ceptors have been suggested to be the primary target of alcohol.[1] We have demonstrated alcohol-like effects in healthy controls and blunted effects in recently detoxified alcoholics when challenged with 2.0 mg/kg Dextromethorphan a non-competitive NMDA antagonist. Induction of craving effect was recorded in patients only.[2]

Main Objective is to compare brain glucose metabolism profiles of alcohol dependent males and healthy controls induced by blocking NMDA receptors with dextromethorphan.

Methods: We compared regional metabolism using [18F] fluorodeoxyglucose (FDG) positron emission tomography (PET) in recently detoxified alcoholic patient and controls (double blind, double dummy, placebo controlled) after challenge with 2.0 mg/kg Dextromethorphan. Controls were additionally challenged with alcohol (0.6 g/kg). Subjects were being assessed with standard measurements.

Results: based on preliminary statistical analyses (so far 5 patients and 10 controls, aim 12/12) indicate:

1. Lower metabolism rate in all brain regions among recently detoxified alcohol dependent males under placebo condition. Alcohol globally reduces regional brain glucose metabolism in controls. (consistent with published findings)
2. In alcohol dependent males dextromethorphan challenge led to no changes, or small reduction in brain glucose metabolism, most pronounced in the cerebellum (-4.9%).
3. In controls dextrometorphan challenge was associated with a small, non-significant increases in metabolism, most pronounced in the frontal region (6.1%), and least pronounced in the cerebellum (2.2%). This finding of "hyperfrontality" is consistent with reported findings from ketamine challenge.[3]

Changes in regional metabolism seem to be different in alcohol dependent males and controls.

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YRP.17

Th1 and Th2 relationship in schizophrenia – immunological, immunogenetic and therapeutic investigations

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We have hypothesised immunological abnormalities characterised by a decreased Th1 and an increased Th2 immune response in a distinct group of schizophrenic patients. To prove this hypothesis we performed biochemical, immunogenetic, and clinical investigations: Cytokine production by in-vitro stimulated lymphocytes; Molecular genetics of candidate Th1/Th2-related genes: IFN-gamma, IL-4, IL-12, IL-13 (patients/controls n=170 each); Clinical study using a COX2 inhibitor added to an antipsychotic medication (n=50 patients).

Our results suggest a subgroup of schizophrenic patients with reduced IFN-gamma production and increased IL-4/IL-13 production. The IL-13 gene A1082G promotor polymorphism, accompanied with more pronounced Th2 response, was more frequent in patients. Patients receiving the COX2 inhibitor showed a markedly faster reduction of psychotic symptoms, than patients of the placebo group.

Our complex but systematic results may have great impact for the identification of a subgroup of schizophrenia with immune-related pathophysiology and for the development of an immune-mediated therapy strategy in schizophrenia.

YRP.18

The candidate gene approach in affective disorder: the European Collaborative Project on Affective Disorders

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No abstract was available at the time of printing.

YRP.19

Lithium augmentation in venlafaxine non-responders: an open study

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Thirteen major depressive patients not responding (less than 50% decrease of their baseline MADRS score) to a four-week venlafaxine 300mg treatment were eligible for a four-week open trial of lithium addition. These patients were part of an initial group of 50 patients. If the patients had an insomnia resistant to the allowed sedatives (zopiclone, clorazepate), trazodone could be added to venlafaxine at bedtime during the prelithium phase: 7 of the 13 patients received trazodone. Lithium dose was individually determined according to 24 hrs single dose plasma level: the mean steady state plasma levels ranged between 0.75 and 0.81 mmol/L. Two patients had to stop lithium before the end of the study. Among the 11 other subjects, five patients became responders, including one patient with a dramatic response (dropping of the MADRS score from 40 to 14 in four days) and two patients had a semi-rapid response (within two weeks). The two patients who dropped out did so for similar reasons involving a mixed-manic switch, nausea and trembling. Retrospectively we believe that these may have been moderate cases of serotonin syndrome.

YRP.20

Childhood routines and obsessive–compulsive disorder in a community sample

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Goals: Obsessive–compulsive behavior appears as a part of normal repertoire in young children, and it appears to fade out in a majority, while persisting into school age and further in some.

The study aimed to document the prevalence of compulsive behavior in young children's routines in a community sample, and establish its cross-sectional correlates in demographic, individual and parental behavior characteristics.

Method: 1169 families of children between 9–72 months from a community sample in Istanbul were interviewed about the child's behavior, using Childhood Routines Inventory-Turkish version by Evans et al. Age-specific average scores were calculated. The upper-, middle, and lower- 5-percentile were selected for further detailed interviews about OC behavior /disorder and related problems.

Results: OC behavior described as "childhood routines" is common in all age groups, however, the peak is at around 36–47

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months. Children with higher number of routines appear to belong to families with significantly higher OC scores, and significant family histories for OCD spectrum disorders.

Conclusion: OC behavior is common among young children, and its persistent presence is associated with higher number of OC behaviors as well as the presence of OCD in the household. The frequencies are comparable to Israeli and American findings using the same methodology.

YRP.22

Dissociation, pain threshold and treatment of eating disorders

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Objective: In eating disorders pain sensitivity has been repeatedly described to be changed without plausible explanation. We studied the relation between pain threshold and dissociation scores rated by Body Attitude Test (BAT, Probst et al. 1995) as we hypothesized that the changed body image perception (overestimation of the body size) may result from similar dissociative phenomenon as pain perception.

Methods: The pain threshold and body perception were tested in control group of young healthy women (n=13) and in the DSM IV diagnozed hospitalized patients with eating disorders (n=14) at the admission and discharge period. The pain threshold latency was measured 3 times both in rest and stress conditions using thermal Analgesia Meter. The rest periods were followed by mental arithmetic task (MAT-subtraction 7 from 700), alimentary test (AT-consumption of sweet biscuits) and cold pressor test (CPT – left hand was immersed in ice-water mixture about 2°C.) BAT was administered at the beginning and unpleasantness of stresses was assessed using 100-mm visual analogue scale at the end of the experiment. Data analysis was done using Pearson's correlation and ANOVA.

Results: Our results showed a significant relation between pain threshold measured during the rest and mental and cold stress and the BAT 2 subscale scoring the degree of dissociation. The scores of unpleasantness during AT only correlated positively with BAT subscales 1,2 and total score and with the 3rd pain threshold during the AT and during the rest preceding the AT. The unpleasantess of MAT correlated negatively with the 3rd measurement of pain threshold and positively with the illness duration. The pain perception and BAT changed during the treatment in correlation with BMI and diagnostic subtype (anorexia and bulimia nervosa).

Conclusion: Our results reflect the associatin between pain perception and dissociation and its changes with the course and the severity of the illness as shown in previous study (Yamamotová, Papežová 2001). The correlation analysis revealed that 1st and 3rd measurements of pain threshold had different values. The 1st modified by higher general arousal of new task corresponds to anticipatory anxiety and subscale of BAT with affective dimension. The 3rd may be considered habituated and objectively reflecting intensity of specific stressor (sweet food offer during alimentary stress in eating disorders). Subjective unpleasantness during AT corresponds to several factors of BAT and therefore could measure the intensity of diagnose specific stressor as well. Futher studies are needed to specify clinical benefits and predictive value of changes of the pain treshold answer to different stresses in diagnostic eating disorders subtypes.

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YRP.24

The candidate gene approach in affective disorder: the European Collaborative Project on Affective Disorders

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Linkage analyses and association studies are the two common types of strategies used in genetic studies. Linkage analyses aim at detecting a cosegregation of a specific variant (allele) of a genetic marker with a particular disorder in families. Association studies aim at demonstrating a significantly different distribution of gene variants (alleles) in control and affected populations. Evidence supporting the possible role of neurotransmitter changes in the pathogenesis of some psychiatric disorders has led to a candidate gene strategy in association studies. The European Collaborative Project on Affective Disorders (ECPAD) «Interactions between genetic and psychosocial vulnerability factors», involving 14 european centers apply a multicenter-based methodology to examine the possible role of candidate genes (see table) in affective disorders. Special attention is given to statistical analysis, the statistical power of the samples and the interaction with psychosocial variables. More than 3000 subjects have been recruited for case-control association studies with candidate genes. This material provides a powerful tool in the search for susceptibility genes in affective disorders and also takes into account non-genetic aetiological factors. Phenotypic heterogeneity has been considered and subgroups analyses have been conducted with relevant variables: age at onset, family history, suicidal behaviour, psychotic features and diagnostic stability. The results of association studies in Bipolar and Unipolar affective disorders will be presented.

Gene	Name	Position
TH	Tyrosine Hydroxylase	11 p 15-5
TPH	Tryptophane hydroxylase	11p15.3-p14
DRD3	Dopamine receptor D3	3q 13-3
DRD2	Dopamine receptor D2	11 q 22 - q 23
GABRA1	gamma-aminobutyric acid - A receptor, alpha 1	5 q 34 - q 35
DRD4	dopamine receptor D4	11 p 15.5
HTR2a	5 hydroxytryptamine receptor 2a	13 q 14 - q 21
HTR2c	5 hydroxytryptamine receptor 2c	Xq24
HTT	Serotonin transporter gene	17 q 11.1 - q12
GABRA5	Gamma-aminobutyric acid-A receptor, α 5	15 q 11 - q 13
GABRA3	Gamma-aminobutyric acid-A receptor, α 3-	Xq 28
NOS	Nitric Oxyde Synthetase	12q24.2-12q24.31
PLA2	Phospholipase A2	12q23-12qter

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