Olanzapine treatment in children with oppositional defiant disorder (ODD) and aggressive, antisocial behavior

D.H. Shawu1, I. Shawu2. 1Hospital for Sick Children, Toronto, Pediatrics, Toronto, Ontario, Canada; 2University of Western Ontario, Undergraduate science, genetics major: Toronto, Ontario, Canada

Purpose: Six prepubertal children with ODD all demonstrating aggressive, antisocial behavior were studied using an open-label trial of olanzapine (2.5–5 mg/day). The children were treated with the goal of decreasing serious symptomatology and helping the caregivers to cope.

Method: All six patients met the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for ODD. Three also met the DSM-IV criteria for attention deficit hyperactivity disorder (ADHD). In all patients, treatment began with a behavior modification program, family counseling, and classroom modifications. The three patients with co-morbid ADHD were also treated with a psychostimulant and one of them received a trial of risperidone. When it was determined that these interventions were not effective treatments for the children’s ODD and aggressive, antisocial behavior, all families chose the option of an open-label trial of olanzapine. Parents were told that there is presently no indication for the use of olanzapine in the treatment of ODD. Studies using olanzapine in the treatment of children with pervasive developmental disorder and aggressive or antisocial behavior were reviewed. An information sheet outlining reported and potential side effects of olanzapine was provided. Graceus (2001) suggested a starting dose of 2.5 mg olanzapine with 2.5 mg increments every 3 to 7 days. The authors began more conservatively with a starting dose of 1.25 mg and slowly titrated upwards in 1.25 mg increments. Using the Clinical Global Impressions (CGI) General Scoring Sheet, a pretreatment CGI ‘Severity of Illness’ score was determined. The effect of olanzapine treatment was determined using the CGI General Scoring Sheet: post treatment CGI ‘Severity of Illness’ score, post treatment CGI ‘Global Improvement’ score, and post treatment CGI ‘Efficacy Index’ score. The following laboratory tests were followed: complete blood count; aspartate aminotransferase, alkaline phosphatase, total bilirubin; hemoglobin A1C; fasting blood glucose; electrocardiogram. It was not necessary to exceed the lowest dosage cited in previous studies: 5–10 mg (Malone 2001) or 5–20 mg (Potenza 1999).

Results: The pretreatment CGI ‘Severity of Illness’ score was ‘5 or 6—Markedly or Severely mentally ill’ in all six patients. The post-treatment CGI ‘Severity of Illness’ score is ‘1 or 2—Not at all mentally ill or Borderline mentally ill’. The results of the CGI ‘Global Improvement’ score are ‘Much or Very much improved’. The presence of brain receptor

Conclusion: The findings suggest that olanzapine, at low doses, may be a useful pharmacologic agent for controlling aggressive, antisocial behavior in children with ODD.

Effects of early parental separation due to divorce on young adults – assessment of the hypothalamic-pituitary-adrenal axis using the corticotropin releasing hormone stimulation test

M.Bloch1, I. Peleg2, D. Koren2, E. Klein2. 1Tel Aviv Sourasky Medical Center, Psychiatry, Tel Aviv, Israel; 2Rambam Medical Center, Psychiatry, Haifa, Israel

Childhood trauma may result in long term alterations in HPA axis activity that may mediate adult psychopathology. While such alterations are well documented in animal models and in women survivors of childhood sexual abuse, data reflecting early parental loss in humans is scarce. We investigated the long term effect of early parental divorce on HPA Axis activity in adults, using a standard CRH stimulation test. Twenty two healthy males and females (age 18–25) whose parents divorced before they reached age 10, and 22 controls were included. All were interviewed using a structured interview (SCID) and a demographics and trauma questionnaire. Exclusion criteria were major physical illness, current or past psychopathology, and significant past trauma. Psychiatric symptomatology and parental bonding were assessed by self administered questionnaires (BSI, PBI). Subjects and controls did not differ at baseline. ACTH levels were consistently higher and cortisol levels lower in subjects compared to controls at all time points (ANOVA – n.s.). Cortisol level was lower in subjects at 5 minutes after CRH administration (p<0.05). When the groups were reanalysed while excluding subjects with high baseline ACTH (n=27), a significant group X time effect was observed for cortisol (F5,21=3.4; p=0.022). Our data suggest that children experiencing early divorce of their parents may have lifelong lasting effects on the HPA axis, which may be either the result of marginal psychopathology or, alternatively, make them predisposed to developing psychopathology later in life. However, the effect found is small and may be biased by the selection of “super healthy” subjects. This effect and the effect of intervening factors should be further studied.

Acute and subchronic effects of gammahydroxybutyrate (GHB) on isolation-induced aggression in male mice

J.F. Navarro, F. Gonzalez, C. Pedraza. Faculty of Psychology, University of Málaga, Department of Psychobiology, Málaga, Spain

Gammahydroxybutyrate (GHB) is a new drug with abuse potential popularly known as "liquid ecstasy". It is an endogenous compound of the mammalian brain, synthesized from GABA, which can traverse the blood-brain barrier. The presence of brain receptor sites as well as brain mechanisms for synthesis, release, and uptake provides evidence that GHB may act as a neuromodulator on specific neuronal populations. In this sense, there are experimental data suggesting the existence of a central interaction between GHB and dopamine receptor (1). This study was designed to assess the effects of low (5 mg/kg) and high doses of GHB (25, 75, 100 mg/kg), acutely or subchronically administered for 15 consecutive days, on isolation-induced aggression in male mice, using an ethopharmacological approach. Albino adult male mice of the OF:1 strain were used. Animals were randomly allocated to one control group (N=12) receiving physiological saline and eight...
experimental groups (N=11 each) receiving acute or subchronic doses of GHB (5–100 mg/kg, ip). Individually housed mice were exposed to anomic "standard opponents" 30 min after drug administration. Ten min of diadic interactions were staged between a singly housed and an anosmic mouse in a neutral area. The encounters were videotaped and the accumulated time allocated by subjects to ten broad behavioural categories was estimated using an ethologically based analysis. The names of categories were as follows: 1. Body care; 2. Digging; 3. Non social exploration; 4. Exploration from a distance; 5. Social investigation; 6. Threat; 7. Attack; 8. Avoidance/flee; 9. Defense/ submission; 10. Immobility. As statistical analysis, nonparametric Kruskal-Wallis and Mann-Whitney U-tests were used. As compared with the control group, acute treatment with GHB (25, 50 and 100 mg/kg) provoked a significant reduction of offensive behaviours (threat and attack) without affecting immobility, whereas with the lowest dose used (5 mg/kg) a significant increase of these behaviors was observed (p<0.05). This behavioral profile was maintained when GHB (25–100 mg/kg) was administered during 15 consecutive days, suggesting an absence of tolerance to the initial antiaggressive action of the drug. However, the subchronic treatment with 5 mg/kg of GHB produced an opposite effect to that observed after single treatment, suggesting a possible desensitization of post synaptic dopaminergic receptors. In conclusion, it is proposed that low doses of GHB (5 mg/kg) could exert their effects by binding to high affinity receptors, thus provoking an increase in dopamine releasing, responsible for the increased offensive behaviours of mice. On the other hand, higher doses of GHB (25–100 mg/kg) could produce a reduction of dopamine releasing and, consequently, a decrement of aggression. In fact, it has been proposed that GHB exhibits an antihypomimergic and neuroleptic-like activity in agonistic encounters between male mice (2).

References

P6.008 An ethopharmacological assessment of the effects of SKF 10047, a sigma-1 selective agonist, on social interactions between male mice
D. Beldan, M. Cavas, J.F. Navarro. Faculty of Psychology, University of Malaga, Department of Psychobiology, Malaga, Spain

Although the sigma binding site was initially described as a subtype of opiate receptor, subsequent studies led to reclassification of these binding sites as unique entities. The sigma-1 receptor, localized intracellularly within neurons, is a 223-aminoacid protein, cloned in several animal species and humans. Its regional distribution indicates moderate to intense staining in most of the dopaminergic structures. From a behavioural point of view, sigma-1 receptors have been implicated in cocaine's rewarding effects and the motivational actions of ethanol. Furthermore, sigma receptor ligands exhibit anxiolytic (anti-stress), anti-amnesic, antidepresant and neuroprotective effects. Sigma receptors are high affinity binding sites for many drugs with psychotropic activity. Thus, both sigma-1 and sigma-2 receptors exhibit high to moderate affinity for typical neuroleptics, such as haloperidol (1). Most typical neuroleptics agents are effective antiaggressive agents (2, 3). However, to date, there is no information with respect to the possible effects of sigma-1 ligands on aggressive behaviour in laboratory animals. Therefore, the aim of this study was to examine the effects of acute treatment with SKF 10047 (0.5, 1, 2, 4, 6 and 8 mg/kg, ip), a classical sigma-1 selective agonist, or saline, on isolation-induced aggression in male mice, using an ethopharmacological approach. This procedure permits to evaluate realibly whether the antiaggressive action of a given drug is specific or non-specific. Individually housed mice were exposed to anomic "standard opponents" 30 min after drug administration. Ten min of diadic interactions were staged between a singly housed and an anosmic mouse in a neutral area. The encounters were videotaped and the accumulated time allocated by subjects to ten broad behavioural categories was estimated using an ethologically based analysis. The names of categories were as follows: 1. Body care; 2. Digging; 3. Non social exploration; 4. Exploration from a distance; 5. Social investigation; 6. Threat; 7. Attack; 8. Avoidance/flee; 9. Defense/ submission; 10. Immobility. As statistical analysis, nonparametric Kruskal-Wallis and Mann-Whitney U-tests were used. SKF 10047 (6 mg/kg) produced a significant reduction of attack behavior, as compared with the control group (p<0.05). No significant differences were found between experimental and control groups in the rest of the behavioural categories analyzed. Further studies are needed to confirm the possible implication of sigma receptors in aggressive behaviour.

References

P0.009 Possible psychosocial factors for sexual dysfunctions of Turkish males: A descriptive study
S. Uguz1, M.L. Soylu2,1 Cukurova University Faculty of Medicine, Psychiatry, Adana, Turkey; Adana State Hospital, Psychiatry, Adana, Turkey

This paper describes the demographic characteristics, related factors, and clinical symptomatology of 40 male patients with various sexual dysfunctions attending the psychiatric outpatient clinic of Cukurova University, in Turkey.

Method: The first forty consecutive male subjects in whom the main problem was a sexual dysfunction or a psychiatric illness with accompanying sexual dysfunction, were included in this study. Cases which proved secondary to an organic cause were excluded from the study.

Results: The mean ages is 37.7±10.5 years. All the samples were Muslims. None of the participants stated that they had homosexual experience or interest. 97.5 % (n=39) of all cases were regularly masturbating in adolescence. 56.6 % (n=18) stated that there is a sense of guilt because of masturbation. 73.8 % (n=7) had stated that premarital sex or masturbation, would be a religious sin. 67.5 % (n=27) stated that they had their first sexual intercourse in a brothel. 65 % (n=26) learned the facts of life from a friend 25 % (n=10) from books and 10% (n=4) from movies. The onset of the dysfunction ranged between 13 and 57 years with an average of 31.33 years. The average duration between

References