15-days old rats showed hypoactivity, while the 21- and 36-days old pups demonstrated hyperactivity and an increased anxiety level. On the 57th day of life the anxiety level was enhanced in males, while decreased in females. Prenatal hypoxia also resulted in altered learning and memory of newborn rat pups. The preliminary intranasal infusion of peptide complex (ACTH4-7-PGP and β-casomorphin-7, 0.1 mg/kg) to pregnant female rats eliminated all the observed prenatal hypobaric hypoxia influences on bioamine balance, behavior and anxiety level.

D35. Instrumental learning of active avoidance of rats in the model of hypokinesia

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Limited locomotor activity becomes a feature of contemporary life style. Hypokinesia is considered the chronic multicomponent stress that causes pathological changes in different organs. Lasting hypokinesia was documented to induce cognitive disabilities and disturbances of learning and memory. The aim of the present research was to study potential hypokinesia-induced learning deficits in active avoidance paradigm of instrumentary learning in rats. Male unlined white rats were placed for 22 hours daily during 7 days into the narrow cages restricted their motor activity. Instrumentary escape behavior test (20 sessions daily) was performed during last three days of hypokinesia (1st experimental group) and starting 12 days after termination of hypokinetic regimen (2d group). Rats of the 1st group displayed lower scores of acquisition of active avoidance compared to intact controls. In rats of 2nd group, the higher scores of task acquisition were obtained compared to the 1st group. There was insignificant difference between the learning scores of these animals versus control group, suggesting memory restoration mechanisms in posthypokinetic period. Thus, 7-day hypokinesia leads to a deficit of instrumentary learning of active avoidance that can be restored 12 days after termination of hypokinesia. This finding needs to be studied in other memory paradigms, including instrumentary learning of passive avoidance and tasks for hippocampus-dependent memory.

D36. Behavioral characterization of WAG/Rij rats with pure absence and mixed form of epilepsy

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The WAG/Rij rats are a suitable genetic model of human non-convulsive epilepsy form. All rats of the WAG/Rij strain show in EEG spontaneous, generalized spike-wave discharges, which are the main indicatives of absence epilepsy. Some WAG/Rij rats (up to 30%) have a mixed form of epilepsy (absence + audiogenic fits). In the present study, behavior of WAG/Rij rats with pure absence (WR-abs) and mixed form of epilepsy (WR-mix), and behavior of Wistar rats with no signs of any seizure pathology was compared. All WAG/Rij rats as compared with Wistar rats were found to exhibit depressive-like behavioral alterations: decreased activity in the open field test, increased immobility in the forced swimming test

and decreased sucrose intake and preference (anhedonia). WR-abs rats as compared with Wistar rats were not more anxious in the light-dark choice, elevated plus-maze and social interaction tests. WR-mix rats as compared with WR-abs rats were less active in the open field test and more anxious in the elevated plus-maze test. In the light-dark choice test, differences between WR-abs and WR-mix rats indicating increased anxiety were not revealed. Results suggest that increased anxiety is most likely associated with convulsive form of epilepsy than with absence epilepsy. WAG/Rij rats might be regarded as new putative animal model of depressive-like behavior accompanying absence epilepsy. Increased anxiety is behavioral characteristic only of those WAG/Rij rats which are susceptible to audiogenic seizures.

D37. Neurocognitive effect and psychopathological presentation of the HIV and AIDS in the brain. Study in adult mexican population

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Pathology associated to HIV effects in the brain from the beginning of the disease shows changes on the cognitive performance in tasks such as motor/visuoconstructive, executive function, learning and memory. In psychopathological factors slow thinking, anergy**,** social anxiety, apathy and depressive mood are the early HIV infectious disease, its suggests a subcortical affection in the evolution of the illness. Despite AIDS pathology has been reported in the world literature few neuropsychological and psychopathological studies have been reported in mexican population. This study examined the association between neurocognitive complaints and psychopathological factors and objective neuropsychological performance in HIV/AIDS states. Eighty nine subjects with HIV (22 adults with HIV diagnosis and 67 with AIDS diagnosis) completed a neuropsychological test battery (Abbreviated Barcelona Test), and psychiatric structured interview (Present State Examination). Mean age and education (31.4 and 11 years). Psychiatric, neurological history and neuroinfection, among others were excluded. Conclusion: In AIDS state exists cognitive failure in attention, information processing speed, function motor in HIV; in AIDS state the failure intensify in language abstraction/executive functions and memory and learning Student t, Mann Whitney, Wilks's Lambda tests classified correctly 84% of the subjects; 91% (AIDS) and 63 % (HIV).

D38. Sexuality and mania

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Objective: Retrospective assessment of the presence of hypersexuality in hypomanic/manic bipolar patients. Method: Retrospective assessment of a wide range of items related to sexuality by means of a self-administered, confidential and anonymous questionnaire in a sample of 29 bipolar I or II (DSM-IV criteria) outpatients (17 men and 12 women). The assessment was carried out when patients were euthymic (Hamilton Depression Rating Scale <8, Young Mania Rating Scale <5). Statistical analysis was performed by the SPSS (version 10.0). Results: In hypomanic/manic phases, 17 patients (59%) experience a growth of their sexuality, 12 (41%) report increasing frequency of their sexual activity, and 14 (48%) have a rise of their sexual thoughts. Six patients (21%) report a switch in their sexual practices, whereas 10 (35%) experience an increasing tendency to sexual phantasies. Nine patients (31%) think that hypersexuality resulted in negative consequences on work, health, economics and couple. Seven percent (n = 2) of the subjects felt that they were unable to control their hypersexuality, 55% (n = 16) viewed their hypersexuality as a desirable condition, though 17% (n = 5) of them feel guilty about it. Conclusion: Hypersexuality in bipolar disorder is a frequent condition (3/5 of the sample) which can result in a negative consequences for the life of patients (1/3 of the sample).

D39. Verbal learning abilities in benign partial epilepsy with centro-temporal spikes

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The purpose of this study was to assess verbal learning abilities in children with benign partial epilepsy with centro-temporal spikes (BPECTS). The sample consisted of 12 children aged 7-11 years with BPECTS compared to a group of 26 children with other forms of idiopathic partial epilepsy and a group of 31 healthy children. The Auditory-Verbal Learning Test (Rey 1964) was used. The results have shown subtle memory deficits in the group of children with BPECTS compared to the age-matched healthy group of children, but they performed better when tested than the group of children with other forms of idiopathic partial epilepsy.

D40. Visual functions in children with benign partial epilepsy with centro-temporal spikes

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Visual and visuo-constructional abilities were assessed. The sample consisted of 12 children aged 7-11 years with benign partial epilepsy with centro-temporal spikes (BPECTS) compared to a group of 26 children with other forms of idiopathic partial epilepsy and a group of 31 healthy children. The Test of Visual-Perceptual Skills (non-motor) – revised by Morrison F. Gardner (1996) – and Rey-Osterrieth Complex Figure Test (Rey 1941, Osterrieth 1944) were used. Compared to the control group, children with BPECTS were impaired in their visuo-constructional abilities.

E1. Sensitization to the rewarding effects of morphine in mice

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The rewarding effects of morphine can underlie its abuse liability and the sensitization process can be a determinate role in the development of addiction. In the present study, an unbiased place conditioning procedure was used to determine whether sensitization to the morphine-induced conditioned place preference (CPP) develops in male mice. For five days animals were pre-treated with a daily injection of one of the following doses of morphine (0, 5, 10 and 20 mg/kg). After an interval of three days, animals started the place conditioning procedure. During the conditioning phase mice were injected with different doses of morphine (0, 2, 3 and 5 mg/kg) to evaluate the acquisition of place preference. Animals which received physiological saline during pre-treatment only develop morphine-induced CPP with 5 mg/kg. Only the pre-treatment with 20 mg/kg of morphine produces the acquisition of CPP in animals conditioned with 2 mg/kg of morphine. Thus, morphine produces conditioned rewarding effects with doses above 5 mg/kg and the pre-treatment with 20 mg/kg of morphine potentiates the effects of an ineffective, sub-rewarding dose of morphine, demonstrating the induction of sensitization to its rewarding effects.

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E2. Physical, verbal and indirect aggression: sexual differences and hormonal correlations in 7-8 years old children

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Objective: This study analyses the sexual differences and hormonal correlations in three types of aggression. Method: To this end, we selected a sample of 7-8 years old children (34 boys and 44 girls). Their scores in three types of aggression (verbal, physical and indirect) were obtained thanks to a specific questionnaire (Direct and Indirect Aggression Scales, DIAS) administered by the subjects' teachers. Hormonal levels (testosterone and estradiol) were measured using an enzyme immunoassay in saliva samples. Results: Significant sexual differences were found in physical aggression (with higher scores among boys than among girls) and in indirect aggression (with higher scores among girls than among boys). No differences were found regarding verbal aggression. With regard to the hormonal correlations of these differences, a significant relationship was found between the scores for indirect and verbal aggression and estradiol levels in girls. No relationship was found between testosterone levels and any of the different types of aggression. Conclusion: We believe that estradiol may be a useful biological marker for indirect and verbal aggression in 7-8 years old girls. This finding should be confirmed by further studies.

E3. Effects of Anterior Cingulate Cortex (ACC) lesion in the control of stress responses in the rat

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The Anterior Cingulate Cortex (ACC) is an area of the Prefrontal Cortex related to fear, stress and anxiety. The aim of this study was to evaluate the effect of the ACC lesion on two tasks: inhibitory avoidance (conditioned fear) and one-way escape (unconditioned fear) in the elevated T-maze. In a second experiment, the effect of a previous acute stress procedure was assessed in the same tasks. Twenty-nine Sprague Dawley (OFA-SD) adult male rats (250-350 g) were used. Animals were randomly assigned to four groups: ACC lesion ($n = 8$), sham lesion ($n = 8$), ACC lesion + immobilization during 3 hours ($n = 8$), sham lesion + immobilization during 3 hours ($n = 5$). Each task was preceded by a 30 min habituation period. Our results indicate that ACC lesion (Cg1, Cg2 and Cg3) reduces anxiety responses in the passive avoidance task. Moreover, acute stress induces enhanced conditioned and unconditioned responses mediated by the activation of the ACC. This could suggest that the ACC regulates the intensity of the conditioned fear responses as a modulator of other brain areas implicated in the control of these emotional responses.

E4. Relationships between illness, stress and social behavior in 5-6-year-old children

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Objective: This study analyses the influence of illness on stress levels and types of social behavior demonstrated by 5-6 years old children. Method: The behavior of a sample group of 47 children (23 boys and 24 girls), during free play in the playground, was studied for two school years by means of systematic observation. Each child's level of cortisol was measured in saliva samples, which were collected on two non-stress related occasions and one stress-related occasion. Furthermore, the children's pediatricians provided information regarding each individual's state of health/illness. Results: The results show a positive relationship between chronic illnesses suffered by the children and their basal cortisol levels. Behavior, divided into factors, also showed a relationship with chronic illness. The behavioral factors positively related to the existence of chronic illness were subordination and receipt of aggression; a negative relationship was found between chronic illness and the avoidance-receipt of threat and the manipulative leadership behavioral factors. Conclusion: Chronic illness may represent a source of early stress that modifies a child's relationship with his or her environment from both a physiological and social perspective.

E5. Differential regulation of PSA-NCAM in CA3 – mossy fibers of rat hippocampus induced by chronic stress and spatial learning

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Exposure to chronic restraint stress (CRS) induces a variety of morphological changes in the hippocampus and impairs spatial learning (SL) (Magariños and McEwen 1995, Sandi et al. 2003). Polysialylation of the neural cell adhesion molecule (PSA-NCAM) regulates cell-cell interactions and contributes to synaptic remodelling. We found previously that CRS and SL induce contrasting patterns in PSA-NCAM immunoreactivity (PSA-NCAM-ir) in the associated temporal cortex-hippocampus circuit. Moreover, CRS induced a loss of simple unperforated synapses in striatum lucidum of CA3, whilst SL reversed this effect; a finding which provides a neuroanatomical basis for the suggested stress-suppressing and learning-inducing plasticity properties. Here, we investigated whether modulation of PSA-NCAM-ir in CA3-Mossy fibers of the rat hippocampus was related to the observed CRS- and/or SL- induced synaptic remodelling. Rats were exposed for 21-days to CRS and/or SL, and PSA-NCAM-ir in the CA3 was evaluated using combined immunocytochemical light and electron microscopic analyses. Data show that CRS and SL exert contrasting effects on PSA-NCAM-ir. Interestingly, a positive correlation was found between learning and PSA-NCAM-ir. Therefore, these results provide further support to the idea of involvement of PSA-NCAM in hippocampus-dependent memory processes.

E6. Archistriatal lesions in quail chicks impair adult fear behaviour

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The avian archistriatum appears to be at least in part homologous with the mammalian amygdala. In order to investigate the function of the archistriatum, 3-5 day-old quail chicks from a line selected for long duration of tonic immobility (a fear-related behaviour) were given bilateral archistriatal lesions (ARCH), bilateral lateral cerebral area lesions (LCA), or were unoperated (U). At 12 weeks old, the quail were given 3 tests of neophobia: 1) response to a novel object, 2) response to a human and 3) response to novel food. The quail were then killed and their brains taken for histology to verify the lesions. Behavioural data were analysed with the Kruskall-Wallis test followed by post-hoc comparisons with the Mann-Whitney U test. There were significant effects of treatment on response to a novel object (P=0.023), latency to peck novel food (P=0.013) and time spent pecking/eating (P=0.007), but response to a human just failed to reach significance (P=0.065). There were no significant differences between U and LCA quail in response to a novel object, latency to peck novel food and time spent pecking/eating. Therefore, U and LCA quail data were pooled. ARCH quail showed significantly less avoidance of a novel object (P=0.022), shorter latencies to peck novel food (P=0.004) and more time pecking/eating novel food than U+LCA quail. These results support a role for the archistriatum in the expression of fear behaviour.

E7. Effects of chronic stress and learning on 3-dimensional synapse and spine morphometry in CA3 of rat hippocampus

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Exposure to chronic restraint stress (CRS) in rats results in cognitive impairment and a variety of morphological changes in hippocampus, including loss of dendritic arborisation. We have demonstrated that CRS induces a loss of simple unperforated synapses in stratum lucidum of CA3, whilst spatial learning reverses this effect (Sandi et al., Europ J Neurosci, in press). Here, detailed quantitative electron microscope analyses were made of the thorny excrescences in CA3 and their synaptic contacts following CRS and/or spatial learning. Thorny excrescences are spine complexes which consist of a stalk connected to several thorns which have both perforated and unperforated post-synaptic densities (PSDs). We utilized 3D reconstruction of over 100 serial ultra-thin sections from each group of rats. Following stress, there is a marked retraction of thorns with a change in the structure of the PSDs; these processes are reversed 24 h following water maze training. In addition, in water maze trained rats, there is an increase in endosome content, particularly multivesicular bodies in thorns and an increase in polyribosomes (rough endoplasmic reticulum and free polysomes) for both dendritic segments and thorny excrescences.

E8. What does noradrenaline do in the hypothalamus during oestrus?

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During oestrus, exposure of ewes to male cues induces an increase in noradrenaline (NA) concentration in the medio basal hypothalamus (MBH (1)). Similar observations have been made in rats after mating (2). These results suggest that NA is implicated in the perception and/or the behavioral response of the female to the male. To test this hypothesis, we observed behavioral changes (proceptivity and receptivity measured according to (3)) after administration by retrodialysis of NA or NA antagonist (phenoxybenzamine: Phe) through probes aimed at the MBH. NA (10 µg/ml) was administered for 2 hours to ovariectomized ewes submitted to artificial oestrus cycle (Progesterone priming followed by E2 IM injection). When given 15 h after E2 NA increased both proceptivity and receptivity 30 min later (n = 7, P<0.03 and 0.05) and only proceptivity 2h later (P<0.05). When given 18 h after E2, only proceptivity was increased 30 min later (P<0.05). On the reverse Phe (100 µg or 1 mg/ml) administration to intact ewes during oestrus decreased proceptivity 30 min in 4/4 ewes (1 mg) or 3/4 ewes (100 µg) and in all ewes 2 h later with both doses. No other change in behaviour could be detected in the females after NA or Phe. These results support our hypothesis.

(1) Fabre-Nys et al. (1997) Eur J Neurosci 9: 1666-1677
(2) Etgen et al. (1992) J Neuroendocrinol 4: 255-271
(3) Fabre-Nys and Venier (1987) Appl Anim Behav 17: 289-304

E9. Sensitization to the conditioned reinforcing properties of Diethylpropion

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Diethylpropion (DEP) is an appetite-suppressing catecholaminergic agent widely used in Brazil and other countries. It has been proposed that sensitization plays a critical role in drug addiction. The aim of the present study was to evaluate whether sensitization occurs to the reinforcing properties of DEP, assessed through the unbiased conditioning place preference paradigm (CPP). In the sensitization phase rats received injections of Saline (Control Group) or 20 mg/kg DET (Sensitization Group) for 5 consecutive days. A place preference pre-conditioning session was run 72 h after the last injection of the sensitization phase, followed by four conditioning sessions with 5 mg/kg DET. Both groups demonstrated CPP in the test session, and such effect was enhanced in the Sensitization Group. After the CPP test two extinction sessions were conducted. No difference in resistance to extinction was observed between groups. This is the first study demonstrating sensitization to the reinforcing properties of DEP in the CPP paradigm. Besides, place preference was conditioned to a DEP dose lower than those previously reported. The results confirm the abuse potential of DEP.

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E10. Hippocampal mineralocorticoid receptors are related to anxiety behavior and spatial learning abilities

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Individual differences in anxiety-related behavior could be the consequence of several factors, such as differential activation of neural circuits and/or hypothalamic-pituitary-adrenocortical axis, coping style, or previous experiences. Central mineralocorticoid (MR) and glucocorticoid (GR) receptors have been shown to be involved in emotional and cognitive processes, two psychobiological functions which could mutually interact. In this study we investigated: i) the relationship between hippocampal MRs and GRs and anxiety levels and; ii) whether anxiety can modulate performance in a spatial learning task. For this purpose, male Wistar rats were firstly tested in an elevated-plus maze and classified according to the time they spent in its open arms, as HA (high anxiety) and LA (low anxiety). For each anxiety trait, one group of rats was left undisturbed and sacrified one week later; whereas another group was handled, trained in a Morris Water Maze (6 trials), and subsequently sacrified. The results show that, both in untrained and trained animals, there is a positive correlation between hippocampal MR levels and time spent in the open arms, with MR levels being higher in LA than in HA rats. Moreover, in the water maze, HA had a slower acquisition curve than LA rats, mainly because they used a less effective strategy (thigmotactic swimming) during the trials. In conclusion, hippocampal MRs seem to be associated with the expression of anxiety-related behavior and spatial learning abilities in the water maze.

E11. X-linked gene dosage effects on fear, pre-frontal dopamine and GABAA alpha-subunit gene expression

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We examined the role of X-linked gene dosage effects on brain functioning in mice. We found a gene dosage effect on fear reactivity as measured by the elevated-plus maze in 39,XO compared to 40,XX mice, that was unconfounded by activity and reactivity to novelty. Specifically, 39,XO mice spent less time on and made fewer entries into the open arm. Furthermore, when we examined the monoamine content of dissected regions of the brains of these mice we found a reduction in dopamine (DA) levels in the medial prefrontal cortex (mPFC) compared to 40,XX mice. Given the role of GABAA receptors in fear mediated behaviours, and in particular of those receptors containing the X-linked alpha3 subunit in mediating monoamine turnover, we looked at the relative levels of alpha subunit gene expression in the brains of our mice using Real Time quantitative PCR. We found significant changes in expression of the alpha1 (decrease) and alpha3 (increase) subunits in the brains of 39,XO compared to 40,XX mice. Expression levels of the alpha2 subunit and a number of other genes were unaltered between the two groups. These results imply that there is a gene(s) on the X-chromosome that acts in a dosage dependent manner to influence alpha subunit expression, and possibly therefore the subunit composition of GABAA receptors. This in turn effects DA levels in the mPFC and fear reactivity.

E12. Normal and anomalous grooming in stress and behavioral genetics research

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Grooming (G) is a sensitive marker of stress in neurobehavioral research in rodents (1). Its traditional measures include latency, frequency and duration. However, sophisticated ethological analysis of G may reveal behavioral alterations not detected by traditional approaches (2). In the open field or holeboard tests, (peripheral:central G), (G in:out of protected homebase), (G associated with defecation (D)/urination (U):unassociated) are the markers of stress. Pre-U/D vs. post-U/DG indicates increased anxiety. In the elevated plus maze, (closed arms:open arms G) increases in stress. Stress also increases abortive (incomplete) vs. complete G and/or shifts abortive G to more aversive areas. Anomalous G type (observed in totally inappropriate situations, when it is physically difficult to groom) is a unique marker of behavioural abnormalities. This pattern is useful for behavioural genetics studies since it is common for many transgenic animals (e.g., ablation of neurosteroid Vitamin D receptors produced anomalous G (paw licking and head wash) in 10-20% and 50% of mice in vertical screen retention and the horizontal rod balancing tests. These patterns are seen with other stress-dependent behavioural abnormalities. In our research we show how ethologically analysed G can be a useful marker of behavioural alterations induced by stress, genetical manipulations or both. References: (1) Kalueff A. (2002) Grooming and stress, Moscow, 164p; (2) Kalueff A. (2000) Measuring grooming in stress and comfort, MB-2000 Abstracts.

E13. Programmed fertility is impaired by sympathetic nerve activation. Role of stress-induced hypothalamic TRH secretion

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Activation of sympathetic nerves develops polycystic ovary in the adult rat. In women, polycystic ovary (PCO)syndrome is usually developed before puberty and expressed during adulthood. In this work, we studied the consequence of a prepubertal ovarian nerve stimulation on fertility during adulthood in the rat, the participation of stress (cold) and the role of TRH as mediator in such stress. Prepubertal activation of sympathetic nerves accelerates puberty, steroid secretion and develops PCO during adulthood, changes reversed after section of ovarian nerves. Cold stress also activates sympathetic nerves and develops ovarian cysts. To know the central neurotransmitter involved, we applied *in vivo* TRH into the third ventricle and we also found activation of sympathetic nerves as cold stress did, suggesting that TRH released at paraventricular nucleus (PVN) participates in the sympathetic responses to stress. To test this possibility, we used push-pull canulla implanted in PVN to study the changes in the *in vivo* TRH secretion during the stress. Cold stress during 64 h increased TRH secretion, suggesting that TRH mediates the cold-induced ovarian sympathetic nerves stimulation and participating in programming the infertility condition that is maintained during adulthood.

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E14. Homologizing human reward systems

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Comparative psychology has established that variations in the magnitude of food rewards produce motivational shifts in performance. Theories of motivation suggest that a number of distinct psychological processes, with distinct neural substrates, contribute to such motivational effects, including both Pavlovian and instrumental incentive processes. In the current study, we examined whether the neural circuits mediating the motivational effects of cultural (monetary) rewards in humans are homologous to those mediating the motivational effects of food rewards in other mammals. Nine healthy volunteers were scanned with H2[15]O PET whilst performing a spatial search task that involved searching for hidden monetary rewards of different values (zero, low, medium, high). PET data were analyzed with SPM 99. Behaviourally, increased reward magnitude was associated with improved task performance. A correlational analysis revealed that activity in several regions, including the amygdala, pulvinar, anterior cingulate and orbitofrontal cortex, increased with increasing reward magnitude, areas previously established as critical for food-related Pavlovian and instrumental motivational processes in rodents and primates. Thus, the neural circuitry mediating the motivational influences of money in humans appears homologous to that mediating the motivational effects of food rewards in other mammals.

E15. Differential involvement of mesocortical and thalamocortical pathways during either acquisition or retention of morphine self-administration into the lateral septum

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To test the hypothesis according to which the septum represents an interface between learning and reward processes, we trained mice to self-administer morphine (5 or 20 ng) into the lateral septum (LS) by a spatial discrimination in a Y-maze. We then used complementary pharmacological and c-fos imaging approaches to identify the neuronal substrates of this behavior at different stages of learning, i.e., after either 6 (acquisition) or 11 (retention) self-administration (SA) sessions. During acquisition, vehicle-pretreated (NaCl i.p.) mice acquired SA behavior, whereas mice pretreated with either an opiate antagonist (naloxone 4 mg/kg i.p.) or a dopaminergic antagonist (D1: SCH23390 mg/kg i.p. or D2/D3: sulpiride 50 mg/kg i.p.) did not. Twenty-five self-administering animals displayed specific high levels of Fos expression in the dorsal hippocampus, mammillothalamic pathway, prelimbic, cingulate and retrosplenial cortices. Concerning retention, mice pretreated with an antagonist during the last 5 sessions showed a rapid extinction of SA performance whereas vehicle-pretreated mice maintained their SA response. Patterns of Fos staining specific to self-administering animals was then restricted to the mammillothalamocortical tract. The results provide evidence for an influence of the LS, *via* the dopaminergic system, on the time-dependent involvement of mesocortical and thalamocortical pathways in instrumental conditioning.

E16. The "one-trial tolerance" effect is modulated by the base-line of anxiety of rats

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One of the most popular animal models of anxiety is the elevated plus-maze. It is argued that this model is highly sensitive to the influence of benzodiazepine/GABAA manipulations (Rodgers et al. 1997). However, an intriguing feature in this model is the absence or attenuation of the effects of benzodiazepines in a second trial in the maze, an effect known as "one trial tolerance" (File 1990). As the efficacy of drugs may depend on the animal's basal level of anxiety (Landgarf and Wigger 2002), the purpose of this study was to asses if the "one-trial tolerance" effect can be modulated by the base-line of anxiety. Although most studies employ a test-retest design, we were interested in studying the effects of Diazepam along various trials. Thus, a group of rats were divided into high- and low-anxiety based in a median split of their performance in a test trial on the elevated plus-maze. During five more trials, rats were injected with Diazepam and retested in the maze. We found that low-anxiety, but not high-anxiety rats, are responsive to Diazepam in a second trial in the maze. These between-groups differences are attenuated in successive trials.

E17. Individual differences in schedule-induced polydipsia: pharmacological and behavioural evidences

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Schedule-Induced polydipsia (SIP) belongs to a larger class of adjunctive behaviour, characterised by excessive, non-regulatory drinking by food deprived animals in response to the delivery of small amounts of food. However, some, but not all, rats given food intermittently display SIP. The current experiments were designed to examine in more detail if high and low drinker animals (HD-LD) exhibit different patterns of behaviour following a known model which asses anxiety, such as the elevated plus maze, and pharmacological manipulations of the gabaergic and the dopaminergic systems. After SIP was acquired animals were tested in the elevated plus maze. No differences were found between HD and LD on this test. Rats were then tested to evaluate the effects on SIP of an anxiolitic drug like diazepam (0, 0.3, 1, 3 and 5 mg/kg), an anxiogenic drug like PTZ (0, 5, 10, 15 and 20 mg/kg) and two dopaminergic drugs such as d-amphetamine (0, 0.25, 0.5, 1, 1.5, 2, and 4 mg/kg) and cocaine (0, 0.25, 5, 10 and 20 mg/kg). Only d-amphetamine and cocaine showed a different effect on HD and LD while animals with PTZ and diazepam behaved similarly. Altogether, these data seem to suggest that the dopaminergic system could be underlying these differences between HD and LD.

E18. Ten days social chronic stress induces astrocytary changes and behavioral alterations in young rats

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Some social stimuli increase glucocorticoid levels affecting brain function and behavior in young individuals. Previous studies have shown changes with 40 days stressed rats. Young male rats (21 days old) were assigned for 10 days to Control (C), Overcrowding (O), Noise (N) and Overcrowding/Noise (ON) groups. Hole-Board and Morris Water Maze were used as behavioral tests. Astrocytic changes were analyzed using anti-glial fibrillary acidic protein (GFAP) and anti-proliferating cell nuclear antigen (PCNA). In cortex, only ON showed a significant increase of GFAP immunoreactivity (GFAPi) (P<0.05), although N and O also had higher levels than C. CA1 showed increased GFAPi for N and ON (P<0.01) as well as high PCNAi for N (P<0.05). An elevation of GFAPi and PCNAi in CA3 and dentate gyrus (DG) was observed in O and N (P<0.05). These changes were stronger in hippocampus than in cortex, probably due to the higher glucocorticoid receptor density of the former. Stressors had a differential effect in their hippocampal impact: O and N were associated with astrocytary changes in CA3 and DG, whereas ON was related with CA1. Compared to C, all groups had higher locomotor activity and less central visits in their exploration and had worse spatial learning and memory. Stress situations probably increased excitability and anxiety in the exploratory behavior due to glucocorticoid increase.

E19. Dissociation of maternal care and adult offspring's stress and fear responses in rats

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In mammals, the early mother-infant relationship plays a crucial role for the offspring's later responses to environmental challenge. In rats, brief (15 min) daily maternal separations during postnatal days 1-10 (PH) reduce adult stress reactivity and fearfulness compared to undisturbed controls (UC). These effects have been proposed to be mediated by enhanced maternal care induced by PH. In contrast, long (4 h) daily maternal separations (MS) from postnatal day 1-10 were claimed to produce opposite effects to PH. However, present evidence indicates that MS and UC have similar effects on the offspring's stress and fear responses, while the effect of MS on maternal care remains to be studied. To examine whether the effects of PH and MS on the offspring's stress and fear responses can be explained by effects on maternal care, maternal behavior was scored at 3-min intervals for 60 min every third hour from postnatal day 1-10 in Lister hooded rats subjected to PH, MS or UC. Both PH and MS induced enhanced maternal care compared to UC, while only PH, but not MS, resulted in reduced plasma ACTH and corticosterone responses to 20 min restraint stress and behavioural signs of reduced fear to novelty in the adult offspring. Thus, neonatal maternal separations have dissociable effects on maternal care and on the offspring's stress and fear responses.

E20. Exposure to acute stress blocks the induction of long-term potentiation of the amygdala-prefrontal cortex pathway *in vivo*

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In recent years, attention is given to the interaction between the emotional state of the animal and its ability to learn and remember. Studies into the neural mechanisms underlying these interactions have focused on stress-induced synaptic plasticity impairments in the hippocampus. However, other brain areas, including the amygdala and the prefrontal cortex (PFC), have been implicated in stress-mediated effects on memory. The present study examined whether stress, which impairs hippocampal long-term potentiation (LTP), also affects LTP of the basolateral amygdala (BLA)-PFC pathway *in vivo*. We first confirmed that the stress protocol we employed, i.e., the elevated platform stress, was effective in blocking LTP in the CA1 area of the hippocampus. We then characterized activity and established the ability to induce LTP at the BLA-PFC pathway. Finally, we examined the effects of an exposure to the elevated platform stress on the ability to induce LTP in this pathway. The results indicate that, at the same time when LTP is blocked in the hippocampus, it is also inhibited in the BLA-mPFC pathway. These results call for a shift from a focused attention on the effects of stress on plasticity in the hippocampus to a system level approach that emphasizes the possible modification of interactions between relevant brain areas following an exposure to a stressful experience.

E21. A correlational study of TH mRNA expression with the HPA axis and behavioural traits in Sprague-Dawley rats

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Some studies have shown a relationship between the activation of the hypothalamic-pituitary-adrenal (HPA) axis and some behavioural traits in rats (anxiety or novelty seeking). In addition, other studies have demonstrated differences in dopaminergic (DA) system related to novelty seeking trait. We then studied the relationship between basal tyrosine-hidroxilase (TH) mRNA in some DA nuclei (ventral tegmental area, VTA; substantia nigra pars compacta, SNc; and A13) and: (i) anxiety (as measured by the elevated plus maze) and novelty seeking (as measured by activity in a circular corridor) traits, (ii) basal expression of some variables related to HPA axis. Anxiety was negatively correlated with TH mRNA expression at VTA and A13, whereas novelty seeking negatively correlated with TH mRNA at SNc. SNc TH mRNA did not correlate with any variable of the HPA axis. In contrast, TH mRNA levels in VTA and A13 showed a negative correlation with hippocampal glucocorticoid receptors mRNA levels, and a positive correlation with CRF mRNA levels in the paraventricular nucleus and the central amygdala. The present correlational studies suggest new interesting relationships between the DA system, the HPA axis, and anxiety and novelty seeking traits in rats.

E22. Sexual attraction through pheromones in mice: from behaviour to brain

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Using chemically naive females, we demonstrated that they were innately attracted by male-derived non-volatile chemicals. We have undertaken the search for the neural pathways underlying this innate attraction by assuming that: 1) non-volatile pheromones are detected by the vomeronasal organ, and 2) the attractive properties of sexual pheromones are indicative of their rewarding value. Thus, here we report the neural connections linking the vomeronasal organ with the tegmento-striatal pathway (reward system), as revealed in mice by the intraaxonic transport of stereotaxically injected dextranamines. The results indicate that the accessory olfactory bulb projects to the medial amygdala (Me), bed nucleus of the stria terminalis (BST) and posteromedial cortical amygdala (PMCoA). Dextranamines injected into the nuclei of origin (ventral tegmental area, VTA) and termination (accumbens, Acb) of the tegmento-striatal pathway retrogradely labelled a few cells in the anterodorsal Me and BST. However, a massive projection to the Acb arises from the basolateral and basomedial amygdaloid nuclei, which, in turn receive convergent projections from the Me and PMCoA. Thus a direct but weak projection to the VTA and an indirect one to the Acb arise as the more likely pathways mediating of vomeronasal stimuli to the reward systems of the brain.

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E23. Bidirectional plasticity in CA3 cells of the hippocampus, following chronic stress

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Chronic stress leads to cellular atrophy in the hippocampus and consequent loss of hippocampus dependent memory. Our previous study showed that the chronic immobilization stress (CIS) causes more atrophy compared to that of the chronic unpredictable stress (CUS). Moreover, CIS leads to an increase in spines and CUS causes a decrease. Surprisingly, long-term potentiation (LTP) of the CA3 cells following 10 days of CIS did not show any change, although CUS showed a marginal increase. This effect was striking because memory impairment following chronic stress does not seem to follow the synaptic changes. As an important follow-up of this finding to understand how the deficits in hippocampal memory correlate with the degenerating cells, we extended our 10 days chronic immobilization stress protocol to 21 days. Following 21 days of chronic immobilization stress, basal synaptic transmission is increased as measured by input-output curve and paired-pulse facilitation. We also found that the depotentiation, a measure of reversibility of potentiation, was completely blocked, in contrast to normal animals and also animals subjected to 10 days of chronic immobilization stress. Our results indicate a perpetual increase in excitability of the CA3 cells, following exposure to chronic stress. Since, the CA3 cells form the central element of the hippocampal tri-synaptic circuit, which encodes new memories, the structural and functional changes in them will act as a potential factor that underlies stress-related memory deficits.

E24. Innately attractive sexual pheromones induce c-fos in the accumbens but not in the ventral tegmental area

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Chemically naive female mice are attracted by male-derived non-volatile chemicals. To understand the neurobiological basis of this attraction, c-fos expression was studied in the brains of chemically naive females (n = 12) that were introduced in a two-choice testing cage where they could explore clean vs. male-soiled bedding. After 90 minutes within the testing cage, the females were perfused and the c-fos was revealed in their brains with specific antibodies. Using a novel image analysis protocol, the labelling obtained in these females was quantified and compared with that of control females that had clean bedding in both sides of the cage. Significant differences in the expression of c-fos between control and pheromone-exposed females were observed in the accessory olfactory bulb. Induction of c-fos in the shell (but not the core) of the accumbens by sexual pheromones suggests an activation of the tegmento-striatal "reward" pathway. However, the ventral tegmental area showed no c-fos expression in either control or pheromone-exposed females. Thus, vomeronasal stimuli should reach the accumbens using alternative neural pathways, such as amygdalo-accumbens projections. This possibility is being explored by analysing the induction of c-fos by male pheromones in the nuclei of the amygdala that project to the accumbens in chemically naive females.

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E25. Brain c-fos expression after open field stress in rats: influence of social position and responsiveness to novelty

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This study was aimed to verify the hypothesis that animals showing individual differences in behavioral characteristics would have different pattern of the central activatory processes when exposed to open field stress. Male Wistar rats were divided into the subgroups of high (HR) and low (LR) responders on the basis of their locomotor response to a novel environment (Columbus actometer) and into the dominant (D) and submissive (S) ones on the basis of the social interaction test. A week after completion of behavioral screening each animal was placed for 30 minutes in the open, brightly lighted field (OF) (1000 x 1000 x 600 mm). The control rats were placed in their home cages next to the OF. Immunohistochemical detection of Fos protein was performed 30 minutes after the end of an experimental session. It was found that exposure to stressor evoked marked increase in the brain c-fos expression in all behavioral groups. HRs had higher number of Fos+ neurons in the majority of brain structures in comparision to LRs, significant for the globus pallidum, lateral and medial septum, amygdaloid nuclei, bed nucleus of the stria terminalis, ventromedial thalamic nuclei and zona incerta. C-fos expression was higher in D rats than in the S ones in all tested structures. The highest overall brain c-fos expression was found in the D/LR rats.

E26. Individual differences and hypothalamic-pituitary--adrenal axis after chronic stress in Sprague-Dawley rats

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The aim of this study is to ascertain the relationship between individual differences in anxiety (as measured by the elevated-plus maze) and novelty-seeking (as measured by the circular corridor) and the hormonal reactivity of the hypothalamic-pituitary-adrenal axis (HPA) (as measured by ACTH and corticosterone) to immobilization stress (IMO) after a chronic variable stress (CVS) procedure. To this end, the behavior in the plus-maze and the circular corridor was assessed and then the Sprague-Dawley rats (n = 64) were divided into two groups: control and CVS. The CVS procedure lasted 12 days and consisted of the exposure to several stressors: novel environment, restraint in tubes, electric shocks and forced swimming test. After this, all the animals were exposed to IMO stress for 30 min. Blood samples were taken immediately before the stress, just after the ending of IMO, and at 45, 90 and 180 min post-IMO. Results showed that CVS decreased ACTH levels in the post IMO period. Moreover, CVS increased basal corticosterone and immediately after IMO and 45 min post-IMO levels whereas slowed the recovery at 180 min. The animals that showed greater motor activity in the circular corridor (HR) presented higher ACTH levels immediately after IMO in comparison to the low-motor activity animals (LR), regardless of the previous stress experience. The CVS stress procedure only increased basal corticosterone levels in LR rats. These data suggest minor influences of CVS in the effect of the novelty-seeking trait on HPA activity.

E27. Stress-associated "readthrough" acetylcholinesterase enhances hippocampal long-term potentiation and fear memory

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Exposure of animals to conditioned stimuli paired with aversive stimuli is often used to reinforce memory consolidation of unpleasant events. The potentially pathogenic impact of this treatment makes it a suitable model for studying molecular mechanisms underlying psychiatric disorders (e.g., depression, post-traumatic stress disorder). Here, we report that mice exposed for 1 h to predominantly emotional stress (immobilization) showed a shift from the abundant "synaptic" acetylcholinesterase variant (AChE-S) to the normally rare "readthrough" variant (AChE-R) in CA1 hippocampal neurons. Hippocampal AChE-R levels reached their maximum 2-3 h after immobilization. These time points following stress exposure were paralleled by increased contextual fear conditioning and enhanced hippocampal long-term potentiation. Antisense oligonucleotides inducing selective AChE-R mRNA downregulation prevented the enhancement of contextual fear in stressed mice and eliminated stress-induced LTP facilitation. Our results suggest that stress-induced AChE-R upregulation enhances long-term contextual fear memory.

E28. Partial implication of cerebral protein synthesis and NMDA receptors in HPA axis desensitization after a single exposure to immobilization

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It has recently been demonstrated that a single exposure to different stressful stimuli induces a few weeks later a sensitization in the HPA axis response to a novel stressful situation. In contrast, we have observed that a single exposure to immobilization (IMO) causes in rats, days or weeks later, a central and peripheral desensitization of the HPA axis response to the same (homotypical) but not to a novel (heterotypical) stimulus. In addition, this desensitization process accentuates over time. Therefore, our results suggest that a single exposure to IMO triggers a learning-like process that maturates over time. In the present work we tried to block the induction or consolidation of this process using two different strategies: NMDA receptor blockade with MK801 (i.p.), and central protein synthesis inhibition with cycloheximyde (i.c.v.). In the two experiments we obtained a partial blockade of HPA desensitization at the level of corticosterone, but no changes observed in ACTH. The results suggest a partial implication of cerebral protein synthesis and NMDA receptors in the induction of the phenomenon, and a clear dissociation between ACTH and corticosterone, suggesting an ACTH-independent regulation of the adrenal gland after a previous experience with IMO.

E29. Comparison of the effects of two methods of main olfactory system impairment on olfactory discrimination and selective nursing of lambs by ewes

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Recently, Booth and Katz (2000) proposed that early olfactory recognition of the lamb by its dam depends mainly on the vomeronasal system (VNO), while Lévy et al. (1995) reported a role of the main olfactory system. This discrepancy could be partly due to a more invasive technique in the study of Lévy et al. (large quantities of $ZnSO_4$ solution were used), which would have resulted in lesions of the VNO. In contrast, Booth and Katz used small amounts of solution which may have induced incomplete lesion of the main olfactory epithelium. Two studies were performed comparing 1) olfactory impairment induced by each technique, and 2) their consequences on acceptance of an alien lamb at the 24 h postpartum. Both treatments resulted in behavioural anosmia in a two-choice test between food associated or not with a repulsive odour. However, in contrast with the results of Booth and Katz (2000), both techniques resulted in the loss of maternal selectivity, whereas intact dams were clearly selective. The histological examination of the VNO did not provide clear evidence that lesions of this structure were implicated in the loss of maternal selectivity. We conclude that the role of the VNO in selective nursing of ewes remains to be confirmed.

E30. Effects of neonatal handling on basal forebrain cholinergic system function, hippocampal corticosteroid receptors and spatial learning and memory in male and female rats

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A number of factors, including the basal forebrain cholinergic system, as well as corticosteroid receptors, type I (MR) and II (GR), along with the levels of circulating corticosteroids, influence the ability for spatial learning and memory, a process controlled by the hippocampus. The early experience of "handling" affects HPA function, which is also known to be sexually dimorphic. Based on the above we investigated the effects of "neonatal handling" in adult males and females on: (1) the number of ChAT cells and on AChE activity in the hippocampus-as indexes of BFCS function; (2) the ability for spatial learning and memory (in the Morris water maze) following an acute restraint stress (30 min) either prior to learning or recall; and (3) the number of hippocampal GR and MR after the termination of the Morris water maze test. In the females handling resulted in increased number of ChAT positive cells in the medial septum and increased AChE activity in the hippocampus, indicating a higher turnover in the BFCS system, an increase in hippocampal GR levels, but spatial learning and memory were not affected. In contrast, in the males, handling resulted in a higher ability for learning and memory, when the acute stress preceded learning of the MWM. This beneficial effect of handling on male cognitive abilities was accompanied by increased GR and decreased MR levels.

E31. Central cholinergic systems in rats of different responsiveness to novelty

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Individual differences in responsiveness to novelty are frequently used as an index of susceptibility to stress and drug addiction. In the present study we examined whether differences in behavioral characteristic can be attributed to the activity of the central cholinergic systems. Brains of rats divided according to their locomotor activity in a new environment (Columbus activity meter) into high (HR) and low (LR) responders were subjected to immunohistochemical staining of cellular choline acetyltransferase (ChAT). Density of the active cholinergic cells was estimated within the Ch1-Ch6 groups and in both dorsal and ventral striatal structures (interneurons). Generally, HR rats showed higher density of active cholinergic cells than LRs in the diagonal band nuclei (groups Ch2 and Ch3), medial septum (Ch1), pedunculopontine tegmental nucleus (Ch5), laterodorsal tegmental nucleus (Ch6), basal nucleus of Meynert (Ch4), ventral pallidum and nucleus accumbens. The results obtained indicate that behavioral differences between HRs and LRs are reflected in brain morphology, e.g., in the activity of the central cholinergic systems.

E32. Stress-induced activation of Fos-like immunoreactivity in the Japanese quail brain

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Little is known about the central control of behavioural stress responses in birds. Therefore, an experiment was designed to investigate the neural activation induced by stressful stimulation of Japanese quail. Adult quail were taken from their home cage and tonic immobility (TI), a fear-related behaviour, was induced for a minimum of 10 min. These quail were then placed in a holding cage with a companion quail. A second group of quail ("hold") were transferred from their home cage to a holding cage containing a companion. TI and "hold" quail were humanely killed 2 h after the beginning of the stressful stimulation and "control" quail were killed immediately after removal from their home cage. The brains were then processed for Fos immunocytochemistry, to reveal neuronal activation. Small numbers of cells with Fos-like immunoreactivity (FLI) were scattered throughout "control" brains. The density of FLI in a number of regions of TI and "hold" quail brains (including the lobus parolfactorius, ventral paleostriatum and paraventricular hypothalamic nucleus) exceeded that in "control" brains. However, there was no apparent difference in the neural distribution of FLI between TI and "hold" quail. Therefore, transferring a quail from its home cage to a novel environment, which is considered to be a mild fear-inducing situation, induced neural activation qualitatively similar to that associated with TI, a very strong fear reaction.

E33. Behavioral effects of oral Al exposure and restraint stress

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The aim of the present study was to evaluate the behavioral effects of long term oral aluminum (Al) exposure and stress. Male Sprague-Dawley rats (n =70) were randomly assigned to 6 groups: control (n = 11), prenatal stress (n = 12), Al (n = 12), pre and postnatal stress (n = 11), Al + prenatal stress (n = 12) and Al + pre- and postnatal stress (n = 12). Al was administered orally 0 and 100 mg/kg/day from conception. Stress consisted in 2 h/day of restraint on gestation days 7-20 (prenatal) and during 15 days before test (postnatal). Animals were monitored weekly for body weight, water and food consumption. At one year of age, rats were evaluated in an open-field and in a water maze task. Results show body weight differences between control or prenatal stressed and all the other groups (P<0.001). An overall effect of stress was observed on activity levels (P=0.033). This effect was mainly due to prenatal stress. In the water maze, although animals in the Al group performed worse than the rest of subjects, no significant differences could be seen during the acquisition period. In the probe trial, time spent in the target quadrant was significantly lower in the Al only group. In general terms, prenatal stress increases activity during the first 5 minutes. This increase was only maintained in rats exposed to both Al and prenatal stress. Learning was only impaired in rats given Al only while stress seems to reverse Al effects.

E34. Postnatal manipulation leads to increased behavioural and cardiophysiological reactivity to aversive challenge in adult Fischer rats

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Early life stress is known to enhance vulnerability to develop neuropsychiatric diseases, including depression, in adulthood. A major diagnostic symptom of depression is negative mood, including feelings of helplessness. A common associated feature of depression is altered cardiophysiological function, including hypertension. We investigated the effects of postnatal environmental manipulation in pups of the inbred Fischer strain on behavioural and cardiophysiological responses to aversive challenge in adulthood. On days1-14 rat pups were isolated for 4 hours (early deprivation, ED), isolated for 15 minutes (early handling, EH), or left completely undisturbed (non-handling, NH). Adult males were tested in terms of: 1) effects of mild footshock pre-exposure (US-PE) in two-way active avoidance (2WAA); 2) blood pressure and heart rate responses to tone-footshock (CS-US) conditioning using telemetry. Following US-PE, ED rats demonstrated increased escape failure in 2WAA compared to their NH and EH counterparts. Following CS-US exposure, ED rats demonstrated a prolonged increase in blood pressure and heart rate compared to NH and EH. This study provides behavioural and cardiophysiological evidence that ED in the Fischer rat constitutes an animal model for the study of depression.

E35. Cost-benefit assessment in rats

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Wistar rats (n = 10) were trained in two different paradigms as part of a research programme into the underlying neuromechanisms of long term efficiency in behaviour. Rats were trained in two maze learning tasks measuring different kinds of cost-benefit analysis: balancing the amount of palatable and non-palatable pellets and balancing the height of barriers and number of pellets. Rats showed a consistent individual different sensitivity for the amount of sugar pellets, and learned to obtain either 3 (n = 5) or 5 (n = 5) sugar pellets in one arm of the maze and 1 pellet in the other. After a stable baseline response (75% choices on the high reward side per 20 trials) rats were either: (i) exposed to a test situation in which the net gain of the high reward and low reward side was gradually changed in favour of the low reward side by including gradually more and more quinine saturated sugar pellets per 10 trials, or (ii) exposed to a test situation in which the net gain of the high reward and low reward side was gradually changed in favour of the low reward side by including gradually more and more barriers per 10 trials. Rats only partially (3 pellet) or not at all (5 pellets) shifted their preference to the most favourable side in the first test condition while they did fully so in the second test condition with no relative difference between 3 and 5 pellets. These data suggest that rats assess the costs of crossing barriers to obtain pellets different by the costs of running into non-palatable pellets.

E36. Effects of a sub-chronic diazepam exposure on social behaviour related to food in rat groups exposed to the diving-for-food situation

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The “diving-for-food” situation is a complex social task that consists of rats swimming in apnea to reach food through a fully immersed swimming pool, bringing a pellet back to the cage and eating it. The progressive immersion of the way of access to the feeder induces the emergence of a social differentiation in a group of 6 rats between the “carrier” rats who dive and swim to get food, and the “non-carrier” animals who never dive and get their food only by stealing it from carriers. Previous results suggested a role of anxiety toward water in the acquisition of the carrier profile. The purpose of this study was to investigate the anxiogenic aspect of the social context of this task and its implication in the carrier/non-carrier differentiation. Six carrier/non-carrier differentiated groups of 6 rats each were treated with diazepam (0.5 mg/kg/day, i.p., 5 days) (DZ) whereas control animals were injected with saline (SAL) (6 groups) or vehicle (VEH) (6 groups). DZ as VEH had no effects on the carrier/non-carrier ratio compared to SAL. Concerning the food exchanges, DZ significantly decreased the quantity of food lost by theft in both carriers and non-carriers whereas VEH did not. These results suggest that DZ-treated rats are more efficient to protect their food through the reduction of the level of emotionality and confirm that anxiety related to the social context may participate in the emergence of the behavioural differentiation.

E37. Reward, prediction errors, uncertainty and dopamine neurons

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Results from lesioning and psychopharmacological studies suggest an involvement of dopamine systems in processing reward information. We found that dopamine neurons respond to rewards, reward-predicting stimuli and certain attention-grabbing stimuli. Rather than signalling rewards as they occur, dopamine neurons detect the extent to which rewards occur differently than predicted. This discrepancy can be called an "error" in the prediction of reward. Using formal learning paradigms, we found that the acquisition of dopamine responses was governed by reward prediction errors, as was the learning of behavioral reactions. Both behavioral and neuronal learning occurred predominantly when dopamine neurons registered a reward prediction error at the time of the reward. In another formal paradigm (conditioned inhibition) we assessed the extent to which dopamine neurons responded to the attentional components of rewards and found only a limited response. The suggestion of prediction error-coding was further tested with different reward probabilities. We found that phasic activations varied monotonically across the full range of probabilities. In addition, we observed a slower response which increased gradually until the potential time of reward. This response reflected the uncertainty of reward, as it was maximal at P=0.5 and decreased at higher and lower probabilities. These data suggest that dopamine neurons emit two different phasic reward signals related, respectively, to prediction errors and uncertainty.

E38. Behavioral phenotyping of GSK-3beta*f* knockout mice

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Glycogen synthase kinase-3 (GSK-3) is a multi-substrate serine/threonine protein kinase, highly abundant in brain. GSK-3 beta*f*s' substrates include: transcription factors, regulatory enzymes and structural proteins and it is suggested to play a role in multiple cellular processes including: metabolism, proliferation, differentiation and development, particularly neurodevelopment. GSK-3 beta null mutant mice are unviable and heterozygote mice do not show any obvious physical abnormality. No difference was found in brain morphology and histology of heterozygote mice. Reflexes, sensory and motor abilities were normal. Heterozygotes were not different from wild type in the prepulse inhibition model of schizophrenia or Porsolt forced swimming test model of depression. However, heterozygotes showed higher anxiety level, in the Open field test. Heterozygote females have clear deficits in maternal behavior, leading to maternal infanticide. *f*n 77% of heterozygous females (n = 34) killed all their pups, whereas in cages of only 13% of wild type females (n = 31) were dead pups. Neither pre-partum vanilla-smell, nor diazepam treatment prevented the infanticide. This finding could suggest a deficit in control of aggression or in bonding, and will be studied in specific behavioral paradigms.

E39. Early life experiences affect the serotoninergic system in the rat brain

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Early life events, particularly a perturbed mother-infant relationship, have been recognized as major factors for the development of psychopathology in adult life. An animal model simulating such conditions is "neonatal handling", in which rats are exposed to brief periods of maternal deprivation during the first 3 weeks of life. "Neonatal handling" is known to affect the hypothalamic-pituitary-adrenal axis and the responsiveness to stressful stimuli. Moreover, in the females "handling" enhances the expression of "depressive" behavior in animal models of the disease. Since the serotoninergic system, and especially 5HT1A receptors, has been implicated in the etiopathogenesis of depression, we investigated the effects of handling on the distribution of 5HT1A receptors in the adult rat brain. We employed *in vitro* binding quantitative autoradiography, using 3H-8-OH-DPAT as the ligand. Statistical analysis revealed that handling decreased the density of 5HT1A receptors in the hypothalamus, the frontal and the orbital cortex, in both sexes, whereas in the hippocampal dentate gyrus a decrease was found in females while an increase was detected in males. These data indicate that "neonatal handling" markedly affects serotoninergic receptors specifically in areas involved in emotional behavior. Moreover, the effects of handling on the serotoninergic system are sexually dimorphic thus possibly explaining the increased expression of "depressive" behavior by handled female rats.

E40. Generalisation of conditioned fear and its behavioural expression in C57Bl/6 inbred mice

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Mice are favourite subjects in molecular and genetic memory research and frequently studied with classical fear conditioning paradigms that use an auditory cue (conditioned stimulus, CS) to predict an aversive, unconditioned stimulus (US). Yet the conditions that control fear memory specificity and generalisation and their behavioural expression in such conditioned mice have not been analysed systematically. We addressed these issues in the most widely used mouse strain of behavioural genetics, C57Bl/6. First, various behavioural parameters were tested for their validity to describe conditioned and generalised fear in these animals. In keeping with findings in other species we could then demonstrate the dependence of fear memory generalisation on training intensity (i.e., both US intensity and the number of CS and US applied) after both excitatory (explicitly paired presentation of CS and US) and inhibitory training (explicitly unpaired presentation of CS and US). Inhibitory overtraining was further associated with changes of uncued anxiety-like behaviour in a light/dark exploration test, indicative of an emotional sensitisation reaction as consequence of a lack of US predictability. Our results describe the behavioural response to conditioned stimuli of different salience and identify training conditions that lead to fear memory generalisation and emotional sensitisation in C57Bl/6 inbred mice.

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E41. Functional involvement of hippocampal neurogenesis in antidepressants therapeutic efficacy following an unpredictable chronic stress procedure in mice

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Recent studies suggest that hippocampal neurogenesis modulation might underlie some functional changes implicated in depression and might be required for the therapeutic effects of antidepressants (ADs). However, this assumption is only based on correlational approaches. Therefore, we decided to explore the functional significance of the hippocampal neurogenesis modulation in depression pathogenesis and treatment. We used a X-ray irradiation specific to the hippocampus to disrupt neurogenesis in the dentate gyrus and confronted Balb/c mice with a five weeks chronic unpredictable stress (CUS). Various ADs treatments were applied from the third week of chronic stress until the end of the behavioural tests. The consequences of CUS were assessed on different measures (coat state, weight) and on two behavioural tests (Novelty Suppressed Feeding Paradigm-NSF- and Splash Test-ST-). CUS procedure induced a deterioration in coat state, an increase of the latency to eat in the NSF, a modification of grooming behaviour in the ST, and a decrease of hippocampal neurogenesis. ADs treatment reversed the behavioural and neurogenic effects of CUS in the non-irradiated mice, while irradiated mice were unresponsive to this treatment. On the other hand, we observed a lack of irradiation effect in no-stressed mice. This last result indicates that hippocampal neurogenesis disruption per se is not sufficient to induce a "depressed-like" state, whereas its relief would appear necessary for the ADs effects. This study provides evidence of a relation between hippocampal neurogenesis and depression, and suggests a functional involvement of hippocampal neurogenesis in ADs therapeutic efficacy.

E42. Dependence of phasic dopamine responses on reward magnitude

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Dopamine neurons are phasically activated by unpredicted reward, depressed when a predicted reward fails to occur and unaffected when a reward occurs as predicted. This indicates that they report an error in the prediction of reward which could be used as a reinforcement signal suitable for learning reward-driven behavior. According to formal learning theories, the effectiveness of such a signal is dependent on the magnitude of reward. We recorded extracellularly from single dopamine units in the ventral tegmental area and the substantia nigra. When reward was entirely unpredicted, or deviated from a standard magnitude, dopamine neurons reported the error in reward magnitude. In a second series of experiments, conditioned stimuli predicted one of two specific reward magnitudes at a probability of 0.5. Responses to the conditioned stimuli were roughly proportional to average reward magnitude they predicted. At the time of reward, neurons were depressed by outcomes smaller than predicted average and activated by outcomes larger than average. However, these depressions and activations were not graded by magnitude. These data suggest that dopamine neurons encode reward magnitude of unpredicted rewards but not magnitude of predicted rewards.

E43. Decrease in anxiety levels related to aging

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Two sessions of elevated plus maze were conducted in rats of different ages: young (3.3 months), middle-aged (16.8 months) and old (23.7 months). Old rats showed lower anxiety response than young rats in several variables: higher number of entries in open arms in the first session (P=0.002), higher time spent in open arms (P=0.012), and higher number of head dipping in the open arms (P=0.008). Middle-aged rats shown an intermediate anxiety pattern, with scores in the above mentioned variables intermediate from young and old rats (not statistically different from one or another), except for the number of open arms entries that is equal to young rats and lower to old rats (P=0.004). We conclude that there is a decrease in the levels of anxiety during aging that can be clearly seen in old animals. Middle-aged animals present a subtle (non significant) decrease in anxiety that must be taken into account in experiments dealing with anxiety related variables such as some kind of learning tasks.

E44. Long term effects of chronic stress on cognitive performance and hippocampal expression of cell adhesion molecules in HR and LR rats

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This study was designed to evaluate (i) whether differences in reactivity to novelty at youth could be related to long term effects of chronic stress on cognitive performance at senescence and (ii) whether individual differences in stress-induced cognitive alterations could be related to the hippocampal expression of cell adhesion molecules of the immunoglobulin superfamily. Four month-old rats were classified according to their locomotor reactivity to a novel environment, as either low (LR) or highly (HR) reactive, and then either submitted at 12 month-old to unpredictable stress for 28-days or left undisturbed until behavioral testing at 18 months. The results showed that unpredictable stress induced a marked deficit in spatial learning in the water maze in HR, but not in LR rats. Although chronic stress induced a reduction on the hippocampal expression of the NCAM180 isoform and L1, the levels of these molecules did not differ between HR- and LR-stressed aged rats. Nevertheless, when compared with their corresponding unstressed counterparts, the reduction on hippocampal expression of NCAM180 induced by prior stress exposure only reached statistical significance in HR, but not in LR rats. Therefore, our results support the view that HR rats are particularly susceptible to develop cognitive deficits at ageing as a consequence of prior stress exposure, and highlight NCAM180 as a possible molecule mediating such effects.

E45. Effects of chronic social stress on astrocytary reactivity, spatial memory and exploratory behavior in young rats

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Background: Animal social stress is a good model for human stress response. Some social stimuli elevate glucocorticoids disturbing brain cells and behavior in young individuals. Objectives: To analyze the effects of overcrowding and ultrasonic noise on hippocampal astrocytes, spatial memory and exploratory behavior. Methods: Young male rats (21 days old) were assigned to Control (C), Overcrowding (O) and Overcrowding and Noise (ON) groups. Glial reactivity and astrocytic proliferation were analyzed using anti-glial fibrillary acidic protein and anti-proliferating cell nuclear antigen. Results: The total number and proliferating population of astrocytes were increased in ON and decreased in O, as compared to C ($P<0.05$; Anova-Scheffé). Exploratory behavior in stressed groups showed higher mobility and less central visits in the Hole Board compared to C ($P<0.05$; Anova-Sheffé). Memory had no significant differences among groups. Conclusions: A soft stimulus as O decreases astrocytary reactivity by glucocorticoid-induced inhibition. In contrast, strong ones as ON increase astrocytary reactivity, likely by neuronal death. Both situations probably increased excitability and anxiety in the exploratory behavior due to a glucocorticoid increase. Social stress has important consequences both at brain and behavioral levels in young individuals.

E46. Reduced acoustic startle reflex response in mice lacking the cytosolic (B-CK), mitochondrial (UbCKmit), or both brain-type creatine kinase isoforms, important for maintenance and distribution of CNS cellular energy

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Brain activity, including action potentials, Na+/K+ ATPase activity and neurotransmission, requires fast and fluctuating energy (i.e., ATP) largely fed through the creatine/phosphocreatine-creatine kinase circuitry. Brain-type creatine kinases B-CK (cytosolic) and UbCKmit (mitochondrial) are further considered important for the maintenance and distribution of cellular energy in the central nervous system. We demonstrated that both isoforms are present in many neuronal nuclei along the rostro-caudal axis of the brain. To investigate whether animals with a deficit in their brain energy-metabolism show an impairment in their immediate reaction to sudden stimuli, mice lacking B-CK, or UbCKmit, or both (CK-/-double knockout) were tested in the acoustic startle reflex set-up and compared to wildtype littermates. All groups demonstrated a similar basal activity/background response amplitude of ~40 arbitrary units during the "no stimulus (70 dB)" trials. Wildtype mice showed maximal startle amplitudes of ~400 as response to the 120 dB startle pulses in three consecutive trial blocks, indicating that no habituation to the stimulus occurred. B-CK-/-, UbCKmit-/-, and CK-/- double knockout mice also showed no habituation to the 120 dB startle pulse. However, all three groups demonstrated a significantly reduced startle response (~80-100 arbitrary units). Wildtype animals revealed a clearcut prepulse inhibition (i.e., suppression of the 120 dB pulse-induced startle response when preceded by a weak prepulse of +2, +4, +8, or +16 dB above background) of 60%, whereas B-CK-/-, UbCKmit-/-, and CK-/- double knockout mice demonstrated only a prepulse inhibition of ~20-30%.

E47. Behavioral and neurochemical responses in tumor-bearing mice submitted to social stress

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The aim of this study was to analyze the effects on behavior and neurochemical brain activity in response to the inoculation of tumor cells in mice submitted to social stress. Two groups of male OF1 mice were used, one of which was inoculated with B16 melanoma cells. Both groups were subdivided into two new groups, one being submitted to social stress through sensorial contact with a selected aggressive subject, and the other being handled without social interaction. Subjects were exposed to social stress for a 24-hour period, with three 5-minute intervals of direct physical interaction, which were recorded and assessed. One hour and three days after the stress and/or handling, dopaminergic (DOPAC/DA) and serotonergic (5HIAA/5HT) activities, norepinephrine (NE) content in the hypothalamus (HYP), and the density of D2 dopamine receptors in the striatum (STR) were assessed. Significant behavioral changes were found in subjects with implanted tumors, mainly characterized by an increase in avoidance behavior when faced with an aggressive opponent. Furthermore, subjects presented an increase in DOPAC: DA ratios, 5HIAA/5HT ratios, and NE content in the HYP. The increase of these activities was higher three days after exposure to stress. Similarly, an increase in the density of D2 receptors in the STR was observed in inoculated subjects. These changes may be related to the behavioral strategy shown by the inoculated subjects.

E48. Stressed amygdala: stress-induced structural and functional plasticity in basolateral amygdala

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Previous work on amygdala, stress and anxiety points towards a very strong probability that stress-induced plasticity in amygdala is important for stress-induced plasticity of affective behaviors like anxiety. We detail features of structural plasticity in the basolateral amygdala caused by chronic stress, and explore links of such structural plasticity to stress-induced facilitation of anxiety. Immobilization stress (2 hours/day, 10 days) induces hypertrophy of basolateral amygdala projection neurons and enhances anxiety. Both hypertrophy and anxiety are persistent with time. Another unrelated stress protocol, chronic unpredictable stress, does not cause hypertrophy and anxiety. In addition, we demonstrate negative correlation between hypertrophy and anxiety, precluding a simple relationship between hypertrophy and anxiety. Taken together this suggests a probable link between changes in anxiety and neural processing in BLA. In addition, data demonstrate dissociation in structural plasticity of hippocampus and amygdala. These observations may provide a potential cellular substrate for exploring stress-induced disorders that are characterized by diminished cognitive capabilities and abnormally high fear response. We also describe structural plasticity in output nuclei of extended amygdala, which are important for fear and anxiety.

E49. Functional heterogeneity of the amygdala: disparity of c-Fos expression in alimentary and defensive conditioning in rats

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It is known that plastic changes related to acquisition of fear responses occur in the lateral and basolateral nuclei of the amygdala. However, no data regarding c-Fos expression evoked in different amygdaloid nuclei by the conditioning of the alimentary response have been available so far. The aim of the present study was to compare c-Fos activation resulted from defensive and alimentary learning procedures. The CER and/or instrumental appetitive responses were trained in the same Skinner box apparatus. The rules established by the Ethical Committee of Animal Research of the Nencki Institute were strictly followed. Male Long-Evans rats were divided into four control (C1-4) and two experimental groups (E1-2). c-Fos expression was analyzed: in home-cage controls (C1), after one daily session of habituation (C2), after the first day of alimentary (E1) and defensive training (E2), after the 10th day of alimentary training (C3) and after the 10th day of defensive training (C4). In the cortical nuclei the appetitive conditioning evoked very intense immunostaining, while the defensive learning resulted in more moderate expression. An increase of c-Fos expression in the medial part of the basolateral nucleus was related to both the alimentary and defensive training. However, the defensive conditioning evoked more considerable increment.

E50. Using radiotelemetry to measure stress-induced hyperthermia in rats

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Introduction: Stress-induced hyperthermia is widely used as a measure of anxiety. Generally, body temperature is recorded with a rectal probe which is invasive and distressing and may confound the hyperthermic response. The present study used radiotelemetry transmitters to measure temperature in freely-moving rats and a physiologically-relevant stressor to evoke hyperthermia. Methods: Under isoflurane anaesthesia, male Sprague Dawley rats were implanted with a radiotelemetry transmitter to measure core temperature and locomotor activity. Rats were singly-housed and, once a week, a novel conspecific was introduced into the homecage for 2 hours. Vehicle or test compound was administered i.p. 1 hour before the intrusion. Temperature and activity were measured throughout. Results: Introduction of a novel rat induced a robust and sustained increase in core temperature of up to 2°C. Pretreatment with a known anxiolytic dose of chlordiazepoxide (5 mg/kg) attenuated the hyperthermia by about 75%, causing a maximal increase of 0.5°C. Locomotor activity was unaffected. Conclusion: Radiotelemetry allows the measurement of a hyperthermic response induced by a physiologically-relevant stressor in freely-moving rats. This response is reduced by a known anxiolytic compound, validating the hyperthermia as a measure of anxiety. Future experiments may use this paradigm to assess the effects of putative anxiolytic compounds such as 5-HT2 receptor antagonists on stress-induced hyperthermia.

E51. Changes in brain monoaminergic activity in mice at different repeated defeat experiences and fluoxetine treatment effects

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The aim of the study was to analyze the effects of different social stress treatments on the dopaminergic (DOPAC/DA ratios) and serotonergic (5HIAA/5-HT ratios) activity and the norepinephrine content (NE) in the hypothalamus (HYP) and hippocampus (HYC), in mice treated and not treated with fluoxetine (5 mg/kg, i.p.). Different sample groups were established and the animals subjected to 9, 23 and 52 defeat experiences, using the sensorial contact model. The control groups received the same handling with the exception of social confrontation. An increase was observed in the serotoninergic activity in the hypothalamus only in animals subjected to 9 defeat experiences, although the 5-HIAA levels remained unchanged. Similarly, an increase was observed in the NE levels after both 23 and 52 defeat experiences. No changes were observed in the activity of these neurotransmitters in the hippocampus. Fluoxetine reduced both 5-HT and 5-HIAA levels in the hypothalamus, although no changes were observed in the serotonergic activity. Nevertheless, a reduction in this activity and metabolite levels was observed in the hippocampus. Fluoxetine was found to increase the DA levels in the hypothalamus only in animals not subjected to defeat experiences.

E52. Modulation of midbrain dopaminergic system by arousal- and feeding-related neuropeptides

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We investigated the effects of neuropeptides that affect food intake and/or arousal on activity of ventral tegmental area (VTA) neurons by whole-cell and extracellular recordings *in vitro*. The expression of these peptides and their receptors was studied in identified single neurons by RT-PCR. We found that the orexigenic peptide, neuropeptide Y (NPY, 300 nM) hyperpolarized and inhibited the firing of 40% of dopaminergic (DAergic) and 55% of GABAergic VTA neurons. All NPY-inhibited neurons were excited by orexins (wake-promoting and orexigenic peptides we previously found to excite the majority of VTA neurons). Corticotropin-releasing factor (CRF), an anorectic peptide which is also known to promote arousal, excited 64% of DAergic neurons and all GABAergic neurons tested. Substance P (SP) that promotes arousal but not food intake, excited 78% of DAergic and all GABAergic VTA neurons (300 nM). Neither the orexigenic neuropeptides ghrelin, melanin-concentrating hormone (MCH) and agouti-related protein (AGRP) nor the anorectic peptides CART and leptin affected the firing rate or membrane potential of VTA neurons. These findings suggest a correlation between the ability of neuropeptides to promote arousal and their action on VTA neurons and reveal that they modulate the activity of DAergic and GABAergic midbrain neurons in a similar rather than reciprocal manner.

E53. Effects of U-50488, a selective kappa opioid receptor agonist, on anxiety tested in the mouse defence test battery

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The role of kappa opioid receptor in the regulation of anxiety is controversial. Thus, "anxiolytic-like", "anxiogenic-like" or absence of effects on anxiety have been described after treatment with several kappa selective ligands using different animal models of anxiety. In an attempt for clarifying the role of these receptors on anxiety, we examine the effects of acute treatment with U-50488 (4 and 8 mg/kg, i.p.) on anxiety tested in the "mouse defense test battery". In this well-validated anxiety screening test subjects were directly confronted with a number of threat stimuli: leather glove, rat odour leather glove and cataleptic rat. Measures taken during and after stimulus confrontation were: avoidance distance and frequency, number of stops and orientations during the chase, number of approaches/withdrawals and threat/attack in the straight alley and escape attempts immediately after the forced contact test. Results showed that U-50488 (8 mg/kg) administration produces significant behavioural changes when mice were confronted with all the stimuli. Moreover, almost all the parameters evaluated were significantly modified when mice were directly exposed to the rat. Taken together, our findings suggest that kappa activity may differently reduce flight responses and risk assessment performances, since effects of U-50488 were more evident with the most complex and anxiogenic stimulus condition.

F1. Evaluation of the possible correlation between behavioural responses to acute nicotine and vulnerability to develop nicotine addiction

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Psychopharmacological effects of nicotine are important for tobacco consumption and the majority of smokers become dependent upon nicotine. A different responsiveness to acute nicotine pharmacological effects could be relevant for the individual vulnerability to nicotine addiction. To evaluate this hypothesis, we have characterized the pharmacological responses to acute nicotine on locomotor activity, exploratory behaviour, motor coordination, nociception and anxiety-like behaviour in inbreed C57BL/6J mice. We also have set up a model to evaluate the rewarding effects and the expression of the dysphoric properties of nicotine withdrawal by using the place conditioning paradigm. These two behavioural responses are important for the development of nicotine addiction. From these data, we intend to correlate individual responses to acute nicotine administration with nicotine rewarding effects and motivational manifestations of nicotine withdrawal. This will permit to identify single behavioural markers to predict individual vulnerability to develop nicotine addiction.

F2. Neonatal dopamine depletion in mice induces behavioral changes which involve the dopamine D4 receptor

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By neonatal lesions with 6-hydroxydopamine (6-OHDA) we developed a mouse model that display hyperactivity at young age and paradoxical calming response to amphetamine. When tested in the open field lesioned mice show higher locomotor scores, enhanced exploration of the central area, an lower defecation rates than their sham operated littermates; consistently, when challenged in the elevated plus maze they display no preference for the closed arms. Also, lesioned mice were severely impaired to perform simple tasks when trained in operant chambers, probably due to inattention. We speculated that some of this traits may be affected by the dopamine D4 receptor (D4R), which has been associated with complex behaviors such as novelty seeking and emotionality, both in humans and rodents. To test this hypothesis we introduced 6-OHDA neonatal lesions in D4R knock-out mice. HPLC and immunohistochemical analysis determined that the neurochemical changes induced by the lesion were similar in both genotypes. Moreover, executive motor coordination in the rotarod was equally impaired in lesioned mice of both genotypes. But interestingly, D4R-/- lesioned mice did not display hyperactivity in the open field, and showed avoidance of the central arena; they also behaved normally in the elevated plus maze and in the light/dark box; these results suggest that the DR4 is necessary for the development and/or the manifestation of the most salient features of this model.

F3. Serotonin (5-HT), dopamine (DA) and learning: studies of visual imprinting

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The young of certain animals including the domestic chick come to recognize an object by being exposed to it. Compelling evidence suggests that a region of the chick forebrain, the IMHV, particularly the left, stores the information acquired through this learning process of imprinting (Horn (1998) Trends Neurosci 21: 300). Are 5-HT and DA involved in this process? Chicks were trained by exposure to an imprinting stimulus, their preferences measured and a preference score (PS) calculated. Trained chicks were divided by PS into "good" (GL) and "poor" (PL) learners. One group of chicks remained untrained (UT). Within 2 h of the end of the preference test, samples from left and right IMHV, hyperstriatum accessorium and neostriatum were assayed for 5-HT, its metabolite 5-hydroxyindoleacetic acid (5-HIAA), DA and its metabolite 3,4-dihydroxyphenylacetic acid (DOPAC). There were no significant differences in mean levels of DA or DOPAC between the 3 groups of chicks. Mean levels of 5-HT and 5-HIAA in the left but not the right IMHV were significantly higher in PL than in GL or UT chicks ($P<0.02$). Means of the last two groups did not differ significantly. There were significant negative correlations between levels of 5-HT and 5-HIAA and PS ($P<0.001$ and $P<0.004$ respectively). Levels of DA and DOPAC were not correlated with PS. These results suggest a role of serotonin in imprinting.