

## A decade of the Social, Genetic and Developmental Psychiatry Centre at the Institute of Psychiatry\*

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October 2004 sees the tenth anniversary of the founding of the Social, Genetic and Developmental Psychiatry Centre, established as a partnership between the Medical Research Council (MRC) and the Institute of Psychiatry (now a school of King's College London). This editorial gives an account of how the Centre came to be founded and an introduction to its work, as the first in an invited series of short articles describing the Centre's research. A more detailed account is given by Rutter & McGuffin (2004).

### Social, genetic and developmental research at the Institute of Psychiatry

Social, genetic and developmental streams of research have all existed at the Institute of Psychiatry since its establishment in 1948, but they were not always integrated and indeed there have been times when genetic researchers and social psychiatrists were in a state of open, mutual hostility. Such intellectual warfare reached its height in the 1960s and 1970s when social psychiatry was in the ascendancy, with its practitioners seeing themselves as occupying the moral high ground in the 'nature *v.* nurture' debate. Certainly, things had started off on a better footing at the Institute. Aubrey Lewis, who was appointed in 1948 as the director of the first MRC unit at the Institute of Psychiatry (the Social Psychiatry Research Unit), saw 'social' psychiatry as a broad field that included consideration of the biological substrate of disorders as well as social causes. Indeed, it was he who in the 1930s had encouraged Eliot Slater to study genetics. Slater, now considered the 'founding father' of psychiatric genetics in the UK,

established another MRC unit at the Institute of Psychiatry in 1959 – the Psychiatric Genetics Unit. This unit, which was housed in a prefabricated building known as 'the hut', was closed on Slater's retirement in 1969, and for the next decade psychiatric genetics largely fell out of fashion in the UK. There were, however, a few notable exceptions to this neglect, one of which was a seminal twin study by Folstein & Rutter (1977), suggesting for the first time that childhood autism, far from reflecting the influences of 'refrigerator parents', is substantially genetic.

Michael Rutter's early research path had been established in the MRC Social Psychiatry Research Unit led by Lewis, and he continued, as his career matured, to take an integrated approach. This was a strong feature of the Institute of Psychiatry Child Psychiatry Department under his leadership and continued with the establishment of the MRC Child Psychiatry Unit in 1984. The unit brought together experts in a variety of overlapping fields: early social development, longitudinal studies of the general population and high-risk samples, genetics and statistical methods. The mix proved highly successful, and over the first 10 years of its existence the Child Psychiatry Unit had a major impact on child psychiatric research nationally and throughout the world. Meanwhile, it was the turn of social psychiatry to become unfashionable, at least in the sense of a discipline that was narrowly focused on social influences without much heed for biological or developmental dimensions. In 1993 the MRC took the decision to close the Social and Community Psychiatry Unit (as it had then been named). However, it did not seem either to the MRC or to the Institute a correct decision to abandon social psychiatry entirely after more than 45 years of influential research. Rather, there was a need for refocusing, and reintegration with other strands of research that

were proving fruitful elsewhere in psychiatry. One of these was the now rejuvenated discipline of psychiatric genetics, and the other lay in the proposition that disorders of adult life – not just childhood disorders – might be profitably seen as neurodevelopmental.

### ESTABLISHMENT OF THE CENTRE

Michael Rutter and David Goldberg, then head of the Institute's Department of Psychiatry, opened discussions with the MRC about establishing an interdisciplinary research centre that could, in a comprehensive way, study the interplay of nature *and* nurture in the development of common psychiatric symptoms and disorders. This led to a successful application for an MRC programme grant to provide core infrastructure support for a centre that under Rutter's directorship could harness existing Institute expertise and draw in top-flight recruits from around the world to achieve this ambitious scientific goal. Robert Plomin, a behavioural geneticist at Pennsylvania State University, was appointed as deputy director, and other prestigious appointments soon followed (Table 1).

From the beginning, the Centre was a partnership between the Institute and the MRC, and was successful in obtaining grant funding from a variety of other sources including medical research charities, the US National Institutes of Health, and industry. By the time of Michael Rutter's retirement as director in the autumn of 1998, the Centre had grown to comprise around 90 scientific, technical and administrative staff spread over eight different buildings on the Maudsley/Institute campus. Peter McGuffin, an adult psychiatrist with a longstanding interest in genetics and gene–environment interplay, was appointed as the new director. As the incoming director, he had two major tasks: the first was to secure renewal of the Centre's core funding from the MRC, and the second was to find funding for a building that would accommodate all of the Centre's research groups under one roof. This entailed an application to the UK government and the Wellcome Trust's newly established joint infrastructure fund. Fortunately, both applications were successful and a new round of recruiting could begin. The final element in the

\*This is the first of a short series of editorials being published in the *Journal* to mark the 10th anniversary of the Social, Genetic and Developmental Psychiatry Centre at the Institute of Psychiatry.

**Table 1** Senior staff at the Social, Genetic and Developmental Psychiatry Centre

Name	Research focus	Date of joining
Professor Peter McGuffin (Director)	Psychiatry, statistical and molecular genetics	1998
Professor Robert Plomin (Deputy Director)	Psychology, behavioural and molecular genetics	1994
Professor Sir Michael Rutter (former Director)	Developmental psychopathology	1994
Dr Kathy Aitchison	Psychiatry, pharmacogenomics	2004
Dr Louise Arseneault	Disruptive behaviour, mental disorders and their development	2002
Dr Philip Asherson	Psychiatry, molecular genetics	1995
Dr David Ball	Psychiatry, molecular genetics	1995
Professor Patrick Bolton	Developmental psychopathology	2003
Professor Avshalom Caspi	Developmental psychology and personality	1997
Professor David Collier	Molecular genetics	1995
Professor Ian Craig	Molecular genetics	1995
Professor Judy Dunn	Social developmental psychology	1994
Dr Thalia Eley	Behaviour genetics, developmental psychopathology	1996
Professor Anne Farmer	Psychiatry, classification and measurement	1998
Dr Francesca Happé	Cognitive developmental psychology	1996
Dr Jonna Kuntsi	Genetic basis of cognition and behaviour	2001
Dr Barbara Maughan	Social epidemiology	2000
Professor Terrie Moffitt	Developmental psychopathology	1997
Dr Thomas O'Connor	Developmental psychopathology	2000
Dr Fruhling Rijdsdijk	Statistical genetics	2002
Dr Leo Schalkwyk	Genetics, genomics	1999
Professor Pak Sham	Psychiatry, statistical genetics	1995
Dr Frans Sluyter	Neurobehavioural genetics	2000
Dr Ursula D'Souza	Molecular genetics, gene expression	2000
Professor Eric Taylor	Child psychiatry, classification and measurement	2000

believe that such research is essential to the development of interventions that prevent the onset of disorders, rather than waiting to treat full-blown disorders. In addition, the Centre's approach to development spans the life course: of considerable current interest are adult outcomes of childhood disorders such as hyperactivity and language disorders, and similarities and differences in the forms of depression that emerge in childhood, adolescence, and early and late adulthood, respectively.

### Genetics theme

The Centre's strategy has been to build strength in quantitative genetics as well as in molecular genetics, because both are vital to the understanding of complex traits. Quantitative genetic approaches, such as twin studies, are central to our themes and, properly applied, can tell us as much about the environment as about genetics. Quantitative genetics, which considers complex quantitative traits influenced by multiple genes as well as multiple environmental factors, also provides the foundation for quantitative trait locus (QTL) strategies for molecular genetics (Plomin *et al.*, 1994). The QTL perspective pervades molecular genetic research in the Centre, because much of the liability to common disorders is likely to be on a continuum of variation. Therefore, risk factors for common disorders probably represent the quantitative extreme of the same genetic and environmental factors that create variation in the normal range. In terms of molecular genetics, two strategic directions are part of the Centre's plan.

- (a) We believe that progress in identifying genes associated with common behavioural disorders has been slower than many had predicted because studies have been inappropriately designed and underpowered for finding QTLs of small effect size. A common approach of the Centre's current genetic studies is, therefore, to collect very large samples, establish them as resources and develop designs and methods that are capable of detecting and replicating QTLs of small effect size.
- (b) High-throughput technologies have been adopted and developed. These allow both linkage and linkage disequilibrium mapping and a focus on direct association analyses using functional

configuration of the Centre resulted from integration of the MRC Child Psychiatry Unit under the leadership of Professor Eric Taylor.

### OVERALL STRATEGY AND WORK OF THE CENTRE

The Centre's current focus is on common psychiatric disorders, covering three domains: mood disorders (especially anxiety and depression), 'externalising' disorders (especially disruptive behaviour including hyperactivity) and cognitive disorders (especially language disorders and mild learning disability, including autistic symptoms). The Centre concentrates on the aetiological aspects – developmental as well as genetic and environmental origins – of behavioural disorders. However, there is a strong emphasis on methods

of measurement and classification and an attempt to foresee the practical, clinical and public health implications of the Centre's findings.

### Developmental theme

The Centre's developmental theme leads to research focused on childhood disorders, because relatively little is known about them despite their public health importance. However, a developmental perspective involves more than studying children – it is an aetiological approach that investigates when and how disorders emerge and change during development and how these aspects of course are influenced by genetic inheritance and social environment. This focus on change and continuity in development is the reason why much of the Centre's research is longitudinal. We

DNA variants expressed in the brain, including sets of variants that can be used to explore entire neurotransmitter pathways.

Such gene-finding approaches, although intensive and time-consuming, are only a prelude to functional genomics that will involve developments in bioinformatics and the integration of genomics, gene expression, proteomic and brain research relevant to behavioural analysis. Together with 'top-down' whole-organism studies, these approaches constitute what might be called behavioural genomics (McGuffin *et al*, 2001; Plomin *et al*, 2003).

### Environmental theme

Research on the environment is in many ways more difficult than research on genetics. Genetics is entering a golden post-genomic era (Peltonen & McKusick, 2001) in which the structure and function of the entire genome will eventually be known. In contrast, there is no 'environment' project. Indeed, there are no laws of environmental transmission and there is nothing like a simple triplet code. Another important factor in the slow progress towards understanding the environment has been the traditional tendency of social psychiatry to ignore genetics or to consider environmental influence as in opposition to genetics. In fact, two of the most important sets of discoveries about environmental mechanisms in the past decade have come from genetic research, including work by Centre members. The first finding is that, contrary to most socialisation theories, environmental influences on many traits tend to be of the

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non-shared type (McGuffin *et al*, 2001): that is, they tend to make children growing up in the same family as different as children growing up in different families. A priority for environmental research therefore should be to identify these environmental factors. The second finding, sometimes called the 'nature of nurture', is that genetic factors influence the way we experience our environments (Plomin *et al*, 2001). Thus, some measures ostensibly of environmental risk – such as life events and psychosocial stress – show genetic influence. Similarly, associations between environmental risks and disorders are often substantially mediated genetically (Caspi *et al*, 2002, 2003). Our view of the way forward is to bring together genetic and environmental strategies using environmental measures within genetic designs to investigate co-actions, interactions and correlations between environmental risks and genetic susceptibilities.

### DECLARATION OF INTEREST

P. McG. and R. P. are Director and Deputy Director, respectively, of the centre described in this paper.

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