dendritic branching and loss of dendritic spines in Rett patients. Therefore the study of BDNF promoter-IV may help us to understand the etiology and pathogenesis of Rett syndrome. Recently, Greenburg and Lu group have generated the promoter-IV specific knock-in (KIV−/−) mice. This mice has never been used to understand shared mechanisms of rett and autism.

In this study, we present evidence that the KIV−/− mice share the cellular and behaviour deficits seen in rett and autism models, which includes:

1) reduced distal dendritic branching and spine density in glutamatergic neurons; 2) loss of inhibitory synapses in glutamatergic neurons, thus leading to disinhibition in cortex; 3) lack of circuits plasticity in response to sensory deprivation or stimulation. Despite these deficits, the KIV−/− mice appeared to develop ‘normally’: 1) they have normal brain cytoarchitectonic structure and normal cell density in both glutamatergic and GABAergic cells in the cerebral cortex; 2) they have normal locomotion behaviour and can survive in complex environment and mild stress during 2nd-4th postnatal weeks. However, careful study of their behaviour revels that the mice exhibited deficits in social interaction tests.

1) The cellular and behaviour deficits of the KIV−/− mice were very similar to those in Rett and autism models, 2) future studies is necessary to further differentiate differences and similarities between KIV−/− and MECP2-null mice.

Acknowledgements

The work is supported by NINDS grant 5R01NS057415.

doi:10.1016/j.ijdevneu.2010.07.143

Mutation of Semaphorin-6A disrupts limbic and cortical connectivity and models neurodevelopmental psychopathology

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Keywords: semaphorin; cortical; psychosis; dysconnectivity

Psychiatric disorders such as schizophrenia and autism are characterised by cellular disorganisation and dysconnectivity across the brain and can be caused by mutations in genes that control neurodevelopmental processes. To examine how neurodevelopmental defects can affect brain function and behaviour, we have investigated the consequences of mutation of one such gene, Semaphorin-6A, on connectivity, behaviour and physiology in mice. These analyses reveal a spectrum of widespread but subtle anatomical defects in Sema6A mutants, notably in limbic and cortical cellular organisation, lamination and connectivity. These mutants display concomitant alterations in the electroencephalogram and hyper-exploratory behaviour, both of which are characteristic of

Fig. 1. Lower dendritic spine density in pyramidal neurons in the KIV+ mice.

Fig. 2. Perisomatic inhibition, which are formed by fast-spiking basket cells, is regulated in an activity-dependent manner in neocortex of wild-type mice 9A) (Sun et al., J. Neurosci 2003; Jiao et al., J. Neurosci, 2006) but not in KIV−/− mice (B).
models of psychosis and reversible by the antipsychotic clozapine. They also show altered social interaction and deficits in object recognition and working memory, core endophenotypes of schizophrenia. In humans, the SEMA6A gene and genes encoding the interacting proteins SEMA6B, PLXNA2 and PLXNA4 map to strong linkage peaks for schizophrenia and autism in isolated pedigrees. These findings are supported by association analyses, which we replicate and extend in the Irish population. Mice with mutations in Sema6A or the interacting genes represent a highly informative model for how neurodevelopmental defects can lead to anatomical dysconnectivity, resulting in dysfunction at the level of neuronal networks with associated behavioural phenotypes of relevance to psychiatric disorders. Of relevance to general mechanisms of neurodevelopmental pathogenesis, for example, we consider which of the physiological and behavioural phenotypes in these mutants may be associated with primary defects in circuitry, and which are more readily explained by secondary, network-level, reactive mechanisms, such as alterations in dopamine signalling. Finally, our biological data make these genes highly plausible candidates to explain the human linkage findings and suggest they may be directly involved in the etiology of psychiatric disorders.

doi:10.1016/j.ijdevneu.2010.07.144

[P2.15]

Microglia in the embryonic neocortex - the effect of maternal inflammation

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Keywords: microglia; maternal inflammation; autism

Infection during pregnancy can lead to maternal inflammation. Several studies have suggested that maternal inflammation increases the risk on neuropsychiatric disorders, like autism, in the offspring. The cause of autism remains unknown, it is thought to be a complex interaction of different factors. A study of Vargas et al demonstrated the presence of an active neuroinflammatory process in the brains of autistic patients, with marked microglial cell activation. Microglia colonize the central nervous system early in embryonic development, at the moment that neuronal migration to the cortical plate is peaking and neuronal differentiation and synaptogenesis are underway. By their production of growth factors, it has been suggested that microglia can influence axonal growth and synaptogenesis. Based on these findings, we aim at studying the localization and activation stages of the microglia present in the embryonic murine neocortex in healthy embryos and embryos subjected to maternal inflammation.

Transgenic CX3CR1 +/eGFP embryos were isolated at the desired age. Heads were fixed in paraformaldehyde, cryoprotected with sucrose and frozen in Optimal Cutting Temperature compound. Coronal sections were stained for Iba-1, CD68, CD11b and MHC II.

At E13.5, few microglia are present in the embryonic cortex (5.2 ± 10^5 ± 3.7 ± 10^6 cells/μm², n = 6). Their number has increased at E14.5 (8.1 ± 10^5 ± 2.9 ± 10^6 cells/μm², n = 6). Most microglia reside at the meninges and some are present in the ventricle. They have a round morphology, with one or two ramifications.

| % microglia expressing: | Iba-1 | CD68 | CD11b | MHC II |
|------------------------|-------|------|-------|--------|
| E13.5 (n = 6)          | 97.5 ± 1.1% | 68.1 ± 3% | 17.9 ± 4.9% | 0%    |
| E14.5 (n = 3)          | 98.2 ± 1.8% | 73.6 ± 4.8% | -      | 0%    |

Although their morphology resembles that of (early) activated microglia, their expression profile suggests that they are ‘resting’ cells. The ramifications could indicate that the microglia migrate along radial glia. We expect to find more cells, in a higher activation stage, in embryos subjected to maternal inflammation.

doi:10.1016/j.ijdevneu.2010.07.145

[P2.16]

Behavior of mice with impaired cognition due to deficiency in neural cell adhesion molecule on the elevated plus-maze

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Keywords: Learning; Anxiety; Neuronal cell adhesion molecule-deficient mice; elevated plus-maze

The elevated plus-maze (EPM) test is one of the mostly used tests to screen the levels of anxiety in rodents. In the present study, we studied how impaired cognition due to the deficiency in the neural cell adhesion molecule (NCAM) could affect the behavior of mice in the EPM task. NCAM-knockout mice demonstrated impaired learning and memory functions in both object recognition and fear conditioning tasks. When NCAM-knockout mice were exposed to EPM task they demonstrated “anxiolytic-like” behavior. Further analysis of the behavior of mice in the EPM task using min-by-min fashion revealed profound influence of genotype. While wild-type mice demonstrated quick learning of aversive properties of the open arms during the first minutes of a single EPM session and avoided to enter open arms during following minutes of the session, NCAM-knockout mice were unable to learn aversive properties of the open arms of EPM and entered open arms equally during whole session. When EPM test/re-test paradigm was used in the EPM task, wild-type mice demonstrated habituation as it was evidenced by a decrease in the % entries onto and % time spent on the open arms during the second presentation to EPM. In contrast, NCAM-knockout mice failed to demonstrate habituation during second EPM presentation. Our data show that the “anxiolytic-like” behavior of NCAM-knockout mice is not related only to the levels of innate anxiety, but rather to the inability of NCAM-deficient mice to recognize and learn the danger associated with the open arms in the EPM task.

In conclusion, the results of the present study show that cognitive functions might have great impact on the performance of the mouse the EPM task and this should be considered when EPM test is employed for the evaluation of the levels of the anxiety.

doi:10.1016/j.ijdevneu.2010.07.146

[P2.17]

Mecp2 and breathing symptoms in a mouse model of Rett Syndrome: On the trail of GABA involvement

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Keywords: Mecp2; breathing symptoms; GABA

Rett Syndrome (RTT) is a severe neurodevelopmental disease mainly affecting girls who, after a normal perinatal period, develop complex symptoms including erratic breathing and life threatening apnoeas. RTT is caused by mutations in the methyl CpG binding protein 2 (Mecp2) gene and therefore Mecp2-deficient mice have been generated. Male of Mecp2-deficient mice (Mecp2−/−) normally breathe at birth but develop breathing symptoms after postnatal