And they showed more activation in the bilateral precuneus (Brodmann area 7) only during emotional empathy task. There was no brain region more activated in control subjects during cognitive empathy task. But while carrying out emotional empathy task, control subjects exhibited greater neural activities in the left middle frontal gyrus (Brodmann area 46) and right anterior cingulate gyrus (Brodmann area 32) than ASD subjects.

**Conclusion:** This fMRI study suggested that the brain regions associated with cognitive and emotional empathy in ASD differed from those in healthy individuals. The results of this study might provide some explanation for impaired empathic ability in autism. Further research will be needed to investigate more definite neurobiology of ASD in terms of empathy.

**PM344**

**Association between peripheral cytokine levels and cognitive abilities in children with autism spectrum disorder**

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**Abstract**

**Objective:** Accumulating data in the literature suggest that cytokines may be one of the factors influencing cognitive development of autism spectrum disorder (ASD). The present study investigated whether cytokines influence cognitive development in children with ASD.

**Methods:** The Wechsler Intelligence Scale for Children (WISC-III or WISC-IV depending on the time of testing) was administered to 14 children with ASD (9 boys and 5 girls; mean age (standard deviation) = 11.6 (2.1) years). The serum levels of 10 cytokines (granulocyte macrophage colony-stimulating factor, interferon-γ, interleukin (IL)-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, and tumor necrosis factor-α) were examined using the Human Ultrasensitive Cytokine Magnetic 10-Plex Panel for the Luminex platform. Each serum sample was assayed in duplicate, and all samples were run on the same assay. The relationships between WISC scores and serum levels of the cytokines were examined.

**Results:** The serum level of IL-6 was significantly negatively correlated with IQ in children who were administered the WISC-III (p < 0.001) as well as in those administered the WISC-IV (p < 0.01). Significant correlation of serum IL-6 levels with IQ was also observed when children administered the WISC-III and those administered the WISC-IV were analyzed together (p < 0.001). No other cytokines were significantly correlated with IQ.

**Conclusions:** The present results suggest that peripheral IL-6 levels are negatively correlated with cognitive development in children with ASD. Although the mechanisms underlying the association between cytokines and cognitive development remain to be clarified, our preliminary findings add to the evidence that cytokines may be involved in the neural development of ASD.

**PM345**

**Resveratrol Suppresses Neuroinflammation in the Experimental Paradigm of Autism Spectrum Disorders**

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**Abstract**

**Objective:** Neuroinflammation triggered by the stimulation of matrix metalloproteinases and the subsequent release of pro-inflammatory cytokines, as a result of oxidative stress and mitochondrial dysfunction, leads to neuronal dysfunction and is one of the probable mechanisms involved in the pathogenesis of autism spectrum disorders (ASD). The aim of the present study was to explore the ameliorative potential of resveratrol on neuroinflammation in the experimental paradigm of neuroinflammatory model of ASD in rats.

**Method:** 1M Propanoic acid (PPA)(4μl) was infused over 10 min-utes into the anterior portion of the lateral ventricle to induce ASD like symptoms in rats. Resveratrol (5, 10 and 15mg/kg) was administered starting from the 2rd day of the surgery and continued upto 28th day. Rats were tested for various behavioural paradigms such as social interaction, stereotypy, locomotor activity, anxiety and novelty, depression, spatial learning and memory, repetitive and pervasive behaviour between the 7th day and 28th day. In addition, biochemical tests for oxidative stress, mitochondrial complexes, TNF-α and MMP-9 were also assessed.

**Results:** Intracerebroventricular injection of propanoic acid produced neurological, sensory, behavioural, biochemical and molecular deficits which were assessed as endophenotypes of autism spectrum disorders. Continued treatment with resveratrol for four weeks restored, significantly and dose dependently, all these endophenotypes in PPA induced ASD in rats.

**Conclusion:** The major finding of the study is that resveratrol restored the core and associated symptoms of autistic phenotype by suppressing oxidative-nitrosative stress, mitochondrial dysfunction, TNF-α and MMP-9 expression in PPA induced ASD in rats. Therefore, resveratrol might serve as an adjunct potential therapeutic agent for amelioration of neurobehavioural and biochemical deficits associated with autism spectrum disorders.

**Keywords:** Autism spectrum disorders (ASD), resveratrol, neurobehavioural, oxido-nitrosative stress, TNF-α, MMP-9

**PM346**

**Social defeat stress as juveniles impairs persistent social behaviors and neurogenesis**

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**Abstract**

**Objective:** Adverse childhood experiences, including physical abuse, often have negative physical and mental health consequences later in life. In the present study, we investigated the influence of social defeat stress as juveniles on emotional behaviors, and also the causal role of glucocorticoids in neurogenesis of mice exposed to the stress.

**Methods:** The juvenile and adult male C57BL/6J mice were exposed to social defeat stress induced by exposure to an aggressive ICR mouse for 1, 5, or 10 consecutive days. We assessed social behaviors, serum glucocorticoid levels, and hippocampal neurogenesis in mice exposed to social defeat stress. Mifepristone, a glucocorticoid receptor antagonist, was administrated 15 min prior to each social defeat stress trial for 10 consecutive days.
**PM347**  
Postnatal exposure to valproic acid in postnatal day 2–4 rats shows deficit of social interaction  
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**Abstract**  
Previously, we have reported that postnatal exposure of valproic acid (VPA) stimulates proliferation of glial precursors during cortical gliogenesis. Because prenatal VPA treatment has inhibited neural cell proliferation and shown autistic-like behavior, we were wondering whether increased astrocyte affects neuropsychiatric behaviors. To study the effect of VPA at early postnatal period, Sprague Dawley (SD) pups were injected subcutaneously at dorsal neck region with 300 mg/kg VPA five times on postnatal day (PND) 2 to PND 4. For studying the VPA induced behavioral abnormalities, four different types of behavior tests were performed. We did open field locomotor test for locomotor activity at PND 21. VPA treated rat showed significantly hyperactive behavior (p<0.05). Moreover, the velocity of movement in VPA group increased with highly significant (p<0.01). Elevated plus maze test was performed for anxiety behavior at PND 22. VPA rat expressed significantly more anxiety behavior than control (p<0.05). Also, deficit of social interaction was measured by three chamber social interaction test by calculating Sociability (SI) and Social Preference (SPI) indices at PND 22. In both cases VPA group showed significantly lower interaction with strangers (p<0.05). But in case of passive avoidance test no significant differences were found between control and VPA treated group. Taken together, our results suggest that early postnatal exposure of VPA has been associated with gliogenesis and induced neurodevelopmental problems with some features of autism like behaviors.  

**PM348**  
Association of peripheral BDNF level with cognition, attention and behavior in preschool children.  
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**Abstract**  
Brain-derived neurotrophic factor (BDNF) has been reported to affect development, cognition, attention and behavior (1). However, few studies have investigated preschool children in regard to these topics.  

**Background**: High peripheral BDNF concentration could be a biomarker of these states in preschool children. Therefore, high peripheral concentration could be a biomarker of these states in preschool children. We confirmed the correlation between the psychometric properties and serum and plasma levels of BDNF.  

**Methods**: The serum BDNF level was negatively related with the Full Scale IQ (r=-0.39, p=0.04) and Verbal IQ (r=-0.05, p=0.01), but not with the Performance IQ (r=-0.12, p=0.56). There were no significant relationships between the plasma BDNF level and each scale of IQ. No correlations were found between serum or plasma level of BDNF and CBCT, ARS, CCTT or Stroop color word test. The total behavioral problem and attention problem sections of the CBCL were positively related to plasma BDNF level ([r=0.41, p=0.03], [r=0.44, p=0.02]). However, no relationship was found between the serum levels of BDNF and CBCL.  

**Conclusions**: Our results suggest that high peripheral concentration of BDNF may be related to intelligence, inattention, behavioral problems and clinical symptoms of neuro-developmental disorders such as intellectual disability and ADHD in preschool children. Therefore, high peripheral BDNF concentration could be a biomarker of these states in preschool children.  

**Reference**  
1. Hyungju Park, Muming Poo. Neurotrophin regulation of neuronal circuit development and function. Neuroscience. 2013 14

**PM349**  
Desynchronization of theta-phase gamma-amplitude coupling appeared during the mental arithmetic task in children with attention deficit/hyperactivity disorder  
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**Abstract**  
Objective: Recently, theta- phase gamma-amplitude coupling (TGC) measurement has received attention because it is a feasible method of assessing brain functions such as neuronal interactions. The purpose of this electroencephalographic (EEG) study is to understand the mechanisms underlying the deficits in attentional control in ADHD children by comparing the power spectra and TGC at rest and during a mental arithmetic task.