PR04.01
Factors associated to resistant depression

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Background and Aims: Few studies have been conducted looking at clinical features associated to treatment resistant depression (TRD) defined as failure to at least two consecutive antidepressant trials. The objective of this study was to identify clinical and demographic factors associated to TRD in a large sample of depressed patients who failed to reach response or remission after at least two consecutive adequate treatments.

Methods: A total of 702 patients with unipolar major depression were included in the analysis. 346 patients were considered as non-resistant. The remaining 356 patients were considered as resistant with a HAM-D-17 score remaining ≥ 17 after 2 consecutive adequate trials. Cox regression models were used to examine the association between individual clinical variables and TRD.

Results: Eleven variables were found to be associated with TRD. Anxiety comorbidity (p <0.001, OR =2.6), comorbid panic disorder (p<0.001, OR=2.6) and social phobia (p<0.008, OR=2.1), personality disorder (p<0.049, OR=1.7), suicidal risk (p<0.001, OR=2.2), severity (p<0.001, OR=1.7), melancholia (p<0.018, OR=1.5), a number of hospitalizations > 1 (p<0.003, OR=1.6), recurrent episodes (p<0.009, OR=1.5), early age of onset (p<0.009, OR=2.0) and non response to the first antidepressant received lifetime (p<0.019, OR=1.6).

Conclusions: Our findings provide a set of eleven relevant clinical variables associated to TRD which can be explored at the clinical level. The statistical model used in this analysis allowed for a hierarchy of these variables (based on the OR) showing that comorbid anxiety disorder is the most powerful clinical factor associated to TRD.

PR04.02
Antidepressants - do they decrease or increase the risk of suicidality?

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Several methodological limitations make it difficult to investigate in randomised, controlled studies whether antidepressants affect (increase or decrease) suicidality. Different kinds of studies (epidemiological, quasi-experimental intervention, naturalistic follow-up, etc.) should therefore also be considered in order to obtain the most comprehensive evidence. Taken together, these different approaches supply reasonable evidence that antidepressants are able to reduce both suicidal ideation and suicide in depressive patients. Data on suicide attempts are not robust enough to draw clear conclusions. Even though there are no consistent indications from the different study types of a suicidality-inducing effect of SSRIs or antidepressants in adults in general, the principle possibility of such an adverse effect in single cases or in subgroups of patients should be considered carefully. Different mechanisms could principally lead to suicidality-enhancing effects, for example the pharmacological mode of action related to different transmitter systems, to special pharmacodynamic properties like activating/drive-enhancing effects or to side effects like akathisia. Special dispositions of patients, i.e. personality disturbances such as borderline personality disorder, comorbidity, non-response, bipolarity and other factors, should be considered. In everyday clinical practice the discussion about the possible risks of the SSRIs or antidepressants in general should not result in clinicians forgetting the benefits of these drugs, especially their lower lethal toxicity profile. This is a great advantage, especially in cases with severe suicidality where the choice of a less toxic antidepressant helps to avoid the risk of fatal if the patient should misuse the antidepressant for a suicide attempt.

PR04.03
Ten possible explanations for resistant depression

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Patients for whom the diagnosis of depression was established, yet did not respond to adequate treatment are defined as suffering from resistant depression (RD). As 20-30% of depression is resistant, depression subtypes with distinct pathophysiology are considered.

The neurobiological approach to RD aims to identify and characterize these subtypes. Different underlying mechanisms which may play a role in RD include: tolerance (“escape”), a “kindling” type of phenomenon, or no response to begin with. There are several types of underlying pathophysiological mechanisms proposed for RD, including: HPA axis hyperactivity, thyroid abnormality, estrogen in postmenopausal women, lower availability of l-tryptophan to the brain, frontal or parietal perfusion defects, genetic factors, thyroid abnormalities, a combination of 5HT/HPA axis and brain lesion, 5HT, NA and HPA abnormalities, sleep abnormalities and immunological factors.

In order to gain better knowledge of these mechanisms, studies of RD patients providing a careful evaluation of the HPA axis and of serotonergic and noradrenergic responsiveness, as well as evaluation of the thyroid system, are warranted. Tryptophan depletion and NE depletion have proven to be effective tools in the study of depression and might be of particular interest in RD. Brain imaging, pre- and post-treatment, and a dichotomous comparison of changes in brain activity in patients who responded to treatment for RD might be of value. However, these have not yet been studied systematically.

Patients with RD suffer greatly and need to be treated. Various underlying psychobiological abnormalities might assist us in tailoring treatment especially to the patient.

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