POS-MON-017

GLIAL FIBRILLARY ACIDIC PROTEIN (GFAP) IS UNALTERED IN THE ANTERIOR CINGULATE FROM SUBJECTS WITH MOOD DISORDERS

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Background: We reported increased transmembrane TNF (tmTNF), but not the cleaved soluble TNF (sTNF), in the dorsolateral prefrontal cortex (DLPFC) from subjects with major depressive disorders (MDD)[1] and have shown increased tmTNF in the anterior cingulate cortex (ACC), but not DLPFC, from subjects with bipolar disorder (BPD: data not shown). As TNF is predominantly expressed by neuroglia we have now measured the astrocytic marker, GFAP, to determine if there are generalised changes in astrocytic protein expression in MDD and BPD. **Methods:** Western blots were used to measure levels of GFAP in ACC from 10 subjects with BPD, 10 subjects with MDD and 10 age sex matched control subjects. **Results:** There were no significant changes in the intensities of any of the four GFAP immunogenic bands of molecular weights 37kDA (mean ± SEM: BPD = 1.01 ± 0.52 vs. MDD = 1.17 ± 0.31 vs. Controls = 1.05 ± 0.31 ratio internal control; p = 0.62), 41kDA (BPD = 0.74 ± 0.34 vs. MDD = 0.99 ± 0.33 vs. Controls = 1.06 ± 0.51; p = 0.24), 47kDA (BPD = 0.74 ± 0.60 vs. MDD = 1.33 ± 0.87 vs. Controls = 1.36 ± 0.81; p = 0.20) and 50kDA (BPD = 2.02 ± 2.28 vs. MDD = 2.71 ± 1.96 vs. Controls = 2.73 ± 2.14; p = 0.70) with diagnoses. Conclusions: Our data shows that levels of GFAP do not differ in ACC from subjects with mood disorders and suggest changes in tmTNF in that region in BPD are not associated with generalised changes in levels of astrocyte proteins. [1]Dean B et al (In Press) J.Affect.Dis. 10.1016/j.jad.2009.04.027 [doi].

POS-MON-018

ASTROCYTIC TUMOUR NECROSIS FACTOR UNDERLIES NEURON FUNCTION IN COGNITION

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Pro-inflammatory cytokines have been demonstrated to have a diverse range of actions on the functioning of the CNS, and in particular learning and memory behaviours. Details of the mechanisms of action of cytokines are still to be determined. **Purpose:** This study uses immunohistochemistry techniques (IHC) to investigate cellular changes present in the hippocampal formation as a result of up-regulation of astrocyte-produced tumour necrosis factor (TNF)α (GFAP-TNFα$^{+/+}$), prior to onset of behavioural deficits. These findings are compared directly to the hippocampal formation of a TNFα knock-out model (TNFα$^{-/-}$) in which marked alterations in learning and memory are observed at the same time-point (12 wks) and to age-match wild-type mice (WT). This time period is of critical importance for further elucidating the role of TNFα in hippocampal dependent learning and memory. **Methods:** Hippocampi from TNFα$^{-/-}$, GFAP-TNFα$^{+/+}$ and WT (n = 5) were subjected to indirect IHC for the analysis of TNFα levels and distribution in regions CA1, CA3 and the dentate gyrus (DG). **Results:** In GFAP-TNFα$^{+/+}$ there was a demonstrated accumulation of TNFα in hippocampal neurons prior to the onset of hippocampal-dependent behavioural deficits. GFAP-TNFα$^{+/+}$ mice also showed a significant increase in TNFα in regions CA3 and the DG (p = <0.05) when compared to WT and TNFα$^{-/-}$ mice. WT mice demonstrated immunoreactivity of TNFα in regions CA1 and the DG. **Conclusion:** These findings suggest that astrocyte-produced TNFα is essential for normal development and functioning of the CA1 region of the hippocampus in cognitive processes. However, an overproduction of astrocytic TNFα accumulates in the neurons of the CA3 and DG regions and likely produces functional deficits, as seen in 6 months plus mice, through these regions.

POS-MON-019

SUBJECTIVE MEASURES OF TREATMENT OUTCOME FOR PEOPLE WITH SCHIZOPHRENIA ON ANTIPSYCHOTIC MEDICATIONS

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Purpose: To investigate variability in outcomes and treatment response to antipsychotics as mediated by the perceived pharmacological action by the individual diagnosed with schizophrenia. **Methods:** A questionnaire consisting of subjective scales was sent to outpatients diagnosed with schizophrenia. The survey pack assessed the variables: symptom severity, medication side-effects, attitudes to treatment, quality of life (QoL), psychosocial function, neuro-cognitive deficits, coping skills, parental bonding and personality. Objective clinical measures of symptom severity, neuro-cognitive deficits and functioning were also examined and contrasted. A reliability test was used to assess internal consistency. Multivariate analysis of variance (MANOVA) was performed, with factors including antipsychotic-induced dysphoria and drug compliance, and dependent variables of symptoms, side effects, functioning and QoL. Multiple linear regression (MLR) was used to assess QoL and the contribution of symptoms, side effects, psychosocial functioning and treatment attitudes upon the QoL measures. **Results**: Reliability was upheld across the scales and subscales assessed within this sample population (n=242), with Cronbach's alpha ranging from 0.6-0.9. MLR revealed 69% of variance in QoL was accounted by symptoms, side effects, treatment attitudes and by psychosocial functioning (p<0.01, n=242). Participants were further divided on the basis of subjective negativity towards treatment (ie: dysphoric vs non-dysphoric responses), where the subjectively negative participant appeared to have more severe symptoms, side-effects and a significantly reduced QoL (p<0.01), as did the non compliant participant. **Conclusions:** Subjective evaluation of antipsychotic action leads to differential treatment outcomes for symptoms, side effects and QoL. These results show that self-report measures can be quantified reliably and may provide unique insight into patients with schizophrenia. Such measures may be used to evaluate treatments, both pharmacological and non-pharmacological. This will allow for an assessment of broader outcomes than just symptomatic improvement, such as treatment attitudes and compliance, psychosocial functioning and quality of life.

POS-MON-020

SECETASE EXPRESSION AND NEUREGULIN 1 PROCESSING IN SCHIZOPHRENIA

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Background and Hypothesis: Schizophrenia (SCZ) is a complex neurological illness that affects 1% of the population. The molecular bases contributing to its pathology remain poorly understood. Genetic studies have linked NRG1 polymorphism to SCZ. Recent studies with mouse models have demonstrated that impaired NRG1-erbB signalling, due to knockout of BACE1 or of the gamma-secretase subunit, Aph1B gene leads to SCZ-like phenotypes that can be rescued by antipsychotics. We hypothesized that the expression of BACE1 and Aph1B, and the proteolytic processing of NRG1 may be altered in the prefrontal cortex of patients with SCZ. **Methods:** Samples from Brodmann 6 region (20 SZ with normal levels of M1 muscarinic receptor; 20 SZ with low levels of M1 muscarinic receptor; 20 age-matched healthy controls - HC) were homogenized with TRIzol and the protein analysed by western blotting for BACE1, Aph1B and NRG-1. Band density was quantified relative to actin. Data were analysed with SPSS software using ANOVA and a significance p value of < 0.05. **Results:** Protein levels of BACE1, Aph1B, and NRG1 full-length did not differ significantly between the three groups. In contrast, ~ 50 % decrease in NRG-1 CTF was observed in both SCZ groups compared to the HC group (p < 0.001). There was a positive correlation between BACE1 and NRG-1 CTF n the HC group, but not in the SCZ groups. **Conclusions:** Our data suggest that the proteolytic processing of NRG-1 is impaired in SCZ. The molecular mechanisms that underlie the decrease in NRG-1 CTF remain to be elucidated.