

are often residual symptoms that are not well treated, including cognitive impairment and anhedonia. The development of novel treatment for depression is particularly challenging given the limited predictive validity of animal models. Human neurocognitive models of antidepressant action can help to bridge the translational gap and allow rapid investigation of novel compounds in healthy volunteers and people with depression. In this talk, using the 5-HT₄ receptor as an example of a novel target of interest, I will outline how these objective neurocognitive models can be used as a translational tool to understand antidepressant treatment mechanisms, guide treatment selection and test novel putative antidepressants early in development.

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S0004

Symptom-level effects of SSRIs in depression studies in a large-scale study programme: efficacy, effects of baseline severity, impact on suicidality, and more

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Abstract: Conclusions about the efficacy of antidepressants, such as the selective serotonin reuptake inhibitors (SSRIs), in clinical trials have generally been based on analyses of total sum scores on psychometric rating scales, mainly the Hamilton Depression Rating Scale (HDRS). However, this rating scale has several drawbacks, such as multidimensionality and a tendency of several items to pick up side-effects. Therefore, analyses that only rely on global drug treatment effects on the HDRS and similar scales risk misrepresenting important properties of any drugs investigated.

This presentation concerns the findings of a research project investigating item-level effects of SSRIs in treating depression in a material encompassing 8262 patients having participated in pre- and post-marketing industry-sponsored studies concerning paroxetine, sertraline or citalopram. This has been a fruitful endeavour, having resulted in numerous research papers. Though our main focus at the outset was to investigate if a comparatively low efficacy of SSRIs in clinical trials was an artefact related to the use of HDRS sum scores as the main outcome (which was indeed the case), we have also used this material to investigate a number of other important questions relating to the influence of SSRIs on the various symptoms experienced by patients with depression. Major findings discussed in the presentation include: i) confirmation of early (but not widely known) reports that SSRIs significantly reduce core depression symptoms already after a week of treatment ii) strong evidence for SSRIs being equally effective in treating core depressive symptoms in mild as well as severe depression, earlier reported differences apparently being explained by differences in terms of effects (and prevalence) of non-core symptoms iii) SSRIs do not seem to exacerbate suicidality as measured by the relevant item of the HDRS scale - indeed, both average scores as well as likelihood of worsening are significantly reduced already at week 1. The implications of these, and other, findings are discussed in

relation to both the role of SSRIs in the clinic as well as pre-clinical research into e.g. the mode of action of these drugs.

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S0005

Evidence that Moved Psychedelic Medicine from the Fringe to the Mainstream in 2022

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Abstract: Interest in possible clinical uses for psychedelic drugs has grown steadily over the past decade. Although impressive findings from small studies stimulated considerable speculation and provided a strong justification for further study of psychedelic treatments, until very recently there was a dearth of high-quality evidence for their efficacy, mechanisms of action, and appropriate treatment models for clinical use. However, during the past 2-3 years, there have been dramatic advances in the field. This presentation will focus on 5 publications in the field of psychedelic medicine that exemplify three important aspects of the recent progress in psychedelic research. (1) There has been a rapid increase in the number and size of controlled clinical trials of various psychedelic treatments. (2) Conceptual models for studying and potentially understanding the therapeutic effect of psychedelics have increased in sophistication and comprehensiveness. And (3) progress has been made toward developing models of treatment that would facilitate access to safe and effective psychedelic treatments, if and when they are approved by regulatory bodies. Although progress has been rapid, the field of psychedelic medicine is still in its infancy. Much more work on these and many other fronts will be necessary to discover what the study of psychedelics can contribute to healthcare and neuroscience.

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S0006

Is the total score of the Hamilton Depression Rating Scale affected by side effects of SSRIs and SNRIs?

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Abstract: This talk will focus on the pitfalls of using multidimensional rating scales to measure the severity of depression – with particular emphasis on the Hamilton Depression Rating Scale (HDRS-17). First, the history behind the development of the HDRS-17 will be briefly covered. Second, it will be argued that the HDRS-17 measures symptoms that overlap with common antidepressant side effects (gastrointestinal dysfunction, sexual dysfunction, somatic anxiety and sleep disturbances), making it possible that side effects of antidepressant treatment are erroneously rated as symptoms of depression.

The rest of the talk will focus on the results of a recent study (1) in which we used individual-level data from antidepressant treatment