Risk factors for psychosis

Dr Helen Fisher is a chartered research psychologist focusing on the interplay between childhood victimisation and genes in the development and outcome of psychosis. Here she explains what has motivated her work, the results produced so far and what this could mean for future treatments

To begin, can you reveal what acted as the catalyst to your interest in psychology?

I have always been fascinated by why people think and behave the way they do and thus psychology seemed an obvious subject to study. During my undergraduate degree I spent a year working with a mental health team and the first client I came into contact with on the inpatient ward was an 18-year-old experiencing his first episode of psychosis. It baffled me that he could hold such strong beliefs that had no basis within reality. He was so convinced by them that he was terrified that I and the other members of staff were going to kill him. That experience drove me to want to understand more about how these delusional beliefs could develop and take over someone's entire life. Following several years of intervention research, I finally returned to investigating why these symptoms come about, in a PhD exploring the associations between childhood abuse and psychosis.

How did this interest develop into your current investigation of the interplay between childhood victimisation and genetic risk in the development and outcome of psychosis?

I became acutely aware that environmental factors (such as childhood victimisation) could not be disentangled from genetic influences – our genes affect both exposure to adverse environments and the degree of impact these environments have upon us. The environment can also influence how our genes function. Therefore, in my current Medical Research Council fellowship it seems essential to me that I have to look at the interplay between childhood victimisation and genetic risk (family history of psychosis) in the onset and persistence of psychosis.

Does the subjectivity of childhood adversity mean it is something that is difficult to be judged and measured? In turn, does this result in difficulty in tracking the pathways between childhood victimisation and psychotic symptoms?

Unfortunately, only a very small minority of children who are victimised come to the attention of welfare, social or legal services, and thus it is not possible to rely solely on documented evidence of victimisation. Researchers have to rely on the reports of the individual, their close relatives or teachers to obtain information about victimisation, which can be problematic and may lead to associations with psychotic symptoms being under- or overestimated. In order to reduce the influence of subjectivity, researchers often use instruments that attempt to elicit more concrete examples from individuals rather than just their impression, and also collate reports from different individuals in order to corroborate accounts. Documented victimisation is used to substantiate reports, but this is often not available.

In my previous research, I was able to demonstrate that even individuals with

Childhood adversity – adult psychosis

Exploring the long-term impact of childhood maltreatment and victimisation on both mental and physical health outcomes is a pressing subject. A team at the **Institute of Psychiatry**, King's College London, uses a number of tools and a range of populations to find out how maltreatment and psychosis are linked

psychotic disorders are able to consistently report adverse childhood experiences over long periods of time. This does not entirely resolve the issue, but does give us more confidence in the findings.

In what ways can specific cognitive and affective difficulties in childhood be targeted to minimise the likelihood of adolescents exposed to early trauma developing psychotic symptoms?

Psychological therapies such as cognitive behaviour therapy (CBT) could be employed to tackle unhelpful cognitive styles and emotional difficulties in children and adolescents, either to reduce the likelihood of them developing psychotic symptoms or to prevent initial symptoms from persisting. Preliminary studies indicate some beneficial effects of CBT in victimised children in terms of improving their ability to regulate their emotions and alter faulty cognitions. This therapy is also effective in reducing psychotic experiences in adolescents and preventing psychotic disorders. However, more evidence is required before these therapies can be confidently rolled out amongst children who have cognitive and affective difficulties.

What do you hope to be the far-reaching implications of your research on prevention and treatment of psychosis, as well as on society as a whole?

Improved understanding of how psychosis develops and persists has massive implications for prevention and treatment. Identification of malleable environmental mechanisms will enable clinicians to provide more effective interventions to reduce the risk of vulnerable children developing mental health problems and to promote resilience. Ultimately, this project intends to improve wellbeing across the lifespan for a significant proportion of the population.

ONE OF THE main environmental risk factors associated with the development of psychotic symptoms and disorders is known to be childhood adversity. However, the mechanisms underlying the adversity-psychosis association are not yet well known. It is unclear whether this association is merely due to genetic factors influencing exposure to such risky environments or increasing sensitivity to the detrimental impact of adversity, or both.

Over the past decade, evidence has been accumulating to suggest that exposure to significant adversity in childhood can increase the risk of developing psychotic symptoms in adolescence and clinical psychosis in adulthood. However, it was only this year that a comprehensive review of all of this research was published, which concluded that there does indeed appear to be a substantiated link between childhood abuse and psychosis. Certainly, now that there are sufficient grounds to believe that the adversity-psychosis association is credible, researchers are able to confidently turn their attention to understanding how they are linked.

EXPLAINING THE LINK

It is in this respect that Dr Helen Fisher and colleagues at the Institute of Psychiatry, King's College London, are conducting groundbreaking research. Their recent study sought to explore the interplay between specific forms of childhood adversity and familial genetic risk in the onset of psychosis.

In the investigation they used detailed assessments of a large epidemiological case-control sample (AESOP). From their research thus far, the team has sought to better understand how early victimisation leads to some children developing psychosis, in order to establish suitable interventions to target these intermediary factors. As Fisher explains, this is more beneficial than waiting until an individual has developed a major psychiatric disorder before intervening: "Psychosis is difficult and costly to treat. Even one episode of this disorder is likely to leave the person with emotional scars and adversely affect their chances of gaining employment and maintaining good relationships with others". Therefore, it is imperative that scientists find ways to tackle the early signs of psychosis to reduce the huge potential costs of a full-blown disorder on the individual, their family and society as a whole.

A LONGITUDINAL COHORT STUDY

Longitudinal cohort studies are preferable to cross-sectional studies as they allow researchers to study how the same individuals change over time, rather than providing a snapshot of different individuals at a single moment in time. This model is thus extremely powerful for exploring questions that concern how difficulties, such as psychotic symptoms, can arise several years after exposure to adverse experiences in childhood. Longitudinal cohorts allow researchers to obtain a better picture of how such problems unfold as individuals grow older, and thus bring us closer to establishing cause and effect relationships. Collecting data prospectively also increases confidence in the accuracy of the information obtained, as it is not subject to problems, either with remembering past events due to forgetfulness, or with current emotional states which often plague retrospectively-collected information.

Fisher has exploited her access to four unique and prospectively collected population-based longitudinal samples to address her research questions: "A major advantage of this is that I can explore whether results from one cohort can be replicated in a different cohort and thus instil more confidence in the findings". The cohorts that Fisher and her team use span different age ranges, thus allowing the investigation of the interplay between childhood victimisation and genetic risk. This reveals more about the persistence of psychotic symptoms in early and late adolescence, as well as into middle age. One of the cohorts also comprises clinical patients, allowing the exploration of the impact of these risk factors on both psychotic symptoms and full-blown psychotic disorders.

GENERALISING RESULTS

The major aspect which limits the generalisability of the findings from this research is that all of the cohorts are drawn from developed countries. It is therefore unclear whether the results would

INTERPLAY BETWEEN CHILDHOOD ADVERSITY AND GENETIC RISK IN THE DEVELOPMENT AND OUTCOME OF PSYCHOSIS IN POPULATION-BASED SAMPLES

OBJECTIVES

- Examine qualitative differences in the form and content of psychotic symptoms experienced by environmentally versus neurodevelopmentally vulnerable children and potential links to comorbidity
- Investigate how types of childhood adversity and familial liability steer individuals towards a pathway leading to psychosis rather than other psychiatric disorders
- Explore the role of early environmental adversity versus neurodevelopmental deficits together with familial liability in the persistence and longer-term outcomes of psychosis

KEY COLLABORATORS

Professor Terrie Moffitt; **Professor Avshalom Caspi**, King's College London, UK and Duke University, North Carolina, USA

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be applicable to developing nations. However, as all of the cohorts are representative of specific populations, there is the potential for good generalisability within these particular settings.

The retention rates for two major projects being investigated by Fisher's research group – the Environmental Risk Longitudinal Twin Study and the Dunedin Multidisciplinary Health and Development Study – are almost 100 per cent, so for these studies specifically, they can be confident that their findings are not biased. However, some bias (such as that caused by individuals dropping out of the study who may have different characteristics than those who stay in the study) may be an issue for the other two cohorts. Nevertheless, Fisher and her colleagues will try to address this statistically by adjusting the data to become more representative of the whole population.

RESULTS SO FAR

A year on from the start of Fisher's current Medical Research Council (MRC) fellowship, the King's College London researchers have made some important discoveries. Working with the Dunedin Multidisciplinary Health and Development Study in New Zealand, Fisher has been able to assess data collected on just over 1,000 individuals from the town of Dunedin since birth, and covering almost every aspect of their lives. This project provided an amazing amount of data and has given the team a unique insight into a whole array of physical and mental health problems at different stages of the life course. Using their results, Fisher will now investigate the impact of childhood victimisation and genetic risk on the development and persistence of psychosis within this cohort.

The group has also been involved with the Environmental Risk Longitudinal Twin Study, which is following a representative sample of twins from the UK over time. They explored whether there was evidence of a direct link between being bullied in childhood and self-harming in early adolescence. That bullying is linked to negative outcomes for the victims will surprise very few people. Yet the team was saddened to find that children as young as 12 who had been frequently bullied were around three times more likely to hurt themselves than children who were not victimised.

The link between bullying and self-harm even held when the team studied twins where one twin had been bullied but the other had not – which rules out other influences (such as parents and home life) from explaining this connection. These twins are currently being reassessed at 18 years of age, to look for evidence that their self-harming has continued, as well as to explore the impact of victimisation and genetic risk on psychotic symptoms.

FUTURE WORK

In the final two years of her fellowship, Fisher and her group will conduct analyses on the four cohorts to explore the interplay between childhood adversity and genetic risk on the persistence of psychosis. In 2013, the MRC will be celebrating its centenary and has provided additional funding for her team to investigate the biological underpinnings of the cognitive difficulties that arise following exposure to early victimisation, which may in turn increase the risk for psychosis. This work will focus on linking differences in how genes are expressed following victimisation to variations in neurological reactivity and associated cognitive performance on psychological tests.

Greater understanding of the process by which biological consequences of stress translate into malleable targets for noninvasive interventions will eventually enable clinicians to potentially prevent or at least minimise the long-term impact of victimisation on the health and wellbeing of individuals.

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