S007

The impact of the change trial on physical health in people with schizophrenia

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Life expectancy in patients with schizophrenia is reduced by 20 years for men and 15 years for women compared to the general population. About 60% of the excess mortality is due to physical illnesses, with cardiovascular disease being dominant. The aim of this trial was to improve the cardiovascular risk profile.
Methods The CHANGE trial was an investigator-initiated, randomised, parallel-group, superiority, multi-centre trial with blinded outcome assessment. Patients diagnosed with schizophrenia spectrum disorders and increased waist circumference according (>88 cm for women, >102 cm for men), were recruited and centrally randomised 1:1:1 to 12-months of lifestyle coaching plus care coordination versus care coordination alone versus treatment as usual. The primary outcome was 10-year risk of cardiovascular disease assessed post-treatment and standardised to age 60, secondary outcomes included cardiorespiratory fitness and physical activity. Clinical.Trials.gov NCT01585493.
Findings A total of 428 participants were randomly assigned to the CHANGE intervention ($n = 138$); care coordination ($n = 142$); or treatment as usual ($n = 148$). At 12 months, the mean 10 years risk of cardiovascular disease was 8.4% (SD 6.7) in the CHANGE group, 8.5% (SD 7.5) in the care coordination group and 8.0% (SD 6.5) in the treatment as usual group ($P = 0.41$). We found no intervention effects for any secondary or explorative outcomes, including weight, cardiorespiratory fitness, physical activity, diet or smoking.
Interpretation The CHANGE trial did not support individual lifestyle coaching or care coordination as superior compared with treatment as usual in reducing the cardiovascular risk in patients with schizophrenia and increased waist circumference.
Disclosure of interest The authors have not supplied their declaration of competing interest.

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Symposium: From prediction errors to disorders of compulsivity: A computational framework

S008

Elucidating the neural circuitry underlying individual differences in response to reward-associated cues

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Stimuli in the environment that have been associated with reward can gain control over behavior and, in some cases, lead to maladaptive behavior. Reward cues acquire inordinate control when they are attributed with incentive salience or transformed into "motivational magnets" (i.e. incentive stimuli). Individuals vary considerably in the extent to which they attribute incentive motivational value to reward cues, and we can capture this individual variation using an animal model. When rats are exposed to a Pavlovian conditioning paradigm, in which the presentation of a lever-cue is immediately followed by the delivery of a food reward, some rats preferentially approach the lever (sign-trackers, STs) while others approach the food cup (goal-trackers, GTs). Importantly, while the lever is a predictor for both STs and GTs, only for STs does it become an incentive stimulus. Thus, this model allows us to parse the neurobiological mechanisms underlying predictive vs. incentive learning processes. Using this model, we have demonstrated that dopamine is critical for incentive, but not predictive, learning and that the cortico-thalamic-striatal "motive circuit" is engaged only by incentive stimuli. In addition, we have identified the paraventricular nucleus of the thalamus (PVT) as a central node that differentially regulates sign- and goal-tracking behaviors. We have begun to utilize a chemogenetic approach (i.e. DREADDs) in combination with in vivo microdialysis to further elucidate the neural circuitry underlying individual variation in cue-motivated behaviors. Findings suggesting that STs rely primarily on subcortical mechanisms, whereas GTs utilize more "top-down" cortical processes will be presented and discussed.
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S009

A reinforcement-learning account of Tourette syndrome

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Background Tourette syndrome (TS) has long been thought to involve dopaminergic disturbances, given the effectiveness of antipsychotics in diminishing tics. Molecular-imaging studies have, by and large, confirmed that there are specific alterations in the dopaminergic system in TS. In parallel, multiple lines of evidence have implicated the motor cortico-basal ganglia-thalamo-cortical (CBGTC) loop in TS. Finally, several studies demonstrate that patients with TS exhibit exaggerated habit learning. This talk will present a computational theory of TS that ties together these multiple findings.
Methods The computational theory builds on computational reinforcement-learning models, and more specifically on a recent model of the role of the direct and indirect basal-ganglia pathways in learning from positive and negative outcomes, respectively.
Results A model defined by a small set of equations that characterize the role of dopamine in modulating learning and excitability in the direct and indirect pathways explains, in an integrated way: (1) the role of dopamine in the development of tics; (2) the relation between dopaminergic disturbances, involvement of the motor CBGTC loop, and excessive habit learning in TS; (3) the mechanism of action of antipsychotics in TS; and (4) the psychological and neural mechanisms of action of habit-reversal training, the main behavioral therapy for TS.
Conclusions A simple computational model, thoroughly grounded on computational theory and basic-science findings concerning dopamine and the basal ganglia, provides an integrated, rigorous mathematical explanation for a broad range of empirical findings in TS.
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