Symp 12/4**PREFRONTAL CONTRIBUTION TO INHIBITORY CONTROL AND AFFECTIVE BEHAVIOUR: NEUROPSYCHOLOGICAL STUDIES IN MARMOSETS***A. Roberts**Department of Anatomy, University of Cambridge, Cambridge, CB2 3DY, UK*

The medial and orbital prefrontal cortices have been implicated in the inhibitory control of behaviour as well as specifically, in the expression of emotional and social behaviour. Humans or non-human primates with damage to these regions may exhibit impulsiveness and inflexibility, emotional disturbances and anti-social behaviour. In addition, a variety of neuropsychiatric disorders such as depression, obsessive compulsive disorder, schizophrenia and sociopathy are associated with dysfunction in these regions. However while the precise relationship between inhibitory control, affective processing and the prefrontal substrates underlying these processes is poorly understood recent findings in the common marmoset, a new world primate, have begun to shed light upon these issues. This presentation will describe the dissociable behavioural effects of excitotoxic lesions of the medial and orbital prefrontal cortex on a range of affective and inhibitory control tests including object retrieval, food preference and extinction of a rewarded response. Overall, the results are consistent with the hypothesis that both medial and orbital prefrontal cortex may be involved in the control of affective processing but their roles are differentiated through the nature of the associations governing behaviour.

<p>Symposium 13: Cerebellar plasticity during development and at adult age: structural and behavioural effects</p>

<p>Organized by P. Strata and A. Gramsbergen</p>

Symp 13/1**THE EFFECTS OF OLIVARY DESTRUCTION AT EARLY AND LATER POSTNATAL STAGES ON CEREBELLAR DEVELOPMENT AND MOTOR BEHAVIOUR IN RATS**

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The inferior olivary nucleus together with the climbing fibre system at adult age plays an important role in the processing of information from the spinal cord. Both the climbing fibre system and the mossy fibre system develop late in neuro-ontogeny and mature functioning of both input systems has been demonstrated to occur from the end of the second week of life. This is further illustrated by our finding that cerebellar hemispherectomy at ages before the 10th postnatal day (P10) leads to motor handicaps only from P15. The problem of the present research is how this late development is related to the compensational capacity of the cerebellum after selective lesions. We concentrated upon the

development of the olivo-cerebellar system in relation to motor behaviour as well as on the effects of selectively lesioning the inferior olivary nucleus by 3-Acetyl Pyridine (3-AP) at early ages (P5) and after the major development of this system has taken place (at P15). Lesioning at P5 only temporarily leads to a retardation of motor development and motor behaviour at adult ages is roughly normal. These data are supported by EMG recordings of hindleg and trunk muscles. On the other hand, lesioning at P15 leads to ataxic walking patterns throughout further development. In histological research at LM and at EM level we studied Calcitonin Gene Related Peptide (CGRP) and Corticotrophin Releasing Factor (CRF) immunoreactivity in the rat olivary nucleus and in the cerebellum after 3-AP lesioning. CGRP was used to identify olivary neurons and their climbing fibres and CRF reactivity is strongly present in Purkinje cells at early stages. After 3-AP treatment at P5, CGRP immunoreactivity in somata of olivary nuclei is low after 5 days survival whereas CRF reactivity is more intense than usual. In the cerebellum only a few labeled profiles were observed. After 10 days of survival, CGRP and CRF reactivity in the olivary nucleus is increased. In the cerebellum CGRP reactivity is present around the Purkinje cells bodies and CRF labels strips of Purkinje cell bodies in the anterior lobe of the vermis. This pattern is in contrast with observations after 3-AP treatment at P15. After a survival time of 10 days CGRP and CRF reactivity is almost absent, suggesting that the synaptic connectivity between climbing fibres and Purkinje cells has been established before P15 and that this system has lost its plastic capacities at that age.

Symp 13/2

ROLE OF THE OLIVARY COMPLEX IN MOTOR SKILLS AND MOTOR LEARNING IN ADULT RATS

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No Abstract

Symp 13/3

REGENERATIVE ACTIVITY AND PLASTICITY IN THE OLIVOCEREBELLAR SYSTEM

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Functional recovery following brain injury relies on the capability of the affected neurones to reestablish disrupted connections and to restore the correct projection map distribution. Because of its precise anatomical arrangement and topographic organisation, the adult rodent olivocerebellar system is a most suitable experimental model to investigate circuit rewiring in the adult mammalian brain. Following subtotal lesions of the inferior olive in adult rats, surviving olivocerebellar axons sprout collateral branches and form new climbing fibres to innervate numerous deafferented Purkinje cells. This

reinnervation fully restores the normal climbing fibre-Purkinje cell relationship and reverts the morphological modifications that affect Purkinje cells following climbing fibre loss. Similar sprouting and terminal arbour growth can be induced, in the absence of any lesion or degeneration, by transplanting embryonic Purkinje cells on the surface of the adult cerebellum. Thus, adult inferior olivary neurones are able to expand their terminal domain to innervate supernumerary Purkinje cells and this plasticity is likely induced and regulated by target-derived signals. The plastic potential of intact olivary axons is paralleled by their regenerative capabilities following transection. Injured inferior olivary neurons strongly upregulate growth-associated genes and vigorously regenerate into embryonic neural and Schwann cell transplants. In the latter condition, some of the axons succeed in growing across the graft and reinnervate deafferented Purkinje cells in the cortex beyond the lesion site. Although adult inferior olivary neurones are able to reestablish specific connections at the single cell level, functional recovery also requires that the original projection map is restored. This can be assessed in the olivocerebellar system in which clusters of inferior olivary neurones project according to a precise topographic manner to parasagittally-oriented cortical compartments, defined by the heterogeneous expression of Purkinje cell-specific genes, such as zebrin-II. Indeed, Purkinje cell reinnervation after a subtotal inferior olive lesion in the adult is restricted within the boundaries of such cortical modules, showing that this process is not randomly oriented, but it is aimed at restoring topographically organised connections. Similarly, the correct olivocerebellar projection map is reestablished during the transcommissural reinnervation that takes place following unilateral transection of the inferior cerebellar peduncle in newborn rats. In addition, also the severed olivocerebellar axons that regenerate into embryonic cerebellar grafts selectively innervate zebrin positive or negative Purkinje cell clusters. The plasticity of adult olivocerebellar axons is regulated by intense reciprocal interactions with Purkinje cells leading to restore a specific relationship at the single cell level and to reconstruct topographically arranged connections. This suggests that these reparative processes may actually lead to an adaptive functional recovery.

Symp 13/4

ELECTRICAL ACTIVITY MAINTAINS INNERVATION SPECIFICITY IN THE CEREBELLAR CORTEX

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During development electrical activity plays a basic role in the refinement of the highly specific pattern of connections that leads to the final architecture of the adult brain. Concerning the mature brain it is currently assumed that electrical activity affects the synaptic strength and spine size and density, these changes being related to learning and memory. However, there is no evidence that electrical activity may control afferent projection specificity. Here we show that in the absence of electrical activity, afferent fibers invade an incorrect dendritic region. Purkinje cells provide an excellent model for examining this problem, since the dendrites have two well-defined compartments, each receiving two different afferent