

Tues-P8**IMPROVEMENT OF NEUROCARDIAL VAGAL DYSFUNCTION AFTER SUCCESSFUL ANTIDEPRESSIVE TREATMENT WITH ELECTROCONVULSIVE THERAPY (ECT)**

M.W. Agelink¹*, W. Lemmer¹, R. Malessa², T. Zeit¹, E. Klieser¹.
¹Dept. of Psychiatry, Evangl. Hospital Gelsenkirchen (45879 GE), University of Bochum; ²Dept. of Neurology, University of Jena, Germany

Objective: To assess autonomic neurocardial function (ANF) in relation to response to antidepressive treatment with electroconvulsive therapy (ECT).

Methods: Using a standardised measurement of heart rate variability we prospectively evaluated ANF in 10 patients (m/w 3/7; mean age 44.1 years) with treatment refractory major depression (DSM-III-R) and in 26 age matched healthy controls. Exclusion criteria were cardiac, pulmonary or neurological diseases, thyroid disease, diabetes mellitus, alcoholism or drug dependence. ECT was applied using a Thymatron DG™ (methods see 1). Four patients took lorazepam during the course of ECT, the others were free from medication for at least four days. Patients were re-tested 24–48 hours following their last ECT. Artefact-free single ECG sweeps from a 5-min recording while resting were digitally stored using the software package "Neurodiag" (H. Lambeck, Munich; modified version of the ProSciCard).

Results: Compared to controls we found a significantly higher mean resting heart rate and a reduction of the mean coefficient of variance (CVr; $p < 0.005$) as well as of the root mean square of successive differences (RMSSDr; $p < 0.01$) in depressive patients. They also showed a marked reduction of the HF-power (spectral analysis). The response to ECT was excellent in five, moderate in three in poor in the other two patients. ECT resulted in a marked increase of the mean CVr and RMSSDr as well as in an increase of the mean HF-power ($p = 0.06$). Patients, in whom depressive symptoms did not clearly improve, showed either no change or a slight deterioration in each HRV-parameter.

Conclusion: In contrast to a recently published report by Schultz et al. 1997 (to the best of our knowledge the only one on this issue), our data suggest a marked improvement in ANF after successful treatment of depression with ECT.

- (1) Agelink MW et al.: Benefit and risk of electroconvulsive therapy in medically ill patients of old age. *Nervenarzt* 1998; (in press).

Tues-P9**ADRENALINE AND IMIDAZOLINE DRUG-INDUCED PLATELET AGGREGATION IN PATIENTS WITH MAJOR DEPRESSION**

P.E. Jaquet*, M. Ferrer-Alcon, C. Walzer, J.A. Garcia-Sevilla, J. Guimón. *Department of Psychiatry, University of Geneva, Geneva, Switzerland*

Major depression is associated with supersensitive α_{2A} -adrenoceptors (increased receptor density and aggregation) (1) and increased density of imidazoline receptors (radioligand receptor binding and immunodetection of receptor proteins) (2, 3) in blood platelets. The functions of imidazoline receptors (I_1 - and I_2 -type) in blood platelets are not known. The aim of this study was to compare the aggregation response induced by adrenaline (α_{2A} -adrenoceptor-mediated) with that of imidazoline drugs in control subjects (5 men, 6 women; age, 38 ± 4 years) and in patients (5 men, 4 women; age, 37 ± 3 years) with major depression

(DSM III-R). Platelet aggregation was measured photometrically as described previously (1). Platelet counts were similar in control subjects ($298 \pm 35 \times 1000/\mu\text{l}$) and depressed patients ($268 \pm 24 \times 1000/\mu\text{l}$). In drug-free (more than 2 months) depressed patients, the primary aggregation response induced by adrenaline (0.01 – $100 \mu\text{M}$) was potentiated, which indicated increased α_{2A} -adrenoceptor sensitivity (controls, slope, EC50: $1.07 \pm 0.13 \mu\text{M}$, aggregation, EC50: $0.67 \pm 0.09 \mu\text{M}$, $n = 11$; depressed, slope, EC50: $0.59 \pm 0.07 \mu\text{M}$, aggregation, EC50: $0.44 \pm 0.05 \mu\text{M}$, $n = 9$, $P < 0.05$). In control subjects, as well as in depressed patients, agmatine (up to 1 mM , $n = 4$), one endogenous ligand for imidazoline receptors, cirazoline (mixed α -adrenoceptor and I_1 imidazoline drug, up to $370 \mu\text{M}$, $n = 3$), antazoline (mixed α -adrenoceptor and I_2 imidazoline drug, up to $370 \mu\text{M}$, $n = 6$) and valldemossine (LSL 61122, selective I_2 imidazoline drug, up to $370 \mu\text{M}$, $n = 6$) did not induce platelet aggregation. In contrast, moxonidine (0.1 – $370 \mu\text{M}$), a putative selective I_1 imidazoline drug, induced a weak aggregation response (slope, EC50: $3.81 \pm 0.81 \mu\text{M}$; aggregation, EC50: $3.13 \pm 0.95 \mu\text{M}$, $n = 3$) that was antagonized by the selective α_2 -adrenoceptor antagonist RX 821002 ($1 \mu\text{M}$, methoxyidazoxan), indicating that this drug behaves as an α_{2A} -adrenoceptor agonist on platelet aggregation. These preliminary results further support the existence of supersensitive platelet α_{2A} -adrenoceptors in depression, and suggest that the activation of platelet imidazoline receptors is not associated with the induction of aggregation, even when these receptors are abnormally up-regulated in major depression.

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- (1) Garcia-Sevilla et al., *Arch. Gen. Psychiatry* 43: 51–57 (1986)
 (2) Piletz et al., *Arch. Gen. Psychiatry* 48: 813–820 (1991)
 (3) Garcia-Sevilla et al., *Arch. Gen. Psychiatry* 53: 803–810 (1996)

Tues-P10**CHOLESTEROL AND SEROTONERGIC CONTROL OF PRO-LACTIN SECRETION IN DEPRESSED AND SUICIDAL PATIENTS**

M. Sarchiapone¹*, A. Roy², G. Camardese¹, S. Della Casa³, M.A. Satta³, S. De Risio¹. ¹Institute of Psychiatry, Catholic University of Sacred Heart, Rome; ²Institute of Endocrinology, Catholic University of Sacred Heart, Rome, Italy
³Department of Veterans Affairs, New Jersey Health Care System, East Orange, New Jersey, USA

In depressed and suicidal patients a reduced response of PRL and cortisol to *d*-fenfluramine has been described. On the other hand a correlation between serum cholesterol levels and suicidal behaviour has been reported so that some authors considered the cholesterol to be responsible of the lower serotonergic activity. The aim of our study was to seek the correlation between cholesterol and central serotonergic activity in depressed patients and/or in suicidal behavior. Study participants comprised 18 subjects, 12 patients (mean age: 46.1 ± 15.5 ; M/F: 1/2) and 6 controls (mean age: 39.1 ± 9.5 ; M/F: 1/2). The *d*-fenfluramine challenge test was performed and the serum lipid and protein profile was evaluated in a blood sample, within 24 hours from the act fulfillment. Results showed a reduced total serum cholesterol in suicidal patients and a decreased response of PRL to *d*-fenfluramine challenge test in most depressed patients. The correlation between total serum cholesterol concentration and the PRL peak was not statistically significant. While the serotonergic activity was related to the severity of depression on the HRSD, serum cholesterol levels were related to the total serum protein, BMI, item 3 of HRSD and item 7 of Z-SDS.

The relationship between cholesterol and self-harm behaviour can be, in our opinion, considered the epiphenomenon of a complex and still unclear biological modification that occurs somehow in impulsive and suicidal patients.

Tues-P11

SUCCESSFUL PHARMACOTHERAPY OF COTARD SYNDROME WITH REDUCTION OF D₂ RECEPTORS IN BASAL GANGLIA

S. De Risio*, M. Sarchiapone, G. Camardese, F. Calvosa, A. Buonanno, E. Barbarino. *Institute of Psychiatry, Catholic University of Sacred Heart, Rome, Italy*

A case of "delire de negation", a rare condition described first by Cotard in 1880, is presented here. The syndrome appeared suddenly in a male of 43 years as an acute manifestation of a major depressive disorder. The central symptom was an intense nihilistic delusion with denial of the organs of his body, of his own existence and of all his internal and external world. The regional cerebral blood flow measured by 99mTc-HMPAO-SPECT was normal but the study of the D₂ receptors by 123I-IBZM-SPECT showed a reduction of the striatum uptake of the D₂ receptor ligand bilaterally. The syndrome was successfully treated by a combined therapy with clozapine, fluvoxamine and imipramine. Neurobiological hypothesis explaining the pathogenesis of the disease will be proposed.

Tues-P12

PREDICTIVE POWER OF BECK'S DEPRESSION INVENTORY IN THE GENERAL POPULATION

L. Lasa¹, J.L. Ayuso-Mateos^{1*}, J.L. Vázquez-Barquero¹. ¹*Clinical and Social Psychiatry Research Unit; "Marqués de Valdecilla" University Hospital, University of Cantabria, Santander, Spain*

The aim of the present paper is to study the predictive power of Beck's Depression Inventory (BDI) for depressive disorders in general population sample.

Methods: 1.250 subjects, from 18 to 64 years old, were randomly selected from the Santander (Spain) municipal census. A two-stage method has been used: in the first stage, all individuals selected completed the BDI; in the second, "probable cases" (BDI cut-off ≥ 13) and a random 5% sample of all respondents were interviewed by psychiatrists using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN), which generates diagnoses of depressive disorders.

Results: We can confirm the predictive power of the selected cut-off point (12/13): 100% sensitivity; 98% specificity; 0.73 positive predictive power (PPP); 1 negative predictive power (NPP) and 98% overall diagnostic power. The area under ROC (AUC) was found to be 0.99 ± 0.0001 . There were no statistic differences in terms of sex or age.

Conclusions: The BDI is a good instrument for detecting depressive disorders in the general population.

Tues-P13

HEALTH ECONOMICS OF ANTIDEPRESSANTS: A METHODOLOGICAL REVIEW

T.R. Hylan*, D.P. Buesching, G.D. Tollefson. *Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46285, USA*

In an era of constrained health care financing, clinicians are increasingly faced with considering the economic consequences

in addition to the clinical outcomes associated with initiating a patient on antidepressant therapy. This has increased the demand for health economic studies comparing antidepressant use and associated health care expenditures in clinical practice.

In this study, we review the published health economic literature as it pertains to antidepressants. Our study reveals at least five types of study methods that have been used to conduct health economic evaluations of antidepressant pharmacotherapy: randomized controlled clinical trials, meta-analyses of clinical trials, decision-analytic models, retrospective database studies, and prospective naturalistic economic clinical trials. Each method has certain advantages and disadvantages. Conclusions which are drawn from results consistent across a variety of methods are less subject to criticisms of any one method.

Broadly considered, health economic studies of antidepressants have consistently found differences in clinical practice between the tricyclic antidepressants (TCAs) and the selective serotonin reuptake inhibitors (SSRIs) as well as among the SSRIs. These differences relate to the pattern and duration of antidepressant use as well as total direct health care expenditures. Future health economic research studies in clinical practice should focus on the economic consequences of long-term antidepressant use as well as the impact of antidepressant use on indirect costs such as productivity and absenteeism.

Tues-P14

DOES ST. JOHN'S WORT HAVE AN EFFECT ON AUTONOMIC RESPONSES OF CUTANEOUS CIRCULATION?

M. Mück-Weymann^{1*}, T. Möslers², R. Buche², T. Reclin². ¹*Dept. of Psychosomatic Medicine, Dresden University of Technology;* ²*Dept. of Psychosomatic Medicine, University of Erlangen, Germany*

Intro: High dosages of *St. John's wort* show a strong impact on patients with mild and moderate depressions as well as on patients with somatoform disorders. By measuring skin blood flow one can observe the influence of autonomic functions on cutaneous vessels. A deep inspiration into the chest causes vasoconstriction followed by dilation. Emphasizing the functional side of this autonomic response, we propose to call it "*voluntary inspiratory constrictor episode*" (VICE). The constrictive phase of such VICEs is mediated via efferent sympathetic nerve fibres, the mechanism of the redilation is suggested to be due to central blocking of sympathetic outflow. The aim of this preliminary study was to evaluate the impact of a treatment with *St. John's wort* on VICEs.

Methods and Results: We investigated 25 healthy untreated control subjects and 12 subjects with mild depressions and/or somatoform disorders treated with 900 mg/day of hypericum extract LI 160 (*Jarsin 300*, Lichtwer Pharma, Berlin, Germany) using the PhotoPlethysmoGraphic-technique. VICE-measurements were evaluated off-line by calculating the half time period $\Delta t_{50\%sup}$. We found that $\Delta t_{50\%sup}$ of the *St. John's wort* treated group did differ from those of the control group (mean: 3.2 s versus 4.3 s; SD: 1.2 s/1.9 s).

Conclusion: The finding, that the standardized application of *St. John's wort* did lead to shorter redilation phases of VICEs (under tricyclic antidepressants this period is considerably prolonged), suggests that this drug does not increase central sympathetic activation. The tendency of lower mean values for the redilation