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► **COVER:** 'Mechanically determined' by Patrick Morgan, inspired by the Review on p204.



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In just over a decade, genome-wide association studies (GWAS) have gone from a back-of-the-envelope calculation to multimillion-pound projects to, crucially, fruitful results in the form of genomic regions that might predispose to several complex diseases. The success of GWAS — which aim to identify genetic markers that are more frequent in affected individuals compared with non-affected individuals in a population — was built on the advances in the technology behind SNP identification and genotyping, and on a huge cash injection to support state-of-the-art facilities.

This month the Wellcome Trust, the largest UK charity, announced that its spending budget for biomedical research would go up by 60%, to £4 billion, over the next 5 years. Its investments (£17 million) in GWAS in recent years have amply paid off, as exemplified by the publication in 2007 by the Wellcome Trust Case Control Consortium — the biggest GWAS enterprise yet — of genomic regions associated with seven common diseases.

Where will the new money go? Identifying gene regions associated with a disorder is several steps away from understanding the biological basis of a disease, and even further away from finding a cure. Even for disorders such as type 2 diabetes, for which GWAS have identified six gene regions and pointed to the involvement of  $\beta$ -cell development, much work remains. This ranges from the fine mapping and sequencing of candidate gene regions, to confirming the associations in additional populations, identifying more small-effect variants, assessing the predictive value of the variant(s) and then experimentally probing their biological function.

As progress and investments are made in sequencing and genotyping technologies GWAS will become more routine, allowing tangible benefits to be had for many disorders, including the more challenging and so far least successful subset, those affecting mental health.

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