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Highlights of this issue

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Lithium – mortality and memory

There is substantial literature on the potential of lithium to reduce the risk of suicide, but less on non-suicide mortality. Lithium has an effect on many organs, some beneficial, such as neurogenesis and leucocytosis, and some hazardous, such as thyroid and renal insufficiency. Smith *et al* (pp. 55–63) report that treatment with lithium significantly reduced non-suicide mortality over the first 90 days, relative to treatment with valproate. This beneficial effect did not extend beyond that time and, perhaps equally importantly, there was increased mortality with subsequent discontinuation of lithium treatment before 180 days, again relative to discontinuing valproate. The authors suggest that once lithium is initiated, treatment should be continued wherever possible; they also recommend more research into the differences between treatment with lithium and valproate. When a medication is demonstrated to be beneficial, it is often said that that it might be helpful to put it in the drinking water. Helbich and colleagues (pp. 64–71) examined the relationship between inter-regional levels of lithium in drinking water and the levels of suicidality. They found an inverse relationship between lithium levels in drinking water and suicide, although this did not survive correction for other relevant risk factors. They also examined the levels of lithium prescribing between the different regions and found that this inverse relationship was not evident for the rates of lithium prescription. Lithium has been shown to inhibit glycogen synthase kinase-3 (GSK3), an enzyme involved in neurotrophic cell responses including inflammatory response and oxidative stress, which may have a protective effect in the development of Alzheimer's disease. Lithium treatment in older patients with bipolar bipolar disorder offers a natural model for examining this relationship; Gerhard and colleagues (pp. 46–51) report that continuous treatment with lithium may serve to reduce the dementia risk in these older adults with bipolar disorder. This finding was not observed for their control group, treated with anticonvulsive medication. The authors suggest that this is a promising finding, and whether it is mediated by lithium's impact on the enzyme GSK3 or through reduced numbers of affective episodes, this warrants further investigation given the paucity of treatment options. An accompanying commentary reviews the failure of contemporary treatment trials designed to interfere with the amyloid cascade in Alzheimer's disease. Sutherland & Duthie (pp. 52–54) describe the role of GSK3 as an alternative mechanism in the development of dementia and put forward the case for its role in the link between diabetes and dementia. They also review the recent clinical trial data with GSK3-modulating agents, in the context of the neuroprotective effects of lithium and the increases in cortical gray matter and *N*-acetyl-aspartate levels that have been demonstrated with its use. Overall, they suggest that lithium appears to have the potential to prevent the development of dementia and warrants further investigation.

Sleep, psychosis and risk of death

There is an increased awareness of the existence of psychotic experiences within the general population. The link between these psychotic experiences and the development of schizophrenia fits well into the continuum hypothesis of psychosis. Sleep disturbance in childhood is a putative risk factor for psychotic experiences. Thompson *et al* (pp. 23–29) found that children who experienced nightmares and night terrors at age 12 were more likely to report psychotic experiences at the age of 18 years. The relationship with night terrors was attenuated by other risk factors, while the presence of nightmares remained significant. The authors conclude that the presence of nightmares in individuals with additional risk factors, such as a positive family history, may warrant the introduction of preventive, evidence-based, psychological treatments such as imagery rehearsal therapy or the use of sleep disturbance-specific medication. Interestingly, Sharifi and colleagues (pp. 30–36) found that the presence of lifetime psychotic experiences was associated with a significant increase in overall mortality at follow-up, even after adjustment for psychiatric diagnoses. The presence of baseline psychotic experiences led to a 5-year reduction in median survival time and, for death by suicide, had a vastly elevated hazard ratio of 9. The authors suggest that psychotic experiences confer risk outwith the specific associations observed with a diagnosis of schizophrenia.

Treating heroin addiction with injectable heroin

There is an enormous personal, economic and societal cost associated with heroin addiction. Strang and colleagues (pp. 5–14) note that treating heroin addiction by replacing it with a treatment predicated on pharmaceutical heroin by injection appears counter-intuitive, but their systematic review of the data suggests that heroin is an effective treatment, when offered as part of a highly regulated treatment schedule for a subgroup of patients whose addiction is refractory to other treatments. Indeed, diamorphine is now licensed for this indication in the UK and four other European countries. An accompanying editorial by Farrell & Hall (pp. 3–4) describes the contentious background to the use of heroin-assisted treatment of heroin dependence, and questions the reasons why there has not been wider adoption of this treatment by policy makers. Given the data, they raise the thorny issue of whether the lack of support for this treatment strategy may lie with politicians and policy makers potentially not viewing heroin dependence as a disorder that is truly 'deserving' of treatment.