evidence, that clozapine-induced weight gain is predictive of clinical response in patients with schizophrenia.

**Objectives:** The aim of this study was to determine if weight gain and changes in metabolic measures with olanzapine and risperidone also predict clinical response in patients with schizophrenia, schizoaffective disorder, or bipolar disorder.

**Methods:** Data from a 12 month, randomized, prospective study of the effects of olanzapine and risperidone in 160 patients with schizophrenia (SCH) and schizoaffective disorder (SAD), and bipolar disorder (BPD) on weight gain, BMI increase and metabolic measures including fasting blood glucose, hemoglobin A1c, total cholesterol, triglycerides, HDL, triglycerides/HDL ratio, log triglycerides, LDL to predict improvement in PANSS total scores.

**Results:** Weight gain and increase in BMI predicted the clinical response to olanzapine, but not risperidone, in patients with SCH or SAD, but not BPD, at 1, 3 and 6 months, when used in combination with other psychotropic medications or no concomitant mood stabilizers. Changes in lipid and glucose measures did not predict response to either drug.

**Conclusions:** Olanzapine-induced weight and BMI increase predicted decrease in PANSS total score at 1, 3, 6 months. No such relationship was found for risperidone- treated patients in either diagnostic group. These results suggest weight gain and clinical response to olanzapine and clozapine may be based on similar mechanism which differentiates them from risperidone.

## P0255

Effect of risperidone-induced hyperprolactinemia on bone mineral density in youth

C.A. Calarge [1], L. Acion [1], J.A. Schlechte [2]. [1] *Department of Psychiatry, The University of Iowa Carver College of Medicine, The University of Iowa Health Care, Iowa City, IA, USA* [2] *Department of Internal Medicine, The University of Iowa Carver College of Medicine, The University of Iowa Health Care, Iowa City, IA, USA*

**Background and Aims:** Hyperprolactinemia can inhibit sex steroids, resulting in bone loss. We, thus, set out to evaluate the effect of risperidone-induced hyperprolactinemia on bone mineral density in youth.

**Methods:** Children and adolescent males treated with risperidone for a minimum of six months underwent volumetric bone mineral density (vBMD) measurement using peripheral quantitative computerized tomography of the ultra-distal nondominant radius. Their treatment history was reviewed and their prolactin and testosterone serum levels measured.

**Results:** We recruited 73 males (mean age: 12.1yrs [SD=2.9], mean Tanner stage: 2.6 [SD=1.4]) treated with 0.03mg/kg (SD=0.02) of risperidone per day for an average of 3.1yrs (SD=1.9). Hyperprolactinemia (defined as a prolactin level $>$ 18.4ng/ml) was present in 51% of the sample. After controlling for Tanner stage which was strongly associated with serum testosterone, we found a trend for a negative effect of prolactin on testosterone. As expected, ultra-distal radius cross-sectional area and cortical vBMD, but not trabecular vBMD, increased with pubertal development. After adjusting for prolactin and pubertal stage, in the subgroup of peri/pubertal (i.e. Tanner stage $\geq$ 2) participants with hyperprolactinemia, prolactin was negatively associated with trabecular, but not cortical, vBMD.

**Conclusion:** To our knowledge, our data are the first to describe the negative effect of risperidone-induced hyperprolactinemia on bone mineral density following long-term treatment in youth.

## P0256

Aripiprazole in schizophrenic patients

A. Chinchilla, R. Gonzalez, I. Gobernado, M.F. Pando, A. Loureiro, E. Erausquin, M. Martín, M.D. Crespo, M. Vega. *Psychiatry Department, Ramon Y Cajal Hospital, Madrid, Spain*

We worked with a group of 36 patients diagnosed with schizophrenia (DSM-IV-TR) who were in a chronic condition, with a predominance of negative and depressive-amotivational sympthomatology. They were on a long-term therapy with antipsychotic agents, achieving just a light improvement on the symptoms.

We switched to aripiprazole using a daily dosage of 15-30 mg. We evaluated the results on PANSS and ICG scales at the beginning of the treatment and after the first and third month, whilst paying special attention to the side-effects and adverse reactions that occurred. Concomitantly, we used benzodiacepines and hypnotics during the first two weeks, and antipakinsonism agents were not needed.

From an average initial PANSS score of 74 and ICG score of 3.6, after a month, PANSS average score lowered to 60 and ICG's came down to 3. After 3 months, PANSS average score was 45 and ICG'S was 2.5.

There was no need for discontinuing the treatment in 35 of the patients. One patient discontinued treatment and follow-up. Side-effects were Invaluable in general, though at the start insomia and light jitterness were observed in some of the patients.

We believe that aripiprazole is a very useful antipsychotic drug, not only for controlling acute episodes, but also on chronic patients for its effectiveness and good tolerability.

## P0257

Effects of antipsychotics on aggression during acute hospitalization

A. Colasanti, A. Natoli, D. Moliterno, M.C. Mauri. *Clinical Neurospychopharmacology Unit, Clinical Psychiatry, Ospedale Maggiore Policlinico, Milan, Italy*

Aggression is a transnosographical dimension in psychiatric patients. The aim of the present study was to explore the aggressive dimension in acute hospitalised patients, with regard to the pharmacotherapeutical approach.

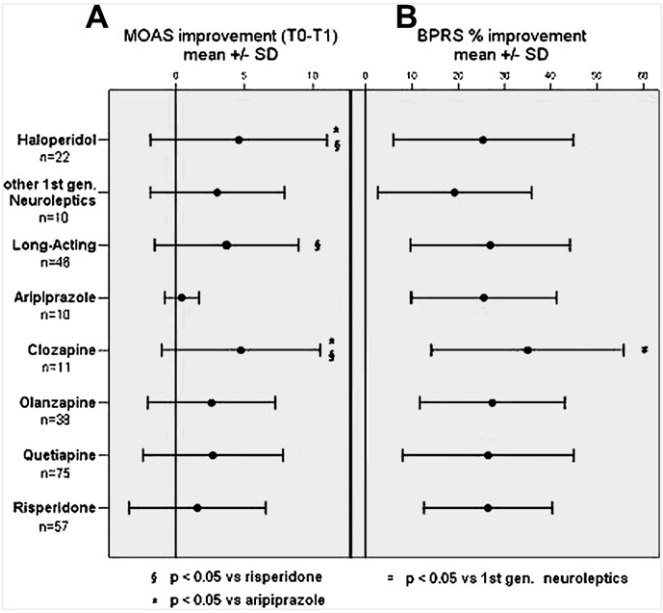
351 patients were consecutively admitted to a psychiatric ward during a 12 months period. Aggressive behaviours were analysed using the MOAS scale, at admission (T0) and at discharge (T1), after 12.4 $\pm$ 8.8 days. General psychopathology was assessed via BPRS, at T0 and T1.

Aggressive behaviours occurred in 8.9% of the cases during the hospitalization. Male gender, compulsory admission status, comorbid substance abuse, a recent history of aggressive behaviours were significantly associated with an increased risk of committing aggressive acts ($p<0.05$). Antipsychotics were the most frequently prescribed medications (76.6% of the cases). The effects of each antipsychotic medication on the amelioration in MOAS score and BPRS score were presented in Fig. 1a and 1b respectively. Percent of amelioration in BPRS score was significantly correlated with amelioration in MOAS score ($r=0.35$, $p<0.0001$).

The results evidenced small but significant differences among antipsychotic drugs regarding the efficacy on aggressive dimension.

https://doi.org/10.1016/j.eurpsy.2008.01.924 Published online by Cambridge University Press

However, further researches are warranted to provide a better qualification of antipsychotic drugs on aggressive dimension

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## P0258

Placebo-controlled clinical trials of new atypical antipsychotics in schizophrenia

P. Czobor [1,2], S. Komlosi [1], I. Bitter [1]. [1] *Deparment of Psychiatry and Psychotherapy, Semmelweis University, Budapest, Hungary* [2] *Nathan Kline for Psychiatric Research, Orangeburg, NY, USA*

**Background:** Placebo-controlled (PC) Phase 3 trials are critical for the registration of new atypical antipsychotic medications (AAP) for schizophrenia but use of placebo when efficacious treatments exist has been questioned.

**Objective:** To investigate evidence for the use of placebo in clinical trials of schizophrenia via a meta-analysis of large, PC trials of new AAPs.

**METHODS:** Using the FDA Summary Basis of Approval reports, we examined outcome data from all Phase 3 clinical trials that evaluated investigational AAPs. Publications from peer-reviewed literature were also identified. The main outcome variables were: symptom improvement in individual treatment arms, clinical response, therapeutic failure.

**Results:** Meta-regression indicated a highly significant difference between improvement in the placebo and the active arm ($p<0.0001$). Effect size (ES) estimate for the placebo arm revealed that patients in this arm obtained a statistically significant but clinically negligible symptom reduction (Cohen d: ~0.15; $p<0.004$) while active-treated patients displayed a substantial symptom reduction (Cohen d: ~0.70; $p<0.0001$). Active treatments showed a highly significant ($p<0.001$) superiority vs. placebo in clinical response and therapeutic failure, with failure rates often exceeding the rate of clinical response. ESs for change varied substantially across trials, with an ES range of d=0.8 for the placebo and the active arms, respectively.

**Conclusion:** Variable ESs across studies support the view that placebo control has major importance in trials of new AAPs. However, efforts should focus on finding design alternatives and to minimize the risks of PC trials so that they may be conducted in ethically acceptable manner.

## P0259

Antipsychotics in psychiatric inpatients: Naturalistic data on first vs. repeated episodes

M. Delic, N. Segrec, U. Groleger. *University Psychiatric Hospital, Ljubljana, Slovenia*

Antipsychotics are widely used in psychiatric patients for various indications, beside psychosis most often in mood disorders, BPSD in dementia and agitation. Official guidelines are based on RCT data which differ from naturalistic data on the use of antipsychotics in real-life clinical setting.

The aim of our cross-sectional naturalistic study of hospitalized psychiatric patients (n=310) was to get insight into prescription patterns for antipsychotics. We were especially interested in the class of antipsychotic, dose and combinations with other antipsychotics and other psychiatric drugs compared with diagnosis and number of hospitalizations. Structured data sheet was used to record data from medical records.

Results have confirmed the use of antipsychotics in variety of indications outside psychosis, especially mood disorders and agitation. Newer antipsychotics predominate although older antipsychotics have been used consistently in patients with longer illness duration and more hospitalizations (especially depot formulations), in acute agitation control as well as in acute mania and in combinations with atypical antipsychotics. Patients with first few hospitalizations are likely to receive antipsychotic therapy according to guidelines with atypical drugs in monotherapy. Equivalent doses for atypical antipsychotics although are usually higher then for typicals and lower for first hospitalizations.

The real-life use of antipsychotics is an important issue for different reasons including long-term treatment, burden of potential serious long-term side-effects as well as the quality of life in patients. Our data show that real-life uses of antipsychotics differ in some patient populations from recommended for various reasons that will be discussed.

## P0260

Hospitalizations and compliance among schizophrenic patients in treatment with clozapine

A. Doll [1], A. Mena [2], M. Domato [1]. [1] *Psychiatry Department, la Paz Hospital, Madrid, Spain* [2] *Psychiatry Department, Gregorio Marañon Hospital, Madrid, Spain*

**Objectives:** Demostrate that clozapine decrease the number of hospitalizations, and improve the adherence to treatment.

The sample consisted of 36 schizophrenia patients who were in treatment with a typical and atypical neuroleptic and then had their medication changed to clozapine. We ascertained the number of inpatient hospitalizations before starting clozapine and compared this with the number of hospitalizations after starting clozapine. We also followed an age- and gender-matched comparison group of other schizophrenia patients who were at treatment approximately the same time. Results indicate that the mean number of rehospitalizations while on other neuroleptic was bigger than after the commencement of clozapine treatment. The decrease in hospitalization rate for the comparison group was also statistically significant. The pre-post change was much greater for the clozapine patients than comparison

https://doi.org/10.1016/j.eurpsy.2008.01.924 Published online by Cambridge University Press