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State of the Art

Research: State of the Art: Adaptive Brain Plasticity Allowing Resilience to Mood Disorders

SOTA001

Adaptive brain plasticity allowing resilience to mood disorders

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Bipolar Disorder runs in families. Close relatives, such as offspring or siblings, of individuals with the disorder are at "high risk" of developing a range of mood problems. Most of this risk can be traced back to genes that affect how the brain grows and works. As a result much research has focused on identifying ways in which changes in brain anatomy and function can increase the risk for Bipolar Disorder. This type of scientific enquiry is essential but overlooks the fact is that the majority of people at "high risk" remain free of any psychiatric disorder. Recognising the factors that promote resilience in the presence of significant genetic risk is very important as it shifts the focus from illness to resilience. Many factors may contribute to resilience in relatives of people with Bipolar Disorder. These can be psychological (e.g. good coping skills), social (e.g. supportive relationships) and biological. Our research group has focused on identifying the biological "signature" of resilience to Bipolar Disorder by studying differences in brain anatomy and function between patients and their well relatives. First, we found that resilient relatives have increased volume in a part of the cerebellum, a brain structure involved in "balancing" mood and movement. Second, resilience relatives had stronger connections between parts of the prefrontal cortex, primarily in regions involved in self- control. Third, the default mode network, considered the functional backbone of the brain, showed greater cohesiveness in resilient relatives. These findings emphasize the ability of the brain to adapt its structure and function to maintain wellbeing in the face of heightened genetic risk for Bipolar Disorder. This line of research also suggests that it is possible to find biomarkers of disease and resilience to Bipolar Disorder and pave the way for the development of interventions that may mitigate the risk of this disorder.

Disclosure of interest.– The authors have not supplied a conflict of interest statement.

Clinical/Therapeutic: State of the Art: At What Level of Severity Do We Need Antidepressive Drugs?

SOTA002

At what level of severity do we need antidepressive drugs?

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The role of baseline severity as effect modifier in various psychiatric disorders is a topic of controversy and of clinical import. This study aims to examine whether baseline severity modifies the efficacy of various antidepressants for major depression through individual participant data (IPD) meta-analysis. We identified all placebo-controlled, double-blind randomised trials of new generation antidepressants in the acute phase treatment of major depression conducted in Japan and requested their IPD through the public-private partnerships between the relevant academic societies and the pharmaceutical companies. The effect modification by baseline depression severity was examined through six increasingly complex competing mixed-effects models for repeated measures. We identified eleven eligible trials and obtained IPD from six, which compared duloxetine, escitalopram, mirtazapine, paroxetine or bupropion against placebo (total $n = 2464$). The best-fitting model revealed that the interaction between baseline severity and treatment was not statistically significant (coefficient = −0.04, 95% confidence interval: −0.16 to 0.08, $P = 0.49$). Several sensitivity analyses confirmed the robustness of the findings. In conclusion, we may expect as much benefit from antidepressant treatments for mild, moderate or severe major depression. Clinical practice guidelines will need to take these findings into consideration.

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Clinical/Therapeutic: State of the Art: Lithium: 70 Years of Treatment in Psychiatry

SOTA003

Lithium: 70 years of treatment in psychiatry

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The introduction of lithium to contemporary psychiatry is marked by the publication of John Cade in Medical Journal of Australia seventy years ago. Cade gave lithium to ten manic patients obtaining spectacular results. In the early 1960s, the first papers on lithium prophylactic efficacy in mood disorders were published and following this, the effect has been widely confirmed. Nowadays lithium is considered the first-line drug for the prevention of recurrences in mood disorders. About one-third of bipolar patients are "excellent lithium responders" in which monotherapy with lithium causes the total cessation of disease expression. Among all mood-stabilizers, lithium exerts the strongest antisuicidal activity, and in some countries, a negative association was found between suicidality and lithium concentration in drinking water. Augmentation with lithium of antidepressants is the best-evidenced procedure for treatment-resistant depression, both bipolar and unipolar. Lithium possesses immunomodulatory and antiviral properties, especially against herpes viruses. A reduction of labial herpes recurrences during lithium prophylaxis was demonstrated in the Poznań-Philadelphia study. In recent years, the evidence for neuroprotective action of lithium has been obtained. Experimental, epidemiological and clinical findings have pointed to the possibility of preventing and therapeutic action of lithium in dementia. In 1988, the International Group for the Study of Lithium-Treated Patients (IGSLI), was created and this group showed a favorable influence of lithium on mortality and prevention of suicides. In 1990-1994 the journal "Lithium" existed. Since 2009, the International Consortium on Lithium Genetic (ConLiGen) has been performing a genome-wide association study (GWAS) on lithium prophylaxis.

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