

## 2014

1. Shoval G, Shmulewitz D, Wall MM, Aharonovich E, Spivak B, Weizman A, Hasin D. Alcohol dependence and suicide-related ideation/behaviors in an Israeli household sample, with and without major depression. *Alcohol Clin Exp Res*. 2014 Mar;38(3):820-5.

### Abstract

#### BACKGROUND:

Suicide-related ideation and behaviors (SRIB) are associated with both alcohol disorders and major depressive disorder (MDD). The objective of this study was to evaluate the relationship of alcohol dependence (AD) and major depression to the risk for lifetime SRIB.

#### METHODS:

Data from a community-based sample of 1,237 adult Israeli lifetime drinkers assessed with reliable diagnostic measures were analyzed using logistic regression.

#### RESULTS:

Lifetime SRIB was reported in 4.7% and was more prevalent among participants with AD (9.0%) than among those without AD (4.1%);  $p$ -value = 0.01. Although both AD and major depression were associated with SRIB (AD: OR 2.2, 95% CI 1.1 to 4.4; MDD: OR 11.4, 95% CI = 6.4 to 20.4), joint analysis showed that AD without MDD increased risk for SRIB as compared to those without AD or MDD (OR 3.1, 95% CI 1.1 to 9.1), but AD did not increase risk among those with MDD (OR 1.1, 95% CI 0.4 to 2.7). Among those with AD, the severity of subclinical depressive symptoms was associated with increased SRIB.

#### CONCLUSIONS:

These findings show that AD increases risk for SRIB among individuals without a history of major depression. Suicidal tendencies may be undetected and underdiagnosed in this group because of the absence of major depression and therefore left untreated. These findings should be considered when adopting suicide prevention or treatment strategies for this high-risk subpopulation.

2. Asherson P, Manor I, Huss M

Attention-deficit/hyperactivity disorder in adults: update on clinical presentation and care  
*Neuropsychiatry* 2014; 4(1), 109–128

**REVIEW SUMMARY** Attention-deficit/hyperactivity disorder (ADHD) is characterized by trait-like symptoms, with stable features frequently emerging in early childhood and persisting throughout adolescence and adulthood. The hallmarks are pervasive, developmentally inappropriate levels of inattention, hyperactivity and impulsivity leading to impairments in family life, social life, academic performance, and occupational functioning. Emotional lability is a commonly associated feature that is a further source of impairment. Diagnosis rests on a comprehensive assessment of developmental psychiatric history and current status, following DSM-5 guidelines on ADHD classification and diagnostic thresholds for adults. Medical and psychotherapeutic interventions can improve psychological functioning, self-confidence, personal/family relationships, professional/academic functioning, cognitive performance, driving safety, and quality of life, and may reduce criminal

behavior. Future efforts should focus on supporting treatment adherence and smoothing transitions from pediatric to adolescent to adult medical services.

3. Gvion Y, Horresh N, Levi-Belz Y, Fischel T, Treves I, Weiser M, David HS, Stein-Reizer O, Apter A.

Aggression-impulsivity, mental pain, and communication difficulties in medically serious and medically non-serious suicide attempters.

Compr Psychiatry. 2014 Jan;55(1):40-50

## **Abstract**

### **BACKGROUND:**

Unbearable mental pain, depression, and hopelessness have been associated with suicidal behavior in general, while difficulties with social communication and loneliness have been associated with highly lethal suicide attempts in particular. The literature also links aggression and impulsivity with suicidal behavior but raises questions about their influence on the lethality and outcome of the suicide attempt.

### **OBJECTIVES:**

To evaluate the relative effects of aggression and impulsivity on the lethality of suicide attempts we hypothesized that impulsivity and aggression differentiate between suicide attempters and non-attempters and between medically serious and medically non-serious suicide attempters.

### **METHOD:**

The study group included 196 participants divided into four groups: 43 medically serious suicide attempters; 49 medically non-serious suicide attempters, 47 psychiatric patients who had never attempted suicide; and 57 healthy control subjects. Data on sociodemographic parameters, clinical history, and details of the suicide attempts were collected. Participants completed a battery of instruments for assessment of aggression-impulsivity, mental pain, and communication difficulties.

### **RESULTS:**

The medically serious and medically non-serious suicide attempters scored significantly higher than both control groups on mental pain, depression, and hopelessness ( $p < .001$  for all) and on anger-in, anger-out, violence, and impulsivity ( $p < .05$  for all), with no significant difference between the two suicide attempter groups. Medically serious suicide attempters had significantly lower self-disclosure ( $p < .05$ ) and more schizoid tendencies ( $p < .001$ ) than the other three groups and significantly more feelings of loneliness than the medically non-serious suicide attempters and nonsuicidal psychiatric patients ( $p < .05$ ). Analysis of aggression-impulsivity, mental pain, and communication variables with suicide lethality yielded significant correlations for self-disclosure, schizoid tendency, and loneliness. The interaction between mental pain and schizoid traits explained some of the variance in suicide lethality, over and above the contribution of each component alone.

### **CONCLUSIONS:**

Aggression-impulsivity and mental pain are risk factors for suicide attempts. However, only difficulties in communication differentiate medically serious from medically non-serious suicide attempters. The combination of unbearable mental pain and difficulties in communication has a magnifying effect on the risk of lethal suicidal behavior.

4. Finzi-Dottan R, Harel G

Parents' Potential for Child Abuse: An Intergenerational Perspective

Journal of Family Violence 2014 May; 29(4):397-408

**Abstract:** This study examined predictors for parents' potential for abusing their children. Two hundred and thirteen Jewish and Arab parents of children up to 6 years of age completed six questionnaires assessing child-abuse potential, childhood history of abuse/neglect, attachment style, emotional control, perceived stress, and cognitive appraisal of parenthood. Results indicated that parents who experienced childhood abuse and neglect scored significantly higher in child-abuse potential than parents without a history of abuse or neglect. A Structural Equation Model indicated that anxious and avoidant attachment mediated the experiences of abuse and neglect in childhood and emotional control; whereas emotional control deficits mediated the relationship between insecure attachment and parenthood as challenge vs. threat, leading to greater child-abuse potential. Clinical implications were discussed.

5. Ebert T, Midbari Y, Shmilovitz R, Kosov I, Kotler M, Weizman A, Ram A.

Metabolic effects of antipsychotics in prepubertal children: a retrospective chart review.

J Child Adolesc Psychopharmacol. 2014 May;24(4):218-22

## Abstract

### OBJECTIVE:

Antipsychotics, especially atypical ones, are in common use in children and adolescents with psychotic or affective spectrum disorders, as well as in various other psychopathologies. The adverse effects of atypical antipsychotics in children and adolescents are similar to those seen in adults, and include weight gain, elevated blood glucose levels, and hyperlipidemia. In this retrospective chart review, we compared these adverse events in children who were treated with typical, atypical, or no antipsychotic treatment.

### METHODS:

The medical charts of 72 children, 65 boys and 7 girls, were reviewed. All children were 6-13 years old (mean age 9.5±1.7 years). In total, 48 children received antipsychotic treatment, and 24 children were in the control group. Data were extracted from the medical charts, including weight, height, body mass index (BMI), blood pressure, aspartate transaminase (AST), alanine transaminase (ALT), triglycerides, total cholesterol, and glucose blood levels. We examined the values in the beginning of the antipsychotic treatment and at release from the hospital in the study group, and at admission and in the end of the drug-free period or at release from the hospital (a duration of at least 4 weeks) in the control group.

### RESULTS:

The average weight gain was 3.9±3.8 kg in the atypical antipsychotic treatment (AAT) group, 1.1±4.4 kg in the typical antipsychotic treatment (TAT) group, and 0.23±2.9 kg in the control group. The average increase in BMI was 15.1±22.0 percentiles in the AAT group, 6.4±14.2 percentiles in the

TAT group, and 1.6±12.5 percentiles in the control group. No statistically significant difference was found in the increase in height percentile. There were no significant differences in the rates of elevated values of serum triglycerides, cholesterol, AST, ALT, or fasting blood glucose.

#### CONCLUSIONS:

We found a significant increase in both absolute weight gain and BMI percentile following atypical antipsychotic treatment. In contrast, typical antipsychotic treatment did not affect weight gain significantly, and the same was true for the control group. In addition, the rates of elevated values of biochemical parameters (AST, ALT, total cholesterol, triglycerides, and fasting blood glucose levels) were very low at the beginning of the study, and were not significantly altered by the various treatments.

#### 6. Bergman J, Pashinian A, Weizman A, Poyurovsky M

The beneficial effect of escitalopram on obsessive-compulsive-related musical hallucinations in elderly patients with hearing impairment: a case series.

Int Clin Psychopharmacol. 2014 Sep;29(5):263-5

**Abstract:** Musical hallucinations (MHs), characterized by the hearing of tunes, melodies, or songs, is a relatively under-recognized phenomenon among elderly individuals with hearing impairment. In some patients, MHs represent a complex psychopathological phenomenon, hallucinatory in content and obsessive-compulsive (OC) in form, justifying trial with an antiobsessive agent. In the present case series, we describe our clinical experience with escitalopram in six (two men, four women; age 74-85 years) elderly individuals with OC-related MH and hearing impairment who did not respond to previous antipsychotic treatment. Switch to escitalopram (mean 12.5 mg) led to a substantial improvement in the MH symptom severity, as reflected in a decrease in the global score of the Yale-Brown Obsessive-Compulsive Scale adapted to OC-related MH (scores before escitalopram, 13.2±0.9; after 12 weeks of treatment, 7.8±2.8; P<0.01). Escitalopram was well tolerated, and the only detected side effects, nausea and headache, were mild and transient. If confirmed in controlled trials, escitalopram and probably other selective serotonin reuptake inhibitors may be a therapeutic option in elderly individuals with OC-related MH.

#### 7. Poyurovsky M, Bergman J, Pashinian A, Weizman A.

Beneficial effect of low-dose mirtazapine in acute aripiprazole-induced akathisia.

Int Clin Psychopharmacol. 2014 Sep;29(5):296-8

**Abstract:** Low-dose mirtazapine was found to be efficacious for neuroleptic-induced akathisia. We evaluated whether mirtazapine is also effective for akathisia induced by the partial dopamine D2 receptor agonist aripiprazole. Medical charts were retrospectively analyzed for eight patients who developed akathisia while being treated with aripiprazole. All scored at least 2 (mild akathisia) on the Barnes Akathisia Rating Scale (BARS) and were treated with mirtazapine (15 mg/day) for a mean of 8.5 days. There was a statistically significant reduction in the BARS subjective, distress, and global (P<0.01 to P<0.001), but not objective (P=0.21) subscales. Five (62.5%) patients fulfilled the criteria of response, a decrease of at least two points on the BARS global subscale. Low-dose mirtazapine was well tolerated, and mild sedation, the only side effect (three patients), was transient. A large-scale controlled investigation is warranted to substantiate clinical utility of mirtazapine for akathisia induced by aripiprazole and other second-generation antipsychotics.

#### 8. Bejerot S, Weizman A, Gross-Isseroff R

Communality between Obsessive Compulsive Disorder and Autism Spectrum Disorders (Book Chapter)

Comprehensive Guide to Autism 2014, pp.671-692

**Abstract:** Obsessive-compulsive disorder (OCD) is a chronic and disabling anxiety disorder which affects approximately 1.5 % of the population. The average age of onset is 15 years, but *OCD* may start at any age although an onset after the age of 35 is viewed as rare. OCD is characterized by obsessions, e.g., images, repetitive thoughts, unwanted impulses to harm, and repetitive behaviors or mental acts (compulsions). Similarly, restricted, repetitive patterns of behavior, interests, or activities characterize autism and are included in the diagnostic criteria for autism spectrum disorder (ASD) in DSM-5. Autistic personality traits are common in patients with OCD, and OCD is likewise common in individuals with ASD. The two conditions share a range of additional communalities: personality disorders within the obsessive-compulsive, avoidant, and schizotypal/schizoid domains; motor clumsiness and soft neurological signs; neuropsychological deficits; serotonergic dysfunction; immunological underpinnings; and a genetic overlap at the molecular level. Cognitive behavioral therapy could be used in OCD regardless of the presence of ASD; however, the outcome is often less favorable in individuals with ASD+OCD compared to those with only OCD or OCD coexisting with a tic disorder.

9. Schneider M, Debbané M, Bassett AS, Chow EW, Fung WL, van den Bree M, Owen M, Murphy KC, Niarchou M, Kates WR, Antshel KM, Fremont W, McDonald-McGinn DM, Gur RE, Zackai EH, Vorstman J, Duijff SN, Klaassen PW, Swillen A, Gothelf D, Green T, Weizman A, Van Amelsvoort T, Evers L, Boot E, Shashi V, Hooper SR, Bearden CE, Jalbrzikowski M, Armando M, Vicari S, Murphy DG, Ousley O, Campbell LE, Simon TJ, Eliez S; International Consortium on Brain and Behavior in 22q11.2 Deletion Syndrome.

Psychiatric disorders from childhood to adulthood in 22q11.2 deletion syndrome: results from the International Consortium on Brain and Behavior in 22q11.2 Deletion Syndrome.

Am J Psychiatry. 2014 Jun;171(6):627-39

## Abstract

### OBJECTIVE:

Chromosome 22q11.2 deletion syndrome is a neurogenetic disorder associated with high rates of schizophrenia and other psychiatric conditions. The authors report what is to their knowledge the first large-scale collaborative study of rates and sex distributions of psychiatric disorders from childhood to adulthood in 22q11.2 deletion syndrome. The associations among psychopathology, intellect, and functioning were examined in a subgroup of participants.

### METHOD:

The 1,402 participants with 22q11.2 deletion syndrome, ages 6–68 years, were assessed for psychiatric disorders with validated diagnostic instruments. Data on intelligence and adaptive functioning were available for 183 participants ages 6 to 24 years.

### RESULTS:

Attention deficit hyperactivity disorder (ADHD) was the most frequent disorder in children (37.10%) and was overrepresented in males. Anxiety disorders were more prevalent than mood disorders at all ages, but especially in children and adolescents. Anxiety and unipolar mood disorders were overrepresented in females. Psychotic disorders were present in 41% of adults over age 25. Males did not predominate in psychotic or autism spectrum disorders. Hierarchical regressions in the subgroup revealed that daily living skills were predicted by the presence of anxiety disorders. Psychopathology was not associated with communication or socialization skills.

### CONCLUSIONS:

To the authors' knowledge, this is the largest study of psychiatric morbidity in 22q11.2 deletion syndrome. It validates previous findings that this condition is one of the strongest risk factors for

psychosis. Anxiety and developmental disorders were also prevalent. These results highlight the need to monitor and reduce the long-term burden of psychopathology in 22q11.2 deletion syndrome.

10. Rosenberg N, Rosenberg O, Weizman A, Veenman L, Gavish M.

In vitro effect of FGIN-1-27, a ligand to 18 kDa mitochondrial translocator protein, in human osteoblast-like cells.

J Bioenerg Biomembr. 2014 Jun;46(3):197-204

**Abstract:** Ligands of 18 kDa mitochondrial translocator protein (TSPO) differ in their cellular effects. We hypothesize that different TSPO ligands might exert different cellular responses. Therefore, following previous studies that showed different cellular responses to two specific TSPO ligands, PK 11195 and protoporphyrin IX, in human osteoblast-like cells in vitro, we now report the cellular response to another specific TSPO ligand, FGIN-1-27 ( $10^{-5}$  M) (MW 436 kDa), in order to characterize the effects of each TSPO ligand. We found in primary culture of the human osteoblast-like cells that cell numbers were decreased by an average of 30% ( $p < 0.001$ ) following exposure to  $10^{-5}$  M of FGIN-1-27 in comparison to vehicle controls. Cellular [(18)F]-FDG incorporation and ATP content were suppressed, by an average of 43% ( $p < 0.001$ ) and 83% ( $p < 0.001$ ), respectively. Mitochondrial mass and  $\Delta\Psi_m$  increased by an average of 26% ( $p < 0.01$ ) and 425% ( $p < 0.0001$ ) respectively. Lactate dehydrogenase activity was enhanced in culture media by 60% ( $p < 0.05$ ), indicating overall cell death, while no increase in apoptotic levels was observed. Cellular proliferation, as determined by BrdU assay, was not affected. Synthesis of mRNA of TSPO, VDAC 1, and hexokinase 2 decreased in 0.3, 0.3 and 0.5 fold respectively, with accompanying decreases in protein expression of TSPO and Voltage Dependent Anion Channel 1 by 23% ( $p < 0.001$ ) and 98% ( $p < 0.001$ ), respectively, but without changes in hexokinase 2 protein expression. Thus it appears that  $10^{-5}$  M FGIN-1-27 reduces cell viability, cell metabolism, and mitochondrial function. Previously we found similar effects of PK 11195 on mitochondrial function and cell metabolism and of protoporphyrin IX on cell death in primary osteoblast-like cells.

11. Schonherz Y, Davidov M, Knafo A, Zilkha H, Shoval G, Zalsman G, Frisch A, Weizman A, Gothelf D.

Shyness discriminates between children with 22q11.2 deletion syndrome and Williams syndrome and predicts emergence of psychosis in 22q11.2 deletion syndrome.

J Neurodev Disord. 2014 Feb 11;6(1):3

**Abstract**

**BACKGROUND:**

22q11.2 deletion syndrome (22q11.2DS) is a common neurogenetic syndrome associated with high rates of psychosis. The aims of the present study were to identify the unique temperament traits that characterize children with 22q11.2DS compared to children with Williams syndrome (WS) and typically developing (TD) controls, and to examine temperamental predictors of the emergence of psychosis in 22q11.2DS.

**METHODS:**

The temperament of 55 children with 22q11.2DS, 36 with WS, and 280 TD children was assessed using the Emotionality, Activity, Sociability (EAS) Temperament Survey, Parental Ratings. The presence of a psychotic disorder was evaluated in 49 children and adolescents with 22q11.2DS at baseline and again  $5.43 \pm 2.23$  years after baseline temperament assessment.

**RESULTS:**

Children with 22q11.2DS scored higher on Shyness compared to WS and TD controls. Children with 22q11.2DS and WS scored higher on Emotionality and lower on Activity compared to TD controls. Shyness was more severe in older compared to younger children with 22q11.2DS. Baseline Shyness scores significantly predicted the later emergence of a psychotic disorder at follow-up, in children with 22q11.2DS.

#### **CONCLUSIONS:**

Our results suggest that shyness is an early marker associated with the later emergence of psychosis in 22q11.2DS.

12. Walsh K, Elliott JC, Shmulewitz D, Aharonovich E, Strous R, Frisch A, Weizman A, Spivak B, Grant BF, Hasin D.

Trauma exposure, posttraumatic stress disorder and risk for alcohol, nicotine, and marijuana dependence in Israel.  
Compr Psychiatry. 2014 Apr;55(3):621-30

#### **Abstract**

##### **BACKGROUND:**

Substance dependence is more common among trauma-exposed individuals; however, most studies suggest that Posttraumatic Stress Disorder (PTSD) accounts for the link between trauma exposure (TE) and substance dependence.

##### **OBJECTIVES:**

This study examined associations between TE and substance dependence (alcohol, nicotine, and marijuana), and whether PTSD accounted for this association.

##### **METHOD:**

1317 Jewish Israeli household residents completed in-person structured interviews assessing TE, PTSD, and substance (alcohol, nicotine, marijuana) dependence between 2007 and 2009. Regression analyses examined associations among TE, PTSD, and substance dependence.

##### **RESULTS:**

In the full sample, mean number of traumatic events was 2.7 (sd=2.2), with 83.7% experiencing at least one event. In the full sample, mean number of PTSD symptoms was 2.5 (sd=3.4), with 13.5% meeting PTSD diagnostic criteria. Prevalence of alcohol dependence was 13.4%; nicotine dependence 52.8%; and marijuana dependence 12.1%. Number of traumatic events was associated with increased odds of alcohol (OR=1.3; 95% CI=1.2-1.4) and nicotine (OR=1.2; 95% CI=1.1-1.3) dependence. Similarly, any traumatic event exposure was associated with increased odds of alcohol (OR=3.1; 95% CI=1.6-6.0) and nicotine (OR=1.9; 95% CI=1.2-2.9) dependence. PTSD symptoms were associated with increased odds of alcohol (OR=1.2; 95% CI=1.1-1.3), nicotine (OR=1.1; 95% CI=1.1-1.2), and marijuana (OR=1.1; 95% CI=1.04-1.2) dependence; similarly, a PTSD diagnosis was associated with increased odds of alcohol (OR=3.4; 95% CI=2.1-5.5), nicotine (OR=2.2; 95% CI=1.4-3.4), and marijuana (OR=2.6; 95% CI=1.2-5.9) dependence. PTSD symptoms accounted for a sizeable proportion of the TE effect on alcohol (46%) and nicotine dependence (31%).

##### **CONCLUSION:**

Individuals with more traumatic events had heightened risk for alcohol and nicotine dependence, and PTSD symptoms partially accounted for this risk. However, marijuana dependence was only significantly related to PTSD symptoms. Clinicians and researchers should separately assess different types of dependence among trauma-exposed individuals both with and without PTSD symptoms.

13. Keyes KM, Shmulewitz D, Greenstein E, McLaughlin KA, Wall M, Aharonovich E, Weizman A, Frisch A, Spivak B, Grant BF, Hasin D.

Exposure to the Lebanon War of 2006 and effects on alcohol use disorders: the moderating role of childhood maltreatment.  
Drug Alcohol Depend. 2014 Jan 1;134:296-303.

## Abstract

### BACKGROUND:

Civilian populations now comprise the majority of casualties in modern warfare, but effects of war exposure on alcohol disorders in the general population are largely unexplored. Accumulating literature indicates that adverse experiences early in life sensitize individuals to increased alcohol problems after adult stressful experiences. However, child and adult stressful experiences can be correlated, limiting interpretation. We examine risk for alcohol disorders among Israelis after the 2006 Lebanon War, a fateful event outside the control of civilian individuals and uncorrelated with childhood experiences. Further, we test whether those with a history of maltreatment are at greater risk for an alcohol use disorder after war exposure compared to those without such a history.

### METHODS:

Adult household residents selected from the Israeli population register were assessed with a psychiatric structured interview; the analyzed sample included 1306 respondents. War measures included self-reported days in an exposed region.

### RESULTS:

Among those with a history of maltreatment, those in a war-exposed region for 30+ days had 5.3 times the odds of subsequent alcohol disorders compared to those exposed 0 days (95%C.I. 1.01-27.76), controlled for relevant confounders; the odds ratio for those without this history was 0.5 (95%C.I. 0.25-1.01); test for interaction:  $X(2)=5.28$ ,  $df=1$ ,  $P=0.02$ .

### CONCLUSIONS:

Experiencing a fateful stressor outside the control of study participants, civilian exposure to the 2006 Lebanon War, is associated with a heightened the risk of alcohol disorders among those with early adverse childhood experiences. Results suggest that early life experiences may sensitize individuals to adverse health responses later in life.

14. Kaminitz A, Barzilay R, Segal H, Taler M, Offen D, Gil-Ad I, Mechoulam R, Weizman A.

Dominant negative DISC1 mutant mice display specific social behaviour deficits and aberration in BDNF and cannabinoid receptor expression.  
World J Biol Psychiatry. 2014 Jan;15(1):76-82

## Abstract



**OBJECTIVES.** Disrupted in schizophrenia 1 (DISC1) is considered the most prominent candidate gene for schizophrenia. In this study, we aimed to characterize behavioural and brain biochemical traits in a mouse expressing a dominant negative DISC1 mutant (DN-DISC1).

#### **METHODS:**

DN-DISC1 mice underwent behavioural tests to evaluate object recognition, social preference and social novelty seeking. ELISA was conducted on brain tissue to evaluate BDNF levels. Western blot was employed to measure BDNF receptor (TrkB) and cannabinoid receptor CB1.

#### **RESULTS:**

The mutant DISC1 mice displayed deficits in preference to social novelty while both social preference and object recognition were intact. Biochemical analysis of prefrontal cortex and hippocampus revealed a modest reduction in cortical TrkB protein levels of male mice while no differences in BDNF levels were observed. We found sex dependent differences in the expression of cannabinoid-1 receptors.

#### **CONCLUSIONS:**

We describe novel behavioural and biochemical abnormalities in the DN-DISC1 mouse model of schizophrenia. The data shows for the first time a possible link between DISC1 mutation and the cannabinoid system.

15. Gothelf D, Law AJ, Frisch A, Chen J, Zarchi O, Michaelovsky E, Ren-Patterson R, Lipska BK, Carmel M, Kolachana B, Weizman A, Weinberger DR.

Biological effects of COMT haplotypes and psychosis risk in 22q11.2 deletion syndrome. *Biol Psychiatry*. 2014 Mar 1;75(5):406-13.

#### **Abstract**

**BACKGROUND:** 22q11.2 deletion syndrome (22q11.2DS) is the most common genetic syndrome associated with schizophrenia. The catechol-O-methyltransferase (COMT) gene is located in the obligatory deletion region, and possible associations between COMT variants and neuropsychiatric manifestations in 22q11.2DS have been reported. The purpose of the current study was to evaluate the effect of COMT hemizyosity and molecular haplotypes on gene expression and enzyme activity and its association with psychotic symptoms in 22q11.2DS.

**METHODS:** Lymphoblast samples were drawn from 53 individuals with 22q11.2DS and 16 typically developing control subjects. We measured COMT messenger (m)RNA and protein expression and enzyme activity using standard procedures. The presence of a psychotic disorder and cognitive deficits were also evaluated using structured testing.

**RESULTS:** There was an approximately 50% reduction in COMT mRNA, protein, and enzyme activity levels in 22q11.2DS samples. Haplotype analysis revealed clear phenotypic differences between various Val-containing haplotypes on COMT-3' untranslated region extended mRNA, soluble COMT and membrane-bound proteins, and enzyme activity. The G variant of rs165599, a 3' untranslated region single nucleotide polymorphism, was associated with low levels of COMT expression and with the presence of psychosis and lower performance IQ scores in our 22q11.2DS sample. Finally, we demonstrate that the COMT rs74745580 "T" mutation is associated with absent soluble COMT expression and very low COMT activity in two 22q11.2DS individuals.

**CONCLUSIONS:** Our findings confirm a robust effect of COMT hemizyosity on COMT activity and show complex interactions of variants within the COMT gene that influence COMT biology and confound conclusions based on associations with the Val158Met genotype alone.

16. Lubow RE, Kaplan O, Manor I.

Latent inhibition in ADHD adults on and off medication: a preliminary study.  
J Atten Disord. 2014 Oct;18(7):625-31.

#### **Abstract**

##### **OBJECTIVE:**

To determine the effects of stimulant medication on performance of ADHD adults on a selective attention task that assesses the processing of irrelevant stimuli.

##### **METHOD:**

ADHD patients and matched controls were given two sessions of a two-stage visual search-latent inhibition (LI) task. In stage-1, they detected the location of a unique shape presented with homogeneous distractors. In stage-2, target detection response time was examined as a function of the stage-1 experience with the target or distractor, or both, providing a within-subject measure of LI. In Session-1, the ADHD subjects were off their customary stimulant medication. In Session-2, they were on medication.

##### **RESULTS:**

Off-medicated ADHD subjects exhibited similar LI to that of controls; medicated ADHD subjects exhibited less LI than controls. Group differences in LI were mediated by RTs to the previously task-irrelevant distractor stimulus.

##### **CONCLUSION:**

The attenuated LI of the on-medication ADHD group is attributable to drug action that reduces attentional resources allocated to distractors.

17. Vinokur D, Levine SZ, Roe D, Krivoy A, Fischel T.

Age of onset group characteristics in forensic patients with schizophrenia.  
Eur Psychiatry. 2014 Mar;29(3):149-52.

**Abstract:** This study aims to empirically identify age of onset groups and their clinical and background characteristics in forensic patients with schizophrenia. Hospital charts were reviewed of all 138 forensic patients with schizophrenia admitted to Geha Psychiatric Hospital that serves a catchment area of approximately 500,000 people, from 2000 to 2009 inclusive. Admixture analysis empirically identified early- (M=19.99, SD=3.31) and late-onset groups (M=36.13, SD=9.25). Early-onset was associated with more suicide attempts, violence before the age of 15, and early conduct problems, whereas late-onset was associated with a greater likelihood of violence after the age of 18 and marriage ( $P<0.01$ ). The current findings provide clinicians with a unique direction for risk assessment and indicate differences in violence between early- and late-onset schizophrenia, particularly co-occurrence of harmful behavioral phenotypes.

18. Bleich-Cohen M, Hendler T, Weizman R, Faragian S, Weizman A, Poyurovsky M.  
Working memory dysfunction in schizophrenia patients with obsessive-compulsive symptoms: an fMRI study.

Eur Psychiatry. 2014 Mar;29(3):160-6.

## Abstract

### BACKGROUND:

A substantial proportion of schizophrenia patients also meets DSM-IV criteria for obsessive-compulsive disorder (OCD). Schizophrenia with OCD ("schizo-obsessive") patients are characterized by distinct clinical characteristics, treatment response and prognosis. Whether schizo-obsessive patients exhibit a distinct pattern of brain activation is yet unknown. To address this question, the present functional magnetic resonance imaging (fMRI) study explicitly compared alterations in brain activation and functional connectivity (FC) underlying a working memory deficit in schizophrenia patients with and without OCD.

### METHODS:

fMRI was applied during the N-back working memory (WM) task in three groups: schizo-obsessive (n=16), schizophrenia (n=17) and matched healthy volunteers (n=20). WM-related activation in the right dorsolateral prefrontal cortex (DLPFC) and the right caudate nucleus, brain areas relevant to schizophrenia and OCD, and FC analysis were used for the evaluation.

### RESULTS:

The two schizophrenia groups with and without OCD exhibited a similar reduction in activation in the right DLPFC and right caudate, as well as decreased FC compared to the healthy controls. Notably, reduced regional brain activation was not related to severity of schizophrenic or OCD symptoms.

### CONCLUSIONS:

Schizo-obsessive patients do not differ from their non-OCD schizophrenia counterparts in brain activation patterns during the N-back WM task. Cognitive paradigms tapping alternative neural networks (e.g., orbitofrontal cortex) particularly relevant to OCD, are warranted in the search for potential distinctive brain activation patterns of the schizo-obsessive subgroup.

19. Haker A, Aderka IM, Marom S, Hermesh H, Gilboa-Schechtman E. Impression formation and revision in social anxiety disorder. *J Anxiety Disord.* 2014 Mar;28(2):133-9.

## Abstract

Interpersonal relations are markedly impaired in social anxiety. Yet, little is known about the ways social anxiety affects social cognition. We examined impression formation and impression revision among individuals with social anxiety disorder (SAD, n = 26) and non-anxious individuals (n = 29). Participants read initial descriptions of protagonists depicted as dominant, neutral or submissive and rated them on social rank and affiliation dimensions. Next, participants were presented with behavioral acts that were either congruent, incongruent or irrelevant to the initial descriptions, and re-rated the protagonists. Individuals with SAD (a) rated others as more extreme on social rank dimension, (b) rated others as lower on the affiliation dimension, and (c) revised their impressions of others to a greater extent than did the non-anxious individuals. Understanding the ways social anxiety affects the formation and revision of perceptions of others can improve our understanding of maintaining processes in SAD.

20. Gershoni A, Hermesh H, Fineberg NA, Eilam D. Spatial behavior reflects the mental disorder in OCD patients with and without comorbid schizophrenia.

## Abstract

### OBJECTIVE:

Resolving the entangled nosological dilemma of whether obsessive-compulsive disorder (OCD) with and without schizophrenia (schizo-OCD and OCD, respectively) are two independent entities or whether schizo-OCD is a combined product of its parent disorders.

### METHODS:

Studying motor activity in OCD and in schizo-OCD patients. Performance of the patients was compared with the performance of the same motor task by a matching control individual.

### RESULTS:

Behavior in both schizo-OCD and OCD patients differed from controls in the excessive repetition and addition of acts, thus validating an identical OC facet. However, there was a significant difference in spatial behavior. Schizo-OCD patients traveled over a greater area with less focused activity as typical to schizophrenia patients and in contrast to OCD patients, who were more focused and traveled less in a confined area. While schizo-OCD and OCD patients share most of the OC ritualistic attributes, they differ in the greater spread of activity in schizo-OCD, which is related to schizophrenia disorder.

### DISCUSSION:

It is suggested that the finding on difference in spatial behavior is a reflection of the mental differences between OCD and schizophrenia. In other words, this could be an overt and observable manifestation of the mental state, and therefore may facilitate the nosology of OC spectrum disorders and OCD.

### CONCLUSION:

It seems as if both the OCD patients' focus on specific thoughts, and the contrasting wandering thoughts of schizophrenia patients, are reflected in the focused activity of the former and wandering from one place to the next of the latter.

21. Moses L, Katz N, Weizman A.

Metabolic profiles in adults with autism spectrum disorder and intellectual disabilities. Eur Psychiatry. 2014 Sep;29(7):397-401.

## Abstract

### INTRODUCTION:

Low levels of blood cholesterol have been found in some children with autism spectrum disorders (ASD). Psychotropic medications, commonly used by people with ASD and people with intellectual disabilities (ID) are frequently associated with altered metabolic profiles.

### PURPOSE:

We aimed to compare metabolic features of adults with ASD or ID with those of a community-based population.

#### **SUBJECTS AND METHODS:**

Data on blood fasting glucose (FBG), lipid profile, liver enzyme profile, TSH, BMI, medications and diagnoses of 80 adults with ASD, 77 adults with ID and 828 control adults were drawn from medical charts/database. Candidates that used glucose or lipid lowering medications were not included.

#### **RESULTS:**

Total-cholesterol levels of people with ASD and ID were significantly lower than those of the controls ( $168.3 \pm 32.78$ ,  $168.2 \pm 32.91$ ,  $185.4 \pm 40.49$  mg/dL, respectively,  $P < 0.001$ ) but after adjusting for gender, age and BMI and using Bonferroni correction, the significance was lost. Compared to controls, ASD and ID had significantly lower FBG (by  $-14.45 \pm 1.81$ ,  $-14.58 \pm 1.54$  mg/dl, respectively;  $P < 0.001$  for both) and liver enzymes, despite using psychotropic medications.

#### **DISCUSSION AND CONCLUSION:**

In contrast to other psychiatric patients receiving similar medications, people with ASD and ID have unaltered lipid profiles and lower glucose and liver enzyme levels compared to a community-based population.

22. Zarchi O, Diamond A, Weinberger R, Abbott D, Carmel M, Frisch A, Michaelovsky E, Gruber R, Green T, Weizman A, Gothelf D.

A comparative study of the neuropsychiatric and neurocognitive phenotype in two microdeletion syndromes: velocardiofacial (22q11.2 deletion) and Williams (7q11.23 deletion) syndromes.

Eur Psychiatry. 2014 May;29(4):203-10.

#### **Abstract**

##### **PURPOSE:**

22q11.2 deletion syndrome (22q11.2DS) and Williams syndrome (WS) are common neurogenetic microdeletion syndromes. The aim of the present study was to compare the neuropsychiatric and neurocognitive phenotypes of 22q11.2DS and WS.

##### **METHODS:**

Forty-five individuals with 22q11.2DS, 24 with WS, 22 with idiopathic developmental disability (DD) and 22 typically developing (TD) controls were compared for the rates of psychiatric disorders as well as cognitive executive and visuospatial functions.

##### **RESULTS:**

We found that while anxiety, mood and disruptive disorders had an equally high prevalence among individuals with 22q11.2DS, WS and DDs, the 22q11.2DS group had the highest rates of psychotic disorders and the WS group had the highest rates of specific phobia. We also found that the WS group demonstrated more severe impairments in both executive and visuospatial functions than the other groups. WS and 22q11.2DS subjects had worse Performance-IQ than Verbal-IQ, a feature typical of non-verbal learning disorders.

## CONCLUSION:

These findings offer a wide perspective on unique versus common phenotypes in 22q11.2DS and WS.

23. Aderka IM, Gutner CA, Lazarov A, Hermesh H, Hofmann SG, Marom S. Body image in social anxiety disorder, obsessive-compulsive disorder, and panic disorder. *Body Image*. 2014 Jan;11(1):51-6.

**Abstract:** Body dysmorphic disorder falls under the category of obsessive-compulsive and related disorders, yet research has suggested it may also be highly associated with social anxiety disorder. The current study examined body image variables among 68 outpatients with primary obsessive-compulsive disorder (OCD; n=22), social anxiety disorder (SAD; n=25), and panic disorder (PD; n=21). Participants filled out self-report measures of body image disturbance, attitudes toward one's appearance, and anxiety. Body image disturbance and attitudes toward appearance did not significantly differ between the groups. However, SAD symptoms predicted body image disturbance, Appearance Evaluation and Body Areas Satisfaction, and OCD symptoms predicted Appearance Orientation. These findings suggest that SAD and OCD may be associated with different facets of body image. Implications for the treatment of anxiety disorders and for future research are discussed.

24. Shoval G, Shmulewitz D, Wall MM, Aharonovich E, Spivak B, Weizman A, Hasin D. Alcohol dependence and suicide-related ideation/behaviors in an Israeli household sample, with and without major depression. *Alcohol Clin Exp Res*. 2014 Mar;38(3):820-5.

## Abstract

### BACKGROUND:

Suicide-related ideation and behaviors (SRIB) are associated with both alcohol disorders and major depressive disorder (MDD). The objective of this study was to evaluate the relationship of alcohol dependence (AD) and major depression to the risk for lifetime SRIB.

### METHODS:

Data from a community-based sample of 1,237 adult Israeli lifetime drinkers assessed with reliable diagnostic measures were analyzed using logistic regression.

### RESULTS:

Lifetime SRIB was reported in 4.7% and was more prevalent among participants with AD (9.0%) than among those without AD (4.1%); p-value = 0.01. Although both AD and major depression were associated with SRIB (AD: OR 2.2, 95% CI 1.1 to 4.4; MDD: OR 11.4, 95% CI = 6.4 to 20.4), joint analysis showed that AD without MDD increased risk for SRIB as compared to those without AD or MDD (OR 3.1, 95% CI 1.1 to 9.1), but AD did not increase risk among those with MDD (OR 1.1, 95% CI 0.4 to 2.7). Among those with AD, the severity of subclinical depressive symptoms was associated with increased SRIB.

### CONCLUSIONS:

These findings show that AD increases risk for SRIB among individuals without a history of major depression. Suicidal tendencies may be undetected and underdiagnosed in this group because of the absence of major depression and therefore left untreated. These findings should be considered when adopting suicide prevention or treatment strategies for this high-risk subpopulation.

25. Tsafirir S, Chubarov E, Shoval G, Levi M, Nahshoni E, Ratmansky M, Weizman A, Zalsman G.

Cognitive traits in inpatient adolescents with and without prior suicide attempts and non-suicidal self-injury.

Compr Psychiatry. 2014 Feb;55(2):370-3.

### **Abstract**

#### **OBJECTIVE:**

Establishing a psychiatric diagnosis and assessing suicidal tendencies is often a challenging task particularly in the early stages of an illness. Cognitive impairments characterize different psychiatric entities, but there is no known specific cognitive deficit profile that could help the clinician in achieving the diagnostic task. This study's aim was to establish a cognitive profile and test its ability to differentiate psychiatric inpatient subgroups, in terms of suicidal risk and diagnosis. The sample constituted of 76 consecutive admissions to the psychiatric adolescent day-care unit, who were admitted for any diagnosis. Assessment included full psychiatric interview and cognitive evaluation, using the COGNISTAT test.

#### **RESULTS:**

Of the 76 participants, 58% reported having suicidal ideation and 29% reported a prior attempted suicide. Subjects who had a prior suicide attempt had better orientation and attention scores in the COGNISTAT. Other cognitive domains did not differentiate between groups or diagnoses.

#### **CONCLUSION:**

These preliminary results suggest a significant association between specific cognitive characteristics and suicidal behavior in adolescents. Those cognitive characteristics might prove clinically useful in the assessment of suicide risk. Further study is needed to establish this association and generalize the conclusion to different populations.

26. Parellada M, Penzol MJ, Pina L, Moreno C, González-Vioque E, Zalsman G, Arango C. The neurobiology of autism spectrum disorders. Eur Psychiatry. 2014 Jan;29(1):11-9.

**Abstract:** Data is progressively and robustly accumulating regarding the biological basis of autism. Autism spectrum disorders (ASD) are currently considered a group of neurodevelopmental disorders with onset very early in life and a complex, heterogeneous, multifactorial aetiology. A comprehensive search of the last five years of the Medline database was conducted in order to summarize recent evidence on the neurobiological bases of autism. The main findings on genetic influence, neuropathology, neurostructure and brain networks are summarized. In addition, findings from peripheral samples of subjects with autism and animal models, which show immune, oxidative, mitochondrial dysregulations, are reported. Then, other biomarkers from very different systems associated with autism are reported. Finally, an attempt is made to try and integrate the available evidence, which points to a oligogenetic, multifactorial aetiology that converges in an aberrant micro-organization of the cortex, with abnormal functioning of the synapses and abnormalities in very general physiological pathways (such as inflammatory, immune and redox systems).

27. Lipschitz-Elhawi R, Itzhaky H.

The contribution of internal resources, external resources, and emotional distress to use of drugs and alcohol among Israeli Jewish urban adolescents.

Subst Use Misuse. 2014 Mar;49(4):475-8

**Abstract:** The contribution of selected background variables (age, gender), internal resources (mastery, emotional maturity), external resources (parental and peer support), and emotional distress to alcohol and drug use among 160 Israeli Jewish urban high school students were examined. Analyzing the variables with hierarchical regression, emotional distress contributed most significantly to both alcohol and drug use, and the contribution of age was somewhat less significant for both of them. Emotional distress also contributed indirectly to drug use through an interaction with one's sense of mastery. Gender, internal resources, and external resources contributed differentially to alcohol and drug use. Whereas gender and internal resources contributed only to drug use, external resources contributed only to alcohol use. Specifically, peer support contributed positively to alcohol use whereas parental support contributed negatively. The discussion provides explanations for these research findings and their implications, and the research's limitations are noted.

28. Walsh K, Elliott JC, Shmulewitz D, Aharonovich E, Strous R, Frisch A, Weizman A, Spivak B, Grant BF, Hasin D.  
Trauma exposure, posttraumatic stress disorder and risk for alcohol, nicotine, and marijuana dependence in Israel.  
*Compr Psychiatry*. 2014 Apr;55(3):621-30.

## **Abstract**

### **BACKGROUND:**

Substance dependence is more common among trauma-exposed individuals; however, most studies suggest that Posttraumatic Stress Disorder (PTSD) accounts for the link between trauma exposure (TE) and substance dependence.

### **OBJECTIVES:**

This study examined associations between TE and substance dependence (alcohol, nicotine, and marijuana), and whether PTSD accounted for this association.

### **METHOD:**

1317 Jewish Israeli household residents completed in-person structured interviews assessing TE, PTSD, and substance (alcohol, nicotine, marijuana) dependence between 2007 and 2009. Regression analyses examined associations among TE, PTSD, and substance dependence.

### **RESULTS:**

In the full sample, mean number of traumatic events was 2.7 (sd=2.2), with 83.7% experiencing at least one event. In the full sample, mean number of PTSD symptoms was 2.5 (sd=3.4), with 13.5% meeting PTSD diagnostic criteria. Prevalence of alcohol dependence was 13.4%; nicotine dependence 52.8%; and marijuana dependence 12.1%. Number of traumatic events was associated with increased odds of alcohol (OR=1.3; 95% CI=1.2-1.4) and nicotine (OR=1.2; 95% CI=1.1-1.3) dependence. Similarly, any traumatic event exposure was associated with increased odds of alcohol (OR=3.1; 95% CI=1.6-6.0) and nicotine (OR=1.9; 95% CI=1.2-2.9) dependence. PTSD symptoms were associated with increased odds of alcohol (OR=1.2; 95% CI=1.1-1.3), nicotine (OR=1.1; 95% CI=1.1-1.2), and marijuana (OR=1.1; 95% CI=1.04-1.2) dependence; similarly, a PTSD diagnosis was associated with increased odds of alcohol (OR=3.4; 95% CI=2.1-5.5), nicotine (OR=2.2; 95% CI=1.4-3.4), and marijuana (OR=2.6; 95% CI=1.2-5.9) dependence. PTSD symptoms accounted for a sizeable proportion of the TE effect on alcohol (46%) and nicotine dependence (31%).



## CONCLUSION:

Individuals with more traumatic events had heightened risk for alcohol and nicotine dependence, and PTSD symptoms partially accounted for this risk. However, marijuana dependence was only significantly related to PTSD symptoms. Clinicians and researchers should separately assess different types of dependence among trauma-exposed individuals both with and without PTSD symptoms.

29. Gil-Ad I, Portnoy M, Tarasenko I, Bidder M, Kramer M, Taler M, Weizman A.  
A novel analog of olanzapine linked to sarcosinyl moiety (PGW5) demonstrates high efficacy and good safety profile in mouse models of schizophrenia.  
*Eur Neuropsychopharmacol.* 2014 Mar;24(3):425-36

**Abstract:** Schizophrenia is a chronic mental disorder related to hypo-functioning of glutamatergic neurotransmission. N-methyl-D-aspartate-receptor (NMDA-R) positive modulators were reported to reduce schizophrenia symptoms. However, their efficacy is low and inconsistent. We developed a novel antipsychotic possessing an olanzapine moiety linked to the positive modulator of glutamate NMDA-R sarcosine (PGW5) and characterized the pharmacodynamic properties of the novel molecule in-vivo using MK-801 and in-vitro using receptor binding analysis. We investigated the pharmacological activity of PGW5 (olanzapine linked to sarcosinyl moiety) in male mice (BALB/c or C57BL). In an open field test, up to 50mg/kg PGW5 did not affect motility while higher doses were sedative. PGW5 (25-50mg/kg po) antagonized MK-801 (0.15 mg/kg ip) and amphetamine-induced (5mg/kg ip) hyperactivity. PGW5 (25mg/kg po/d) treatment for 15 or 22 days exhibited antidepressant and anxiolytic activity in mice. Moreover, PGW5, but not olanzapine, attenuated phencyclidine (PCP)-induced deficits of social preference in mice and promoted the expression of brain derived neurotrophic factor (BDNF) in the hippocampus and the frontal cortex and glutamic acid decarboxylase (GAD67) in the hippocampus. Mice treated with PGW5 (25 and 50mg/kg/d) for 28 days did not show toxic effects in terms of weight gain and blood-chemistry analysis. **CONCLUSIONS:** PGW5 is a novel and safe antipsychotic, efficacious against schizophrenia-like positive and negative symptoms at nonsedative doses. The drug shows anxiolytic and antidepressant activity, and improves impaired social performance in phencyclidine (PCP) treated mice. The mechanism underlying its activity seems to involve potentiation of NMDA receptor as well as stimulation of brain BDNF and GAD67 expression.

30. Golubchik P, Sever J, Weizman A.  
Methylphenidate treatment in children with attention deficit hyperactivity disorder and comorbid social phobia.  
*Int Clin Psychopharmacol.* 2014 Jul;29(4):212-5.

**Abstract:** The aim of this study was to assess the response of social phobia (SP) symptoms to methylphenidate (MPH) treatment in children with attention deficit hyperactivity disorder (ADHD). Twenty-one ADHD patients with SP, aged between 8 and 18 years, received 12 weeks of MPH treatment. The severity of SP symptoms were assessed by the Liebowitz Social Anxiety Scale for Children and Adolescents (LSAS-CA), and the severity of ADHD symptoms was assessed by the ADHD Rating Scale at baseline and at endpoint. MPH treatment was associated with a significant decrease in the ADHD Rating Scale scores ( $P < 0.0001$ ) and in the total LSAS-CA scores ( $P = 0.013$ ), as well as the school-related items of LSAS-CA ( $P = 0.011$ ). A significant correlation was found between the reductions in ADHD score and total LSAS-CA score ( $P = 0.038$ ), especially in school-related SP. The improvement in ADHD symptoms because of MPH treatment correlates with a parallel improvement in SP. MPH treatment appears to be safe and effective in ADHD/SP children.

31. Nahaliel S, Sommerfeld E, Orbach I, Weller A, Apter A, Zalsman G.  
Mental pain as a mediator of suicidal tendency: a path analysis.  
*Compr Psychiatry.* 2014 May;55(4):944-51.

**Abstract:**

## BACKGROUND:

This study used path-analysis to examine the assumption that the presence of mental pain in adults mediates the relationship between self-destruction, number of losses experienced in one's life, and suicidal tendency.

## METHODS:

Fifty suicidal inpatients, 50 non-suicidal inpatients and 50 healthy volunteers were assessed for self-destruction, losses experienced, depression, suicidal tendency, and mental pain.

## RESULTS:

Self-destruction was found to have both a direct effect on suicidal tendency as well as one mediated by the presence of mental pain. Number of losses effected suicidal tendency only indirectly, mediated by the presence of mental pain. Overall, self-destruction was a more significant determinant of suicidal tendency than were the number of losses experienced during one's life. A competing model, with depression replacing mental pain as the mediator, was also found to fit the data.

## DISCUSSION:

These findings provide evidence that the presence of mental pain is a mediator in the relationships between both self-destruction and number of losses experienced, and between suicidal tendencies. More studies are needed in order to further differentiate between mental pain and depression as mediators in suicidal tendency.

32. Shoval G, Bar-Shira O, Zalsman G, John Mann J, Chechik G.  
Transitions in the transcriptome of the serotonergic and dopaminergic systems in the human brain during adolescence.  
Eur Neuropsychopharmacol. 2014 Jul;24(7):1123-32.

**Abstract:** Adolescence is a period of profound neurophysiological, behavioral, cognitive and psychological changes, but not much is known about the underlying molecular neural mechanisms. The aim of this study was to systematically analyze expression levels of the genes forming serotonergic and dopaminergic synapses during adolescence. We analyzed the mRNA expression profiles of genes that code for all components of serotonergic and dopaminergic synapses, in 16 brain areas from human and non-human primates from public domain databases, to detect genes whose expression changes during adolescence. Two serotonin receptors, HTR1E and HTR1B had expression levels that exhibit a sharp transition in the prefrontal cortex in adolescence, but we found no similar transition in the dopaminergic system. A similar but smoother rise in expression levels is observed in HTR4 and HTR5A, and in HTR1E and HTR1B in three other expression datasets published. An earlier rise is observed in HTR1A, and a smooth and significant rise with age is observed in the expression of HTR1E in microarray measurements in macaque monkeys. The expression of HTR1E and HTR1B is correlated across subjects within each age group, suggesting that they are controlled by common mechanisms. These results point to HTR1E and HTR1B as major candidate genes involved in adolescence maturation processes, and to their operation through common control mechanisms. The maturation profiles may also involve several other 5-HT receptors, including the genes HTR5A, HTR4 and HTR1A.

33. Hasson-Ohayon I, Tuval-Mashiach R, Morag-Yaffe M, Gazieli M, Schapir L, Zalsman G, Shoval G.  
Parents of adolescents with psychiatric disorders: insight into the disorder, self-stigma and parental stress.  
Compr Psychiatry. 2014 Jul;55(5):1106-10

## **Abstract**

### **BACKGROUND:**

Parents of adolescents with mental disorders experience stress partially due to the way they perceive and experience their offspring's disorder. The current study assessed the mediator role of self-stigma in the relationship between insight into the disorder and parental stress of parents of adolescents with mental disorders.

### **METHOD:**

A total of 37 parents of adolescents with psychiatric disorders were assessed for their level of insight, self-stigma and parental stress.

### **RESULTS:**

The hypothesized mediation model was confirmed and is consistent with previous study on parents of adults with severe mental illness.

### **DISCUSSION:**

The positive association between insight and parental stress is mediated by these parents' self-stigma, suggesting that insight increases the self-stigma, which in turn increases the parental stress. These results may have clinical implications with regard to the treatment of the family of adolescents with mental disorders.

34. Shelef A, Hiss J, Cherkashin G, Berger U, Aizenberg D, Baruch Y, Barak Y  
Psychosocial and medical aspects of older suicide completers in Israel: a 10-year survey  
International Journal of Geriatric Psychiatry 2014 Aug; 29(8):846-851

## **Abstract**

### **OBJECTIVES:**

The rate of completed suicide among the elderly continues to be the highest of any age group worldwide. The aim of the present study was to investigate the sociodemographic data, mental and physical health characteristics, and suicide methods of the elderly population who completed suicide in Israel.

### **METHODS:**

A national retrospective record-based case series study of consecutive elder (50 years or older) suicide completers who had undergone autopsy over a 10-year period was conducted.

### **RESULTS:**

Three hundred and fourteen consecutive records of suicide completers, 69.6% males, and mean age 64.7 were analyzed. The largest group (38%) emigrated from the Former Soviet Union and 19% emigrated from East Europe. Immigrants from East Europe committed suicide at an older age. Hanging was the predominant suicide method. Jumping from height increased more than threefold in the 'old-old' (older than 75 years) group. Hanging and firearms were more frequently used by males. Females were more likely to employ poisoning and suffocation. A significant minority (30%) had been

diagnosed as suffering from psychiatric morbidity. Most common diagnoses were depression and alcohol abuse or dependence. Physical disorders (mainly cardiovascular disease and malignancy) were present in 27% of cases. Subjects with psychiatric illness were more likely to complete suicide at a younger age compared with subjects with physical illness.

## CONCLUSIONS:

Findings of male predominance, psychiatric morbidity, and physical illness are consistent with previously published studies. Immigrants from East Europe completed suicide at an older age and the older victims had used more lethal methods of suicide.

35. Cohen O, Finzi-Dottan R

Contribution of Health, Coparenting, and Maturity of Defense Mechanisms to the Quality of Life of Divorcing and Divorced Parents: A Longitudinal Study  
Marriage & Family Review 2014; 50(5): 395-415

**Abstract:** This longitudinal study, carried out among 78 divorcing and divorced parents in Israel, examined changes in their coparenting over a 2-year period and the contribution of their coparenting behaviors and defense mechanisms, at three time points, to their quality of life at Time 3. Data were collected between 2007 and 2009. At Time 1 couples appeared in the family court, and Times 2 and 3 were 1 and 2 years later, respectively. The main findings show that (1) both parents' participation and consideration decreased over time, (2) both tension/hostility with the spouse and low level of mature defense mechanisms eroded the participants' quality of life, (3) the ability of tension/hostility to undermine the participants' quality of life exceeded the ability of mature defense mechanisms to improve it, (4) the negative impact of the participants' coparenting relationship and immature defense mechanisms in the first year endured to the third year, and (5) being free of health problems contributed significantly to the participants' quality of life. The limitations, contributions, and practical implications of the study are noted.

36. Golubchik P, Golubchik L, Sever JM, Weizman A.

The beneficial effect of methylphenidate in ADHD with comorbid separation anxiety.  
Int Clin Psychopharmacol. 2014 Sep;29(5):274-8.

**Abstract:** The objective of this study was to assess the response of subsyndromal separation anxiety (SSSA) symptoms to methylphenidate (MPH) treatment in patients with attention-deficit/hyperactivity disorder (ADHD). A group of patients with ADHD and SSSA (n=42), aged 8-17 years, received 12 weeks of MPH treatment. The severity of SSSA symptoms was assessed using appropriate scales including the Screen for Child Anxiety Related Emotional Disorders and the specially designed Child and Adolescent Separation Anxiety Scale (CASAS). The severity of ADHD symptoms was assessed using the ADHD Rating Scale. The severity of ADHD and separation anxiety reduced significantly and significant positive correlations were found between the changes in ADHD Rating Scale and the total CASAS scores (P=0.012), as well as other relevant subscales of Screen for Child Anxiety Related Emotional Disorders and CASAS. The MPH-related attenuation in the severity of ADHD was associated with a corresponding improvement in separation anxiety related to school. SSSA symptomatology may be secondary to ADHD and thus the alleviation in ADHD symptoms achieved by MPH treatment results in corresponding relief in separation anxiety.

37. Kushnir J, Marom S, Mazar M, Sadeh A, Hermesh H.

The link between social anxiety disorder, treatment outcome, and sleep difficulties among patients receiving cognitive behavioral group therapy.  
Sleep Med. 2014 May;15(5):515-21.

## Abstract

## **OBJECTIVE:**

The aim of our study was to examine the association between sleep disturbances and social anxiety disorder (SAD). Another aim was to explore the impact of cognitive behavioral group therapy (CBGT) for SAD on co-occurring sleep difficulties.

## **METHODS:**

Data were obtained retrospectively from patient files receiving CBGT for SAD. The sample included 63 patients with SAD (mean age, 30.42 years [standard deviation, 6.92 years]). There were 41 men and 22 women, of whom 41 participants completed the treatment protocol. Before treatment onset participants completed the Liebowitz Social Anxiety Scale (LSAS), the Beck Depression Inventory (BDI), the Pittsburgh Sleep Quality Index, and several sociodemographic questions. On completion of the treatment protocol, the same measures were completed, with the addition of the Sheehan Disabilities Scale (SDS).

## **RESULTS:**

The results of our study suggest that: (1) subjective insomnia is associated with SAD severity even after controlling for depression severity and additional variables; (2) participants with SAD with co-occurring clinical levels of subjective insomnia present a more severe clinical picture both at treatment onset and termination; and (3) although CBGT lead to reduction in SAD and depression symptoms severity, it had no significant impact on co-occurring sleep difficulties.

## **CONCLUSIONS:**

Sleep difficulties predict SAD severity regardless of depressive symptoms and may be linked to a more severe clinical picture. Clinicians should be aware of these sleep difficulties co-occurring with SAD and consider implementing specific sleep interventions. Future studies should incorporate larger samples sizes from clinical populations outside of Israel.

38. Amitai M, Zivony A, Kronenberg S, Nagar L, Saar S, Sever J, Apter A, Shoval G, Golubchik P, Hermesh H, Weizman A, Zalsman G.

Short-term effects of lithium on white blood cell counts and on levels of serum thyroid-stimulating hormone and creatinine in adolescent inpatients: a retrospective naturalistic study.

J Child Adolesc Psychopharmacol. 2014 Nov;24(9):494-500.

## **Abstract**

### **OBJECTIVE:**

The purpose of this study was to determine if the known side effects of lithium in adults may be generalized to younger patients with psychiatric disorders.

### **METHODS:**

A retrospective naturalistic study design was used. Data were collected from the database of a tertiary pediatric medical center covering the years 1994-2010. Included were patients hospitalized for bipolar and non-bipolar disorders and treated with lithium, alone or in combination with other medications. The electronic medical files were reviewed for changes in thyroid and kidney function and for hematological parameters during the course of treatment.

## RESULTS:

Sixty-one patients 12.5-20.4 years of age (mean 16.94±1.66) met the study criteria: 33 with bipolar disorder and 28 with a non-bipolar disorder. Mean duration of lithium treatment (mean lithium blood level, 0.73±0.24 mEq/L) was 193.68±254.35 days. Mean levels of thyroid-stimulating hormones (TSH) rose significantly from baseline to last measurement (3.16±2.68 vs. 1.52±0.92 mU/L; paired  $t=-5.19$ ,  $df=50$ ,  $p<0.001$ ); in 25% of patients, TSH levels at the last measurement were above normal ( $\geq 4$  mU/L). Only one patient developed TSH values  $>10$  mU/L (the threshold considered clinically significant). Positive correlation was found between pre- and posttreatment TSH levels (Pearson's  $r=0.60$ ;  $n=51$ ,  $p<0.05$ ). White blood cell count (WBC) also increased significantly following lithium treatment (7195±2151 vs. 7944±2096 cells/mm<sup>3</sup>;  $t=2.83$ ,  $df=60$ ,  $p=0.006$ ). No significant changes were noted in serum creatinine levels. There was no difference in these parameters between patients treated with lithium alone or in combination with other medications.

## CONCLUSIONS:

Lithium treatment in adolescents with bipolar or non-bipolar disorders is associated with a significant increase in blood TSH levels and WBC count. Lithium-treated adolescent inpatients with a high basal TSH level may be at risk of developing pituitary-thyroid axis dysregulation. Therefore, baseline measurement of thyroid functions and serial monitoring throughout treatment are recommended.

39. Carmel M, Zarchi O, Michaelovsky E, Frisch A, Patya M, Green T, Gothelf D, Weizman A. Association of COMT and PRODH gene variants with intelligence quotient (IQ) and executive functions in 22q11.2DS subjects. *J Psychiatr Res.* 2014 Sep;56:28-35.

**Abstract:** The 22q11.2 deletion syndrome (22q11.2DS) carries the highest genetic risk factor for the development of schizophrenia. We investigated the association of genetic variants in two schizophrenia candidate genes with executive function (EF) and IQ in 22q11.2DS individuals. Ninety two individuals with 22q11.2 deletion were studied for the genetic association between COMT and PRODH variants and EF and IQ. Subjects were divided into children (under 12 years old), adolescents (between 12 and 18 years old) and adults (older than 18 years), and genotyped for the COMT Val158Met (rs4680) and PRODH Arg185Trp (rs4819756) polymorphisms. The participants underwent psychiatric evaluation and EF assessment. Our main finding is a significant influence of the COMT Val158Met polymorphism on both IQ and EF performance. Specifically, 22q11.2DS subjects with Met allele displayed higher IQ scores in all age groups compared to Val carriers, reaching significance in both adolescents and adults. The Met allele carriers performed better than Val carriers in EF tasks, being statistically significant in the adult group. PRODH Arg185Trp variant did not affect IQ or EF in our 22q11.2DS cohort. In conclusion, functional COMT variant, but not PRODH, affects IQ and EF in 22q11.2DS subjects during neurodevelopment with a maximal effect at adulthood. Future studies should monitor the cognitive performance of the same individuals from childhood to old age.

40. Shelef L, Fruchter E, Mann JJ, Yacobi A. Correlations between interpersonal and cognitive difficulties: relationship to suicidal ideation in military suicide attempters. *Eur Psychiatry.* 2014 Oct;29(8):498-502

## Abstract

### BACKGROUND:

Understanding suicidal ideation may help develop more effective suicide screening and intervention programs. The interpersonal and the cognitive-deficit theories seek to describe the factors leading to suicidal behavior. In the military setting it is common to find over- and under-reporting of suicidal

ideation. This study sought to determine the relationship between these two models and determine to what degree their components can indirectly predict suicidal ideation.

#### **METHODS:**

Suicide attempters (n=32) were compared with non-suicidal psychologically treated peers (n=38) and controls (n=33), matched for sex and age (mean 19.7years). Pearson's analysis was used to quantify the relationship between the variables from the two models and hierarchical regression analysis was used to determine the explanation of suicidal ideation variance by these variables.

#### **RESULTS:**

Suicide attempters have more difficulties in problem-solving, negative emotion regulation and burdensomeness compared with their peers ( $P < .001$ ). These variables are all closely correlated with each other and to suicide ideation ( $r > \pm 0.5$ ;  $P < .001$ ). Prior suicide attempt, loneliness and burdensomeness together explain 65% ( $P < .001$ ) of the variance in suicidal ideation.

#### **CONCLUSIONS:**

Suicidal ideation is strongly correlated with components of interpersonal and cognitive difficulties. In addition to assessing current suicidal ideation, clinicians should assess past suicide attempt, loneliness and burdensomeness.

41. Amit BH, Krivoy A, Mansbach-Kleinfeld I, Zalsman G, Ponizovsky AM, Hoshen M, Farbstein I, Apter A, Weizman A, Shoval G.

Religiosity is a protective factor against self-injurious thoughts and behaviors in Jewish adolescents: findings from a nationally representative survey.

Eur Psychiatry. 2014 Oct;29(8):509-13

#### **Abstract**

##### **PURPOSE:**

Few studies have investigated the association between religiosity and self-injurious thoughts and behaviors specifically in adolescents, yielding inconsistent results. To date, no study has examined this relationship in a Jewish adolescent cohort.

##### **METHODS:**

Self-injurious thoughts and behaviors, as well as depression, were assessed in a nationally representative sample of Jewish adolescents (n=620) and their mothers, using the Development and Well-Being Assessment Inventory (DAWBA) structured interview. Degree of religiosity was obtained by a self-report measure.

##### **RESULTS:**

Using multivariate analysis, level of religiosity was inversely associated with self-injurious thoughts and behaviors (Wald  $\chi(2)=3.95$ ,  $P=0.047$ ), decreasing the likelihood of occurrence by 55% (OR=0.45, 95% CI 0.2-0.99), after adjusting for depression and socio-demographic factors. This model (adjusted  $R(2)=0.164$ ; likelihood ratio  $\chi(2)=7.59$ ;  $df=1$ ;  $P < 0.047$ ) was able to correctly classify 95.6% of the patients as belonging either to the high or low risk groups.

## CONCLUSION:

This is the first study demonstrating religiosity to have a direct independent protective effect against self-injurious thoughts and behaviors in Jewish adolescents. This finding has clinical implications regarding risk assessment and suicide prevention. Further research can potentially elucidate the complex relationship between religiosity, self-injury and suicide in this population.

42. Sagy R, Weizman A, Katz N.

Pharmacological and behavioral management of some often-overlooked clozapine-induced side effects.

Int Clin Psychopharmacol. 2014 Nov;29(6):313-7.

**Abstract:** This article reviews four of the milder but still bothersome side effects of clozapine that are fairly frequent and may have a negative impact on patients' compliance with the treatment regime. We reviewed the available literature on the rate and management of four non-life-threatening side effects of clozapine, including hypersalivation, constipation, tachycardia, and nocturnal enuresis. We found a variety of pharmacological and behavioral strategies to manage these four side effects. There is, however, no consensus on a preferred strategy to control these distressing side effects and there are no guidelines. Psychiatrists should be aware of the relatively high rate of hypersalivation, constipation, tachycardia, and nocturnal enuresis in clozapine-treated patients, of the impact that these side effects may have on patients' quality of life, and should be able to suggest management strategies to the patients.

43. Thompson RG Jr, Shmulewitz D, Meyers JL, Stohl M, Aharonovich E, Spivak B, Weizman A, Frisch A, Grant BF, Hasin DS.

Parental psychopathology moderates the influence of parental divorce on lifetime alcohol use disorders among Israeli adults.

Drug Alcohol Depend. 2014 Aug 1;141:85-91.

## Abstract

### BACKGROUND:

Parental divorce and psychopathology are well-documented risk factors for alcohol use disorders (AUD) in the United States and other countries where divorce is common and per capita total alcohol consumption is moderate to high. However, little is known about these relationships in countries where divorce and alcohol problems are less common, such as Israel.

### METHODS:

Israeli adult household residents (N=797) age 21-45 were interviewed in person between 2007 and 2009. Logistic regression models were used to examine main and additive interaction effects of parental divorce and psychopathology on lifetime DSM-IV AUD, adjusting for age, gender, and ethnicity.

### RESULTS:

Parental divorce (OR=2.18,  $p < 0.001$ ) and parental psychopathology (OR=1.61,  $p < 0.01$ ) were independently associated with lifetime AUD and, when considered together, showed significant interaction ( $p = 0.026$ ). Specifically, the effect of divorce on AUD was only significant among those who also reported parental psychopathology.

### CONCLUSIONS:



This is the first study showing the influence of parental divorce and psychopathology on risk for AUD among Israeli adults, where both divorce and AUD are less common than in the United States. Alcohol prevention and treatment professionals should recognize that children who experience parental divorce and/or psychopathology could be more vulnerable to later developing AUD than those whose parents remain together and without psychopathology.

44. Grinshpoon A, Weizman A, Amrami-Weizman A.

The beneficial effect of trazodone treatment on escitalopram-associated nocturnal bruxism. (Letter, No Abstract)

J Clin Psychopharmacol. 2014 Oct;34(5):662

45. Kilcoyne B, Shmulewitz D, Meyers JL, Aharonovich E, Greenstein E, Frisch A, Weizman A, Spivak B, Edenberg HJ, Gelernter J, Hasin DS.

Alcohol consumption mediates the relationship between ADH1B and DSM-IV alcohol use disorder and criteria.

J Stud Alcohol Drugs. 2014 Jul;75(4):635-42.

## Abstract

### OBJECTIVE:

A single nucleotide variation in the alcohol dehydrogenase 1B (ADH1B) gene, rs1229984, produces an ADH1B enzyme with faster acetaldehyde production. This protective variant is associated with lower alcohol consumption and lower risk for alcohol use disorders (AUDs). Based on the premise that faster ADH1B kinetics decreases alcohol consumption, we formally tested if the association between ADH1B variant rs1229984 and AUDs occurs through consumption. We also tested whether the association between rs1229984 and each of the 11 Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), AUD criteria occurs through consumption.

### METHOD:

A total of 1,130 lifetime drinkers from an Israeli household sample were assessed with a structured interview and genotyped for rs1229984 (protective allele frequency = 0.28). Logistic regression evaluated the association between rs1229984 and each phenotype (AUDs, 11 individual DSM-IV criteria). For phenotypes significantly related to rs1229984, the effect through consumption was tested with logistic regression and bootstrapping.

### RESULTS:

ADH1B rs1229984 was significantly associated with AUDs and six criteria, with odds ratios ranging from 1.32 to 1.96. The effect through consumption was significant for these relationships, explaining 23%-74% of the total ADH1B effect.

### CONCLUSIONS:

This is the first study to show that ADH1B rs1229984 is related to 6 of the 11 DSM-IV AUD criteria and that alcohol consumption explained a significant proportion of these associations and the association of ADH1B with AUDs. Better understanding of the relationship between ADH1B and the DSM-IV AUD criteria, including effects through consumption, will enhance our understanding of the etiologic model through which AUDs can occur.

46. Kertzman S, Avital A, Weizman A, Segal M.

Intrusive trauma recollections is associated with impairment of interference inhibition and psychomotor speed in PTSD.  
Compr Psychiatry. 2014 Oct;55(7):1587-94.

## **Abstract**

### **BACKGROUND:**

Intrusive cognitions that enter consciousness involuntarily are prominent symptoms of posttraumatic stress disorder (PTSD). The present study aimed to identify neuropsychological mechanisms involved.

### **METHOD:**

Fifty PTSD outpatients and 50 healthy controls were tested using Finger Tapping, Simple and Choice Reaction Times and Stroop Tasks, to measure motor, psychomotor speed, response selection, and interference inhibition ability respectively.

### **RESULTS:**

PTSD patients performed poorly in all tests, presumably owing to their generalized slowness of information processing and motor reaction. Psychomotor speed was a predictor of slowness and high error rate during the Stroop. Impaired inhibition, as measured by the interference index of the Stroop task, explained 9.7% of the predicated variance in frequency of re-experiencing PTSD symptoms and 23.5% of the predicated variance in augmentation of the interference response time.

### **CONCLUSION:**

Impaired interference control may be related to internal (re-experiencing) and external (sensory) stimuli that leads to cognitive deficits in PTSD patients.

47. Hochman E, Weizman A, Valevski A, Fischel T, Krivoy A.  
Association between bipolar episodes and fluid and electrolyte homeostasis: a retrospective longitudinal study.  
Bipolar Disord. 2014 Dec;16(8):781-9.

## **Abstract**

### **OBJECTIVES:**

Imbalance of fluid and electrolyte homeostasis has been suggested to be associated with the neuropathological processes underlying bipolar disorder. However, longitudinal data regarding the association of bipolar episodes with fluid balance are still lacking. We hypothesized that mania may be associated with a relative fluid retention and hemodilution, and depression with a relative hemoconcentration.

### **METHODS:**

Patients with bipolar disorder (n = 43) admitted to a mental health center, both with depressive and manic episodes, were retrospectively followed between 2005 and 2013. Fluid balance and electrolyte serum indices were compared between their manic and depressive episodes. We adjusted for physical and psychiatric comorbidities and for psychotropic treatment, using two-way analysis of variance with repeated measures.

## RESULTS:

There was a significant reduction in serum fluid balance indices during mania compared to depression: mean hemoglobin concentration  $13.9 \pm 1.4$  g/dL versus  $14.5 \pm 1.4$  g/dL, paired  $t = -4.2$ ,  $p < 0.0005$ ; mean hematocrit  $41.1 \pm 4.1\%$  versus  $42.3 \pm 3.7\%$ , paired  $t = -3.0$ ,  $p < 0.005$ ; mean albumin concentration  $4.2 \pm 0.3$  g/dL versus  $4.5 \pm 0.3$  g/dL, paired  $t = -4.5$ ,  $p < 0.0001$ ; and mean sodium concentration  $140.3 \pm 2.0$  mEq/L versus  $141.0 \pm 2.0$  mEq/L, paired  $t = -2.1$ ,  $p = 0.04$ , respectively. Controlling for physical and psychiatric comorbidities and psychotropic treatment did not alter these associations.

## CONCLUSIONS:

Our results support the notion of an imbalance of fluid and electrolyte homeostasis among bipolar episodes, which is suggestive for relative hemoconcentration during depressive episodes and relative hemodilution during manic episodes. These findings may eventually lead to novel therapeutic targets.

48. Hochman E, Shelef L, Mann JJ, Portugese S, Krivoy A, Shoval G, Weiser M, Fruchter E. Primary health care utilization prior to suicide: a retrospective case-control study among active-duty military personnel.

J Clin Psychiatry. 2014 Aug;75(8):e817-23

## Abstract

### OBJECTIVE:

About 45% of civilians who died by suicide had contact with a doctor within 1 month of death. Thus, educating primary care physicians (PCP) to detect and mitigate depression is an important suicide-prevention strategy. However, the PCP consulting rate before suicide has not been examined in a military population. We investigated the utilization of primary health care and mental health services by active-duty military personnel suicide cases prior to death in comparison to matched military controls.

### METHOD:

All suicides ( $N = 170$ ) were extracted from a cohort of all active-duty Israeli military male personnel between 2002 and 2012. Applying a retrospective, nested case-control design, we compared primary care services utilization by suicide cases with demographic and occupationally matched military controls ( $N = 500$ ).

### RESULTS:

Whereas 38.3% of suicide cases contacted a PCP within the last month before death, only 27.6% of suicide cases contacted a mental health specialist during their entire service time. The PCP contact rate within 1 month before death or index day did not differ between suicide cases and military controls (38.3% vs. 33.8%,  $\chi^2_1 = 1.05$ ,  $P = .3$ ). More suicide cases contacted a mental health specialist within service time than did military controls (27.6% vs. 13.6%,  $\chi^2_1 = 10.85$ ,  $P = .001$ ).

### CONCLUSIONS:

Even though PCP contact rate by military personnel who died by suicide is slightly lower than that reported for civilians who died by suicide prior to their death, it is higher than mental health specialist contact rate and higher than that by age-matched civilians who died by suicide. These results imply that PCPs education is a viable approach to suicide prevention in a military setting.

49. Meyers JL, Shmulewitz D, Elliott JC, Thompson RG, Aharonovich E, Spivak B, Weizman A, Frisch A, Grant BF, Hasin DS.

Parental alcohol history differentially predicts offspring disorders in distinct subgroups in Israel.

J Stud Alcohol Drugs. 2014 Sep;75(5):859-69

### Abstract

#### OBJECTIVE:

The association between alcoholism in parents and related disorders in their offspring is well established in cultures with intermediate/high alcohol consumption, but not in those with low consumption, such as Israel. This study investigated differences in parental transmission of alcohol problems and related psychopathology between immigrants from the former Soviet Union (FSU) to Israel and other Israelis—two Israeli subgroups with differing alcohol consumption behaviors and social norms.

#### METHOD:

A total of 1,347 adults from a household sample were interviewed. Regression analyses were used to examine associations between parental alcohol problems and participant disorders: alcohol, nicotine, and cannabis use disorders (AUD, NUD, CUD); antisocial personality disorder (ASPD); major depressive disorder (MDD); and posttraumatic stress disorder (PTSD). We also examined the associations of parental alcohol problems with participant disorders characterized with two latent factors: externalizing (EXT: AUD, NUD, CUD, ASPD) and internalizing (INT: MDD, PTSD). Differential parental transmission of alcohol problems in FSU (n = 315) and non-FSU (n = 1,032) Israelis was examined with statistical interaction.

#### RESULTS:

Among emigrants from the FSU, parental alcohol problems predicted AUD, NUD, CUD, ASPD, PTSD, EXT, and INT (mean ratios = 1.38-4.83). In non-FSU Israelis, parental alcohol problems predicted only ASPD and PTSD (mean ratios = 1.08-4.09). Significant interactions were observed for AUD, CUD, PTSD, and EXT; each relationship was stronger in FSU Israelis and null (AUD, CUD, EXT) or less robust (PTSD) in other Israelis.

#### CONCLUSIONS:

Parental alcohol problems were related to substance use and psychiatric disorders differently in FSU and other Israelis, two groups with different alcohol consumption levels and drinking norms. We propose that, in social contexts that vary in the degree to which they constrain alcohol behavior, underlying genetic predispositions may manifest as different disorders.

50. Shrot S, Ramaty E, Biala Y, Bar-Klein G, Daninos M, Kamintsky L, Makarovsky I, Statlender L, Rosman Y, Krivoy A, Lavon O, Kassirer M, Friedman A, Yaari Y.

Prevention of organophosphate-induced chronic epilepsy by early benzodiazepine treatment.

Toxicology. 2014 Sep 2;323:19-25

**Abstract:** Poisoning with organophosphates (OPs) may induce status epilepticus (SE), leading to severe brain damage. Our objectives were to investigate whether OP-induced SE leads to the emergence of spontaneous recurrent seizures (SRSs), the hallmark of chronic epilepsy, and if so, to assess the efficacy of benzodiazepine therapy following SE onset in preventing the epileptogenesis.

We also explored early changes in hippocampal pyramidal cells excitability in this model. Adult rats were poisoned with the paraoxon (450µg/kg) and immediately treated with atropine (3mg/kg) and obidoxime (20mg/kg) to reduce acute mortality due to peripheral acetylcholinesterase inhibition. Electrical brain activity was assessed for two weeks during weeks 4-6 after poisoning using telemetric electrocorticographic intracranial recordings. All OP-poisoned animals developed SE, which could be suppressed by midazolam. Most (88%) rats which were not treated with midazolam developed SRSs, indicating that they have become chronically epileptic. Application of midazolam 1min following SE onset had a significant antiepileptogenic effect (only 11% of the rats became epileptic;  $p=0.001$  compared to non-midazolam-treated rats). Applying midazolam 30min after SE onset did not significantly prevent chronic epilepsy. The electrophysiological properties of CA1 pyramidal cells, assessed electrophysiologically in hippocampal slices, were not altered by OP-induced SE. Thus we show for the first time that a single episode of OP-induced SE in rats leads to the acquisition of chronic epilepsy, and that this epileptogenic outcome can be largely prevented by immediate, but not delayed, administration of midazolam. Extrapolating these results to humans would suggest that midazolam should be provided together with atropine and an oxime in the immediate pharmacological treatment of OP poisoning.

51. Levi-Belz Y, Gvion Y, Horesh N, Fischel T, Treves I, Or E, Stein-Reisner O, Weiser M, David HS, Apter A

Mental pain, communication difficulties, and medically serious suicide attempts: a case-control study

Arch Suicide Res. 2014;18(1):74-87

**Abstract:** Medical severe suicide attempts (MSSA) are epidemiologically very similar to individuals who complete suicide. Thus the investigation of individuals who have made MSSAs may add to our understanding of the risk factors for completed suicide. The aim of this study was to assess the role of mental pain and communication difficulties in MSSA. A total of 336 subjects were divided into 4 groups: 78 meeting criteria for MSSA compared with 116 subjects who made a medically non-serious suicide attempt (MNSSA), 47 psychiatric controls with no history of suicidal behavior, and 95 healthy controls. Mental pain variants (e.g., hopelessness), facets of communication difficulties (e.g., self-disclosure), as well as socio-demographic and clinical characteristics were assessed. The MSSA had significantly higher communication difficulties than the other 3 groups. Moreover, the interaction between mental pain and communication difficulties explained some of the variance in suicide lethality, above and beyond the contribution of each component alone. This report underlines the importance of mental pain for suicide attempts in general while difficulties in communication abilities play a critical role in differentiating MSSA from MNSSA. The co-existence of unbearable mental pain with difficulties in communication significantly enhances the risk for more lethal forms of suicidal behavior.

52. Manor I, Rubin J, Daniely Y, Adler LA.

Attention benefits after a single dose of metadoxine extended release in adults with predominantly inattentive ADHD.

Postgrad Med. 2014 Sep;126(5):7-16

### Abstract

#### OBJECTIVE:

To assess the first-dose effectiveness and tolerability of metadoxine extended release (MDX) in adults with predominantly inattentive attention-deficit/hyperactivity disorder (ADHD-PI).

#### METHODS:

In this double-blind, placebo-controlled, crossover study, adults with ADHD-PI were randomized 1:1:1 to receive a single dose of MDX 1400 mg, MDX 700 mg, and placebo (ClinicalTrials.gov identifier: [NCT01685281](#)). The primary efficacy end point was the mean change in the Test of Variables of Attention (TOVA) ADHD score from baseline to 3 to 5 hours after drug administration. Secondary assessments included TOVA subscores, TOVA response rates (defined as an increase of 0.8 points in the TOVA ADHD score), and the Cambridge Neuropsychological Automated Test Battery. Safety assessments included adverse events and vital signs.

## RESULTS:

The intention-to-treat population included 36 patients (52.8% men; mean age, 32 years). The efficacy of MDX 1400 mg was demonstrated by a statistically significant difference in the mean ( $\pm$  SD) change in the TOVA ADHD score at baseline to 3 to 5 hours after drug administration compared with placebo (2.0 [4.2];  $P = 0.009$ ). The TOVA response time variability subscore was significantly different between MDX 1400 mg and placebo (mean difference, 7.9 [19.2] points;  $P = 0.022$ ). Significantly more adults responded to single-dose MDX 1400 mg versus placebo (97.1% vs 71.4%,  $P = 0.006$ ). There were no statistically significant differences between MDX 700 mg and placebo on any measures. Exploratory analyses of the Cambridge Neuropsychological Automated Test Battery did not yield significant findings. Fatigue and headache were the 2 most frequently reported adverse events. There were no clinically significant abnormalities in laboratory values, vital signs measurements, Columbia-Suicide Severity Rating Scale scores, or electrocardiographic parameters.

## CONCLUSIONS:

Single-dose MDX 1400 mg significantly improved sustained and selective attention in adults with ADHD-PI as measured by the TOVA ADHD score 3 to 5 hours after drug administration. Single doses of MDX 700 and 1400 mg were well tolerated.

53. Lazarov A, Liberman N, Hermesh H, Dar R  
Seeking proxies for internal states in obsessive-compulsive disorder  
*J Abnorm Psychol.* 2014 Nov;123(4):695-704

**Abstract:** Pervasive doubts are a central feature of obsessive-compulsive disorder (OCD). We have theorized that obsessive doubts can arise in relation to any internal state and lead to compensatory reliance on more discernible substitutes (proxies), including rules and rituals. Previous findings corroborated this hypothesis, but were based on students with high and low OCD tendencies and did not control for anxiety. The present study tested our hypothesis in OCD participants using both anxiety disorders and nonclinical controls. Twenty OCD participants, 20 anxiety disorders participants, and 20 nonclinical participants underwent 2 experimental procedures. In the first, participants had to produce specific levels of muscle tension with and without the aid of biofeedback. In the second, participants were asked to subjectively assess their own muscle tension after viewing preprogrammed false feedback showing either increasing or decreasing levels of muscle tension. As predicted, OCD participants were less accurate than anxiety disorder and nonclinical participants in producing designated levels of muscle tension when biofeedback was not available and more likely to request the biofeedback when given the opportunity to do so. In the false feedback procedure, OCD participants were more influenced by the false biofeedback when judging their own level of muscle tension compared with the 2 controls groups. In both procedures, anxiety disorder participants did not differ from the nonclinical controls. These results support the hypothesis that individuals with OCD have attenuated access to and reduced confidence in their internal states, and that this deficit is specific to OCD and not attributable to anxiety.

54. Avril M, Leclère C, Viaux S, Michelet S, Achard C, Missonnier S, Keren M, Cohen D, Chetouani M.  
Social signal processing for studying parent-infant interaction.

Front Psychol. 2014 Dec 10;5:1437

**Abstract:** Studying early interactions is a core issue of infant development and psychopathology. Automatic social signal processing theoretically offers the possibility to extract and analyze communication by taking an integrative perspective, considering the multimodal nature and dynamics of behaviors (including synchrony). This paper proposes an explorative method to acquire and extract relevant social signals from a naturalistic early parent-infant interaction. An experimental setup is proposed based on both clinical and technical requirements. We extracted various cues from body postures and speech productions of partners using the IMI2S (Interaction, Multimodal Integration, and Social Signal) Framework. Preliminary clinical and computational results are reported for two dyads (one pathological in a situation of severe emotional neglect and one normal control) as an illustration of our cross-disciplinary protocol. The results from both clinical and computational analyzes highlight similar differences: the pathological dyad shows dyssynchronic interaction led by the infant whereas the control dyad shows synchronic interaction and a smooth interactive dialog. The results suggest that the current method might be promising for future studies.

55. Cohen O, Finzi-Dottan R, Tangir-Dotan G  
The Fatherhood Experience of Divorced Custodial Fathers in Israel  
Family Relations 2014 Dec; 63(5):639-653

**Abstract:** This qualitative study examines the fatherhood experience of 20 divorced men who are raising children on their own. The findings were gathered from semistructured in-depth interviews. The interviewees' depictions revealed a process of making place for oneself in a multiparticipant arena facing social systems, the mother of the children, and the children themselves. The main findings concern the circumstances of single fatherhood: a constraint and a choice stemming from the mother's incapacity, the nature of the relationships created between mother and children and between father and mother, and the burden and pleasure contained within single parenthood. The discussion looks at the findings through the prism of Baxter and Montgomery's (1996) dialectic theory. It sheds light on the ongoing, contrast-filled process of establishing a perception of fatherhood, and the experiences of divorced fathers raising their children on their own.

56. Finzi-Dottan R, Cohen O  
Predictors of Parental Communication and Cooperation Among Divorcing Spouses  
Journal of Child and Family Studies 2014 Jan; 23(1):39-51

**Abstract:** The present study seeks to identify parental communication and cooperation as predictors of successful co-parenting in Israel during the divorce process. Self-report questionnaires assessing three types of predictors (parent personality characteristics, social and contextual factors and child characteristics) were completed by 123 divorcing mothers and 94 divorcing fathers. Two stepwise hierarchical regressions, one for parental communication and one for cooperation, showed that gender (female) and use of negotiation to resolve conflicts were the major predictors of both. These variables affected co-parenting both independently and in interaction with the personality characteristics of defense mechanism use and optimism. The differential contributions support the hypothesis of communication and cooperation as separate components of successful co-parenting, and the value of studying both. Clinically, these findings may be used to help improve co-parenting during divorce.

57. Schneider C, Taylor D, Zalsman G, Frangou S, Kyriakopoulos M.  
Antipsychotics use in children and adolescents: An on-going challenge in clinical practice.  
J Psychopharmacol. 2014 Jun 5;28(7):615-623

**Abstract:** Antipsychotic medications (APs) are a well-established pharmacological treatment in adults with serious mental health problems. However, many adult mental health disorders have their origins and onset in childhood or adolescence. The understanding that neuropsychiatric conditions of childhood are in part biologically determined, led to an increase in the number of clinical trials supporting evidence on the efficacy of antipsychotic agents as first-line treatment for childhood psychotic disorders and therapeutic augmentation of nonpsychotic conditions. In recent years the use of antipsychotics in children and adolescents for neurodevelopmental, behavioural and psychiatric disorders has significantly increased while the age of prescription has decreased. These trends have not been matched by advances in the understanding of APs' safety profile in this group of patients. It is therefore crucial that current and future practice is informed by up-to-date synthesis of the evidence and clinical guidelines about the use and monitoring of these treatments in paediatric populations, since the effectiveness of early therapeutic interventions in children can affect positively the long-term outcome.

58. Shelef L, Fruchter E, Spiegel DO, Shoval G, Mann JJ, Zalsman G.  
Characteristics of soldiers with self-harm in the Israeli defense forces.  
Arch Suicide Res. 2014;18(4):410-8

**Abstract:** Suicide is the leading cause of soldier death in the Israeli Defense Forces (IDF) in peace time. Suicide attempt (SA) and non-suicidal self-injury (NSSI) are risk factors for death by suicide in civilian studies and therefore their predictive value needs to be determined in the military. All army screening, psychometric and demographic data on consecutive cases of IDF soldier self-harm during the years 2010-2011 were analyzed. The Columbia Suicide Severity Rating Scale was used retrospectively to classify self-harm as suicidal or NSSI. The Suicide Ideation Scale and the Suicide Intent Scale were scored retrospectively by trained clinical psychologists. A total of 107 soldiers reported self-harm during the study period, comprising 70 SA and 37 with NSSI. The most prevalent diagnosis was personality disorder (n = 48). Soldiers with any mood/anxiety disorders comprised the smallest group (n = 21) and included major depression, dysthymia, anxiety, and posttraumatic stress disorder. Soldiers with NSSI (n = 37) did not differ in any of the characteristics from those who attempted suicide (n = 70). Unlike the well-known female dominance in both SA and NSSI patients in other settings, males dominated this army sample in both groups. Soldiers with self-harm (both SA and NSSI) cannot be easily distinguished by any demographics or specific psychological attributes detectable at induction, and the scales used in suicide research cannot predict an attempt or NSSI. Unlike civilian samples, males dominated attempter and NSSI groups and the reason for this may be multifactorial. These retrospective findings, if replicated, indicate the need for different screening strategies at induction into the military.

59. אמיתי מ., קרונברג, ס., כהן, ט., פריש, ע., ויצמן, א., אפרטר, א.

### פרמקוגנטיקה והפרעות חרדה

הרפואה, 153(3-4):210-214, 2014

הפרעות חרדה הן הפרעות כרוניות בעלות שכיחות גבוהה באוכלוסייה, הגורמות לתחלואה ומצוקה רבה ללקימים בהן. הטיפול המקובל כיום להפרעות אלו הוא תרופות נוגדות דיכאון, ובראשן תרופות ממשפחת מעכבי הקליטה הברירניים (הסלקטיביים) לסרוטונין, (SSRI Serotonin selective reuptake inhibitors). אולם למרות יעילותן היחסית של תרופות אלו, קיימת שונות גבוהה בתגובה לתרופות אלו, כאשר שלישי מן המטופלים אינם מגיבים כלל. כיום אין לנו יכולת לדעת מי מהמטופלים יגיב לתרופות, והתקווה היא כי המחקר הגנטי יאפשר לזהות מי מבין המטופלים צפוי להגיב לטיפול, וכך למנוע ניסיונות טיפוליים כושלים והשפעות לוואי. בנקודה זו נכנסת הפרמקוגנטיקה לתמונה. תחום הפרמקוגנטיקה נחלק לפרמקוקינטיקה (גורמים גנטיים המשפיעים על המטבוליזם של התרופה בגוף) ופרמקודינמיקה (גורמים גנטיים המשפיעים על התגובה לתרופה ברמת הקולטנים באברי המטרה).



בניגוד לטיפול בדיכאון, קיים מיעוט מחקרים בתחום הפרמקוגנטיקה של הפרעות חרדה, ורוב הממצאים תואמים לידוע בתחום הדיכאון.

עיקר הממצאים הפרמקוגנטיים קשורים לגנים מהמערכת הסרוטונרגית, עם ניבוי תגובה טובה לטיפול בבעלי האלל הארוך של הגן לטרנספורטר לסרוטונין (5-HTT), וכן מימצאים נוספים בוואריאנטים גנטיים של הקולטן לסרוטונין. הממצאים הפרמקוקינטיים מתרכזים במערכת אנזימי ה-CYP450. התקווה היא, כי עם התפתחות מחקר הפרמקוגנטיקה, יתגלו ואריאנטים גנטיים נוספים שבשילוב עם מאפיינים קליניים של הלוקים בהפרעות חרדה, יאפשרו בניית אלגוריתם טיפולי מותאם אישית לכל מטופל.

60. קרן, מירי

#### **המעבר להורות כגורם דחק משמעותי בקרב מבוגרים פגיעים: הצורך בעבודה משותפת של פסיכיאטר ילדים ופסיכיאטר מבוגרים**

עט השדה, 13: 51-57, 2014

המאמר מעביר את הקוראים מראייה כוללת לעיסוק בנושא חשוב לכשעצמו - המעבר להורות. עוד קודם לעיסוק באתגרי תפקיד ההורים בגידול הילדים, מתמקדים הכותבים באתגרים עת המעבר לתפקיד זה. זאת ועוד, החוקרים מציפים את החיבור בין בריאותם הנפשית של ההורים לבין מצבם ההתפתחותי של ילדים בגיל הרך ושל תינוקות בפרט. הדיון בסוגיה זו חושף בפני הקוראים את האתגרים המורכבים של הולדה והורות מצד אחר - לא רק מתן מענה לבריאות הנפש של האם אלא גם מתן תשומת לב מקצועית לדפוסי ההתקשרות אם-תינוק.

61. שויביץ א, רוסמן י, קריבוי א, שטטלנדר ל, קסירר מ, שרוט ש

#### **פגיעות ארוכות טווח של חרדל גופריתי – עדכונים וחידושים בגישה הטיפולית**

הרפואה, 153(3-4): 199-205, 2014

החרדל משתייך לקבוצת חומרי הכווייה (Vesicants) ומנוצל כחומר לחימה כימי עקב רעילותו ועמידותו הגבוהות, וייצורו הזמין והזול אשר הביאו לניצולו בעימותים צבאיים. האירוע המשמעותי האחרון היה במלחמת איראן-עיראק, שבה נפגעו יותר מ-100,000 איראנים, וכשליש מהם לוקים בהשפעות ארוכות טווח עד היום. שכיחות הסיבוכים הכרוניים ועוצמתם תלויות לרוב בהיקף, אזור וצורת החשיפה החדה לרעל. המערכות העיקריות אשר נפגעות כרונית הן הנשימה, הכוללת מחלות חסימתיות ומיצרות, ומתבטאת בנשמת (דיספנאה), שיעול והפרשות, פגיעה בעיניים כוללת רגישות לאור (פוטופוביה), גרד, יובש, דמעת ופגיעה בראייה, ובנוסף מפתח הנפגע דלקות, עכירות וכיבים בקרנית עד לעיוורון. פגיעה בעור מאופיינת בגרד, צריבה, יובש, הפרעות בצבענות (פיגמנטציה), גרב (אקזמה), שלפוחיות ועוד. למרות שמנגנון הפגיעה של החרדל טרם הובן במלואו, נהוג לייחס את הנזקים הרעלניים שלו לאלקילציה של מולקולות ביולוגיות ממרכיבי התא, בעיקר הדנ"א. אולם שינויים בחלבונים ובליפידים בממברנת התא, יחד עם הפעלת תהליכים דלקתיים משמעותיים, עשויים להוביל בשלב החד למוות תאי מתוכנת, לנמק ולפגיעה במבנה הרקמה.

בעבודה הנוכחית נסקרים הנזקים ארוכי הטווח של חשיפה לחרדל במערכות העיקריות, תוך התמקדות במחקרים קליניים בבני אדם שנבחנו בהם טיפולים אפשריים לשיפור היקף הפגיעה, תפקודיות החולה ואיכות חייו. הטיפולים הנסקרים במאמרנו מתמקדים: (1) בפגיעה הנשימתית: טיפול ב-N-acetyl cysteine, במישלבים של מרחיבי סימפונות (קצרי וארוכי טווח), בסטרואידים במתן פומי, לתוך הווריד או בשאיפה, באינטרפרון גאמא, בפוסיד ובמורפין, (2) בתסמינים בעיניים: בווריאציות שונות של פעולות פולשניות כטיפול בפגיעה המאוחרת בקרנית, כגון בהשתלת קרנית והשתלת תאי אב ללימבוס בשיטות שונות, (3) בפגיעה בעור: בנוגדי היסטמינים, בתרופות נוגדות דיכאון, ב-Pimercrolimus, Unna's, Mentol & boot, Capsaicin, Phenol, אלורה ושמן זית, כורכומין ואינטרפרון גאמא.