Conclusions: the achieved results point to the specific therapeutical response to different groups of antidepressive drugs in adolescence, which may be explained by psychobiological and age factors, and especially to the incomplete morphofunctional brain maturation, and with the hormone and immunological disbalance in puberty. This confirms the necessity to single out adolescent psychopharmacotherapy into a special area and to study it on different levels.

P01.14

Glucocorticoid Receptor-mRNA levels are regulated in human blood cells by different types of antidepressants

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Beside other data, increases in glucocorticoid serum levels and disturbances of the circadian secretion of these hormones in depressive patients point to a putative glucocorticoid receptor (GR)-dysfunction in this illness.

Therefore, the aim of the present study was to investigate the regulatory effects of different types of antidepressants (desipramine, imipramine, mirtazapine and maprotiline) on GR-mRNA levels in blood cells of healthy male probands.

Total RNA was extracted from whole blood samples after 24 h of incubation with the antidepressants using Trizol® reagent and RT-PCR methods were used for the semiquantitative analysis of GR-transcripts. Our results suggest that a concentation of 10^{-7} M of mirtazapine induces a down-regulation of GR-mRNA levels in human blood cells. Interestingly, the same concentration of maprotiline lead to a significant up-regulation of GR-mRNA levels. These treatments did not induce changes in the levels of the house-keeping gene glyceraldehyde-3-phosphate dehydrogenase (GAPDH).

Therefore, antidepressants with different modes of action affect GR-mRNA-levels in human blood cells in vitro, although not in the same direction. These changes further support the assumption that this may represent a relevant mechanism of action in the course of the treatment of diseases such as major depressive disorder.

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P01.15

Duloxetine 60 mg QD is efficacious in the treatment of depression

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This study examined duloxetine (60 mg QD), a potent and balanced reuptake inhibitor of norepinephrine and serotonin, in the treatment of the mood and physical symptoms associated with major depressive disorder. In a multicenter, randomized, double-blind, parallel, placebo-controlled study, adult MDD patients (n=245) were randomly assigned to receive placebo or duloxetine 60 mg QD for a 9-week treatment period. The primary efficacy assessment was HAMD17 total score. Physical symptoms were measured by somatic symptom inventory and a visual analog scale for pain. Duloxetine was statistically significantly superior to placebo at weeks 2 through 9 on the reduction of HAMD17 total score and resulted in an estimated probability of remission of 44%. Duloxetine resulted in a significant reduction in severity of overall pain compared with placebo. Duloxetine was well tolerated and none of the duloxetine-treated patients reported any serious adverse events. These results indicate that duloxetine administered at 60 mg once daily is a safe and efficacious treatment of MDD. Moreover, these results also indicate that duloxetine may be an important treatment for MDD patients with physical symptoms, including pain.

P01.16

Duloxetine in the treatment of depression: a double-blind placebo-controlled comparison with paroxetine

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In this study, duloxetine (40 & 80 mg/day), a potent and balanced dual serotonin and norepinephrine reuptake inhibitor, was compared with the SSRI paroxetine (20 mg QD) and placebo in the treatment of MDD. In this 8-week, randomized, double-blind controlled study in outpatients with MDD, efficacy was evaluated using total HAMD17 (primary), MADRS, CGI-S, and PGI-I. Secondary measures included the HAMA and visual analogue scales for pain. Safety and tolerability were also assessed. Duloxetine at 80 mg/day was superior to both placebo and paroxetine on the reduction of HAMD17 total score. Duloxetine 80 mg/day was superior to placebo on most secondary efficacy measures. The remission rate for duloxetine 80 mg/day was 50%, paroxetine 37%, and placebo 30%. Duloxetine 80 mg/day significantly reduced overall pain. Insomnia was the only adverse event reported significantly more frequently for duloxetine 80 mg/day than for the SSRI paroxetine. The number of cases of hypertension observed did not differ between duloxetine and placebo groups. These results indicate that duloxetine is well-tolerated and efficacious in the treatment of the mood and physical symptoms associated with MDD.

P01.17

Olanzapine-fluoxetine combination in treatment-resistant depression

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Objective: This 8-week, double-blind study compared olanzapine-fluoxetine combination (OFC) with olanzapine (OLZ), fluoxetine (FLX), and nortriptyline (NTP) monotherapies in treatment-resistant depression (TRD). TRD was defined as historic SSRI failure and prospective nortriptyline failure.

Method: 499 subjects failing a 7-week nortriptyline lead-in phase were randomized to OFC, OLZ, FLX or NTP treatment groups, and efficacy evaluated with the MADRS.

Results: OFC subjects demonstrated significantly better total scores than the monotherapies from week 1–4, except OLZ at week 3. OFC maintained treatment effect throughout 8 weeks, however, at endpoint OFC statistically separated only from OLZ (-8.6, -6.5). Sub-analysis of subjects with >3 depressive episodes within the last two years also demonstrated the fast OFC onset of action, and statistical separation from OLZ and FLX at endpoint (-11.33, -4.57, -5.76). Subjects with SSRI failure during the current MDD episode demonstrated fast OFC onset of action, and statistical separation from component monotherapies through week 7, and from OLZ at endpoint (-9.66, -5.16). OFC's safety profile was similar to component monotherapies.

Conclusion: OFC had a rapid onset of action and was particularly efficacious in subsets of more treatment-resistant subjects.

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