have a protective value or may be risk factors and both concur in determining the individual's vulnerability to suicidal behaviour. With the aim of evaluating impact of some psychopathological dimensions on suicidal behaviour, we conducted a study on a sample of depressed psychiatric patients, comparing those with a history of suicide attempt it with those without suicidal tendencies. 170 adult outpatients consecutively enrolled, were the study subjects (mean age: 40.31±12.27; M:F 72/98). 108 patients had a lifetime suicide attempt in psychiatric history. Among suicide attempters, a significantly higher number of subjects were female sex, not married, unemployed and with a high educational status. Results also showed that patients with a suicide attempt had higher Childhood Trauma Questionnaire (CTQ) scores for emotional abuse, physical abuse and sexual abuse, and Brown Goodwin Life History of Aggression (BGLHA) scores in comparison to the control group and lower scores on the resilience scale. In order to evaluate the indipendent contribution of the selected measures, all risk factors were then entered in a logistic regression model, using the lifetime presence of a suicide attempt as the dependent variable.

S30.03

The link between the serotonin system and suicidality

P.A. Saiz. *Deparment of Psychiatry, School of Medicine, University of Oviedo, Oviedo, Spain*

Abnormalities in the serotoninergic system have been associated with suicidality, aggression, and impulsivity. Exactly what role serotonin plays in the initiation, modulation, maintenance, or regulation of such behaviours remains under study. However, recent data suggest that serotonin is involved along the pathway from genetic predisposition and environmental stimulus to expression of psychiatric disorders and suicidal behaviour.

On the other hand, it has been suggested that the seemingly ''robust'' association of low CSF-5HIAA concentration with suicidality and aggression is rather weak, and are likely to represent somewhat premature translations of findings from studies that have flaws in methodology.

Finally, we the review the controversial role of the selective serotonin reuptake inhibitors (SSRI) on suicidality, as they have been suggested: i) to decrease suicide rates in the population, and ii) to increase suicide rates in some individuals in early treatment.

S30.04

Decision making as an endophenotype in suicidal behaviour

P. Courtet. *Université Montpellier 1, Montpellier, France Service de Psychologie Médicale et Psychiatrie, CHU Montpellier, Hôpital Lapeyronie, Montpellier, France [3]Inserm E361, Montpellier, France*

We recently reported that decision-making impairment may be a neuropsychological trait of vulnerability to suicidal behavior (SB), that may reflect a serotonergic dysfunction in the orbitofrontal cortex.

We used the Iowa Gambling Task to assess decision-making in euthymic suicide attempters and controls with a history of affective disorders but no history of SB, and healthy controls. We explored 1) the link between decision-making deficit and relevant clinical variables; 2) the role of serotonin related polymorphisms relevant to SB in decision-making processes; 3) the link between life events on the last 12 months and decision-making.

1) In a sample of more than 300 psychiatric patients, we found that a decision making impairment was associated with the vulnerability to SB independently of the psychiatric diagnoses. Decision making was negatively correlated with emotional dysregulation, but not with impulsivity. No association was found between decision-making performance for suicidal lethality, intent, ideation, number of suicide attempts, age at first suicide attempt. 2) Suicide attempters carrying the 5HTTLPR-ss or the TPH1-AA genotypes, associated with SB, expressed worse learning abilities during the decision making task. 3) Adult life events and decision-making were correlated in suicide attempters.

We confirm that impaired decision making, possibly due to emotional dysfunction, may be a neuropsychological risk factor for SB independently of psychiatric disorders. In suicide attempters, the influence of genetic factors may partly be achieved through their modulation of the learning processes of decision-making, that may constitute a candidate endophenotype in SB.

S30.05

Genetic association studies of aggression-related genes

D. Rujescu. *Department of Psychiatry, University of Munich, Munich, Germany*

Suicidal behavior is a major health problem worldwide. The risk of suicide-related behavior is supposed to be determined by a complex interplay of sociocultural factors, traumatic life experiences, psychiatric history, personality traits, and genetic vulnerability. This view is supported by adoption and family studies indicating that suicidal acts have a genetic contribution that is independent of the heritability of Axis I and II psychopathology. Neurobiological studies have shown that serotonergic dysfunction is implicated in suicidal behaviors. Additionally aggression-related traits are mediated by the serotonergic system. Since both, aggression–related traits and serotonergic activity are partially heritable and correlate inversely, variations in genes of the serotonergic system might then, to some extent, account for variations in aggression-related behavior. Thus, we also investigated the relationship between serotonergic genes and anger, as a subtype of aggression-related behavior.

For that reasons we have initiated a large scale case control genetic association study which comprises of 250 suicide attempters and 1900 healthy volunteers and investigated the role of a comprehensive set of serotonergic candidate genes in this behavior. Additionally we conducted a large-scale gene expression analysis using cDNA-microarrays to identify new candidate-genes for suicide. We found several genes to be differentially expressed in the orbitofrontal cortex of suicide completers. Cross-validation experiments using quantitative RT-PCR validated 9 genes so far. These genes were genotyped as well to look for associations with suicide-, anger- and aggression-related behavior and also these results will be presented.

S31. Symposium: 25 YEARS OF EXPERIENCES WITH VARIOUS TYPES OF ANTIDEPRESSANTS: THE DANISH UNIVERSITY ANTIDEPRESSANT GROUP

S31.01

SSRIs versus tricyclics

K.B. Stage. *Department of Psychiatry, Odense University Hospital, Odense C, Denmark, The Danish University Antidepressant Group*

https://doi.org/10.1016/j.eurpsy.2007.01.196 Published online by Cambridge University Press

The development of antidepressants that appear to selectively affect either serotonin or norepinephrine has renewed interest in distinguishing neurotransmitter systems and coupling them with clinical phenomenology. Parallel to this development, a number of investigators have documented differences in response to antidepressants among depressive subtypes. For the delusional subtype there is some consensus on the specifics of treatment response. Delusional depression may not respond sufficiently to treatment with antidepressants alone but often requires combination with antipsychotics or electroconvulsive therapy (ECT). It has also become more and more clear that selective serotonin reuptake inhibitors (SSRIs) and some other types of never antidepressants are relatively ineffective for treating depressed inpatients. When treating inpatients, the superiority of tricyclic antidepressants (TCAs) compared to never antidepressants is evident, especially in studies using sufficient doses of TCA. Perhaps most intriguing are the data that suggest that depressed patients of the melancholic (endogenous) subtype does not respond adequately to SSRIs but does respond to TCAs and to ECT. This paper will discuss these aspects emphasizing the Danish University Antidepressant Group studies comparing TCAs and SSRIs.

S31.02

The fate of moclobemide

K. Martiny. *Psychiatric Research Unit, Frederiksborg General Hospital, Hillerød, Denmark*

The introduction of the reversible monoamine oxidase-A inhibitor moclobemid was a promising development of the MAO inhibitor principle in the treatment af major depression. The irreversible MAO inhibitors has severe interactions with a broad range of drugs and patients needs to be very alert regarding specific dietary components such as redwine, cheese and so on. In spite of investigations showing promising results and a very beneficial side effect profile, the drug is currently not much used. This presentation reviews the principal studies included the DUAG study on moclobemide and tries to explain the fate of moclobemid.

S31.03

Dose-effect relationships for antidepressants

L.F. Gram. *Department of Clinical Pharmacology, University of Southern Denmark, Odense, Denmark*

Dose-effect studies provide, for groups of patients, information on the probability of therapeutic response and tolerability problems (non tolerability) for different doses and varying duration of therapy.

By such studies it thus may be possible to describe the inter-patient variability in intended and unintended effects and therapeutic range or index of the compound examined.

In several reviews and studies on different types of antidepressants it has been concluded that a dose with optimal balance between intended and unintended effects cannot be indicated, since the dose-effect curves for antidepressant effect and adverse reactions are flat and overlapping. (Gram, NEJM, 1994, 331: 1354, Bollini & al. BJP,1999, 174: 297, DUAG-4, CPT 1999, 66: 152).

For TCA such as clomipramine dose-dependant kinetics and genetic polymorphisms are important. However, for clomipramine the concentration-effect relationship was not better than the dose-effect relationship, suggesting that the variation in dose-effect is as much related to other factors than kinetic variability.

Data on clomipramine (DUAG-4, 1999) suggested that higher doses, not only are more effective, but also is associated with faster response. Indeed higher doses are also associated with more frequent tolerability problems causing drop-out. Clinical dosing should be based on a judgment of the patient's need for rapid effective cure, against the importance of good tolerability.

S31.04

Placebo-controlled relapse prevention trials in unipolar depression

P. Bech. *Psychiatric Research Unit, Frederiksborg General Hospital, Hillerod, Denmark*

Among the treatment modalities in the acute therapy phase of a major depressive episode, ECT (electroconvulsive therapy) has the highest response rate (90%), but also the highest relapse rate in the continuation phase over the next 6 months (65%). Placebo has the lowest response rate (45%), but the highest pharmacological relapse rate (50%). The SSRIs seem to have the lowest relapse rate compared to imipramine (12% versus 30%). Both the SNRIs and mirtazapine (the ''dual action'' drugs) have higher relapse rates (20%) although they have a higher response rate than the SSRIs (70% versus 60%).

S31.05

Prophylaxis in bipolar disorder: methodological implications of an almost completed lamotrigine-vs-lithium study

R.W. Licht. *Mood Disorders Research Unit, Psychiatric Hospital, Risskov, Denmark*

Background and Aims: In 2 drug approval studies lamotrigine has been shown to possess prophylactic potentials comparable with lithium in bipolar disorder. However, the generalisabilty of these results are limited. In 2001, an investigator-driven study was initiated comparing lamotrigine and lithium for prophylaxis aiming at mimicking routine clinical conditions. Data collection is not completed (until end 2006) albeit recruitment is accomplished. Based on preliminary findings, the focus will be on methodological implications.

Methods: This is an open, multicenter, randomised trial conducted within the Danish University Antidepressant Group Subjects suffered from bipolar disorder indicating prophylaxis. Exclusion criteria were kept to a minimum. Randomisation took place when clinically appropriate The primary end-point was the need for additional medication or hospitalization, conditionally that patients were stabilized on monotherapy 6 months after randomisation. Patients were followed up to 6 years after randomisation.

Results: Of the 155 randomised patients, 123 (79%) were recruited at the main center. So far, 25% of the patients were prematurely withdrawn within the first 6 months after randomisation, 25% were withdrawn at 6 months since they were not in monotherapy at this point, 25% have reached the primary end-point and the remaining 25% are still in trial.

Conclusions: The large proportion of patients that needed additional medications even after 6 months indicates that previous long-term studies randomising patients on monotherapies may have limited generalisability. The uneven contribution from the main center and the other centers indicates that multicenter studies may include patients that are selected beyond the selection criteria.

https://doi.org/10.1016/j.eurpsy.2007.01.196 Published online by Cambridge University Press