ENVIRONMENTAL VULNERABILITY AND GENETIC-ENVIRONMENTAL INTERACTIONS JIM VAN OS AND RICHIE POULTON pdf

1: Table of contents for The recognition and management of early psychosis

Gene-Environment Interactions in Schizophrenia: Review of Epidemiological Findings and Future Directions Jim van Os, 1, 2, 3 Bart PF Rutten, 2 and Richie Poulton 4 2 Department of Psychiatry and Neuropsychology, School of Mental Health and Neuroscience, Maastricht University Medical Centre, EURON, SEARCH, PO Box (location DOT

High rates of schizophrenia in large cities, and among immigrants, cannabis users, and traumatised individuals reflect the causal influence of environmental exposures. This, in combination with progress in the area of molecular genetics, has generated interest in more complicated models of schizophrenia aetiology that explicitly posit gene-environment interactions. Unravelling the causes of psychotic disorders Schizophrenia and related psychotic disorders have a complex aetiology. Research has attempted to determine the role of specific biological variables, such as genetic and biochemical factors and subtle changes in brain morphology. According to twin and family studies more than half of the vulnerability for schizophrenia is of genetic origin. However, attempts to discover genes that relate directly to psychotic disorder have been frustrating and often disappointing, and despite enormous investments, the identification of actual molecular genetic variants underlying schizophrenia liability has proven extremely difficult. This difficulty is mainly due to the phenomenon of gene-environment interaction, which is defined as genetic control of sensitivity to the environment. Exciting findings in other areas of psychiatry have motivated researchers to turn their attention to better understanding the complex ways in which genetic factors interact with non-genetic factors to produce psychosis. Biological vulnerability factors with a genetic background interact with complex physical, psychological and environmental vulnerability factors. Conceptualised in a model, gene-environment interaction proposes that genes influencing risk for schizophrenia may not do so directly the dominant model until recently , but indirectly by making individuals more sensitive to the effects of causal environmental risk factors. Gene-environment interaction seems a particularly suitable approach for understanding the development of psychosis because this phenotype is known to be associated with environmentally mediated risks, yet people display considerable heterogeneity in their response to those environmental exposures. In the framework of gene-environment interaction, research is focussing on subclinical symptoms that can be traced to prior persistence of clinically relevant symptoms. For example, in a substantial proportion of patients with bipolar disorder, onset of illness may be seen as the poor outcome of a developmentally common and usually transitory non-clinical bipolar phenotype Tijssen et al. According to the model of psychosis proneness - persistence - impairment, genetic background factors impact on a broadly distributed and transitory population expression of psychosis during development. Hence, poor prognosis, in terms of persistence and clinical need, can be predicted by environmental exposure interacting with genetic risk. Environmental risk factors According to findings from epidemiological research, rates of schizophrenia and related psychotic disorders are substantially influenced by a spectrum of environmental risk factors with significant impact on children and adolescents growing up in European societies. Urbanicity Growing up in an urban area has been shown to be associated with an increased risk of developing psychotic disorder in later life Spauwen et al. For children growing up in big cities a more than twofold risk compared to children in rural environments has been shown, independent of other risk factors. Migration Migration presents an increasing challenge to European countries. In immigrant populations the risk of developing psychotic disorders is much higher compared to the risk in both the host country and the country of origin. These findings point to a significant impact associated with the often problematic social interaction between migrants and majority populations. Cannabis use Apart from alcohol, cannabis is the most widely used drug in Europe. Although its effects were considered to be harmless compared to other drugs until recently, many studies have shown that cannabis use, in particular heavy use during adolescence, increases the risk of psychotic disorders such as schizophrenia. Evidence from epidemiological research pointing to a link between childhood trauma and psychotic disorders is remarkably consistent in showing strong effects on disease vulnerability. Measuring schizophrenia vulnerability caused by

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gene-environment interaction Given substantial gene-environment interaction underlying schizophrenia and related psychotic disorders, the most promising approach to elucidate the causes of schizophrenia is to focus on both genes and environments in the same research project. The study of gene-environment interaction is a multidisciplinary exercise involving epidemiology, psychology, psychiatry, neuroscience, neuro-imaging, pharmacology, biostatistics, and genetics. However, it has proven extremely difficult to bring together these disciplines. Now for the first time in the European Union a rational strategy of focused research collaboration has been devised with a unique, large-scale project, which aims to unravel the causes of schizophrenia and related psychotic disorders EU-GEI project, see below. The EU-GEI project This multidisciplinary project, involving more than 7, patients and their families from 15 countries, is the largest effort to date to find gene-environment interactions underlying schizophrenia risk. It is designed to focus on the effects of gene-environment interactions on brain pathways and psychological vulnerability, and to elucidate how subtle, but measurable, behavioural expressions of vulnerability for psychotic disorder are mediated by cerebral and psychological pathways. Follow-up research in the project is expected to establish why, in some individuals, expression of vulnerability will never progress to overt illness, while in others, schizophrenia will manifest in clinical expression. Psychopathological experiences show essential features such as variability over time and dynamic patterns of reactivity to the environment that need to be captured for a better understanding of their underlying mechanisms. Behavioural expression of vulnerability, occasioned by gene-environment interactions, is best captured as subtle alterations in mood, perception, volition and thought in response to minor stressors in the flow of daily life. Since to date no tools exist to adequately monitor these alterations, European enterprises and start-ups in the EU-GEI project will develop new technology allowing for adequate assessment. Today a prototypic device PSYMATE has been designed which can be carried during the day for easy data input concerning mental state, context and activities at random moments in the stream of consciousness. Clinical implications Given the evidence for detrimental effects of big cities on mental health and a wide range of somatic disorders, the impact of the increasing urbanisation and other environmental risk factors in European countries e. Since genetic factors impact on a rather common, transitory expression of psychosis during development, poor prognosis in terms of clinical need can be predicted by environmental exposure interacting with genetic risk. The current development of tools allowing the actual measurement of vulnerability caused by gene-environment interaction will enable clinicians to monitor, and possibly modify, vulnerability at the behavioural level. The findings of the EU-GEI project are promising with regard to preventing transition from subclinical psychosis to overt illness. Conclusion Until recently, researchers found it difficult to unveil the causes of schizophrenia and related psychotic disorders. Recent research findings in psychiatry indicate that genes are likely to influence disorder mostly indirectly, via their impact upon physiological pathways, and work by increasing the likelihood of developing a psychiatric disorder, rather than as direct causes of disorder per se Van Os et al. A significant proportion of psychotic disorder may be understood as the rare poor outcome of a common developmental phenotype characterized by persistence of detectable subclinical psychotic experiences. The current model of gene-environment interaction is nurturing promising approaches to understand the symptoms of schizophrenia and related psychotic disorders and improve treatment. Evidence that onset of clinical psychosis is an outcome of progressively more persistent subclinical psychotic experiences: Experience sampling research in psychopathology: Does urbanicity shift the population expression of psychosis? J Psychiatr Res ; Prediction of transition from common adolescent bipolar experiences to bipolar disorder: Br J Psychiatry ; Gene-environment interactions in schizophrenia: A systematic review and meta-analysis of the psychosis continuum: Jim van Os Dept.

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2: Gene-Environment Interactions in Schizophrenia: Review of - www.enganchecubano.com

Contents: Rationale for and overview of the 2nd edition of the Recognition and management of early psychosis / Henry J. Jackson, Patrick D. McGorry, and Kelly Allott -- Diagnosis and the staging model of psychosis / Patrick D. McGorry, Kelly Allott, and Henry J. Jackson -- Genetic vulnerability / Daniel Weinberger and Gregor Berger.

Any opinions expressed here are those of the author s and not those of IZA. Research published in this series may include views on policy, but the institute itself takes no institutional policy positions. The Institute for the Study of Labor IZA in Bonn is a local and virtual international research center and a place of communication between science, politics and business. The center is associated with the University of Bonn and offers a stimulating research environment through its international network, workshops and conferences, data service, project support, research visits and doctoral program. IZA engages in i original and internationally competitive research in all fields of labor economics, ii development of policy concepts, and iii dissemination of research results and concepts to the interested public. IZA Discussion Papers often represent preliminary work and are circulated to encourage discussion. Citation of such a paper should account for its provisional character. A revised version may be available directly from the author. Little is known about the mechanisms underlying the transfer of economic status between generations. This paper addresses the question of whether inter-generational correlations in health contribute to the perpetuation of economic status. We examine inter-generational correlations in birth weight, a We examine inter-generational correlations in birth weight, a key indicator of the health of newborns that we link to future educational attainment and earnings using a unique data set based on California births from s to the present. We use names and birth dates to link the records of mothers and children. We also identify mothers who are siblings. Together these findings suggest that intergenerational The new look of behavioral genetics in developmental psychopathology: Gene-environment interplay in antisocial behaviors by Terrie E. Moffitt - Psychological Bulletin , " This article reviews behavioralâ€"genetic research to show how it can help address questions of causation in developmental psychopathology. The article focuses on studies of antisocial behavior, because these have been leading the way in investigating environmental as well as genetic influences on psy The article focuses on studies of antisocial behavior, because these have been leading the way in investigating environmental as well as genetic influences on psychopa-thology. First, the article illustrates how behavioralâ€"genetic methods are being newly applied to detect the best candidates for genuine environmental causes among the many risk factors for antisocial behavior. Second, the article examines findings of interaction between genes and environments G E associated with antisocial behavior, outlining steps for testing hypotheses of measured G E. Third, the article envisages future work on geneâ€"environment interplay, arguing that it is an interesting and profitable way forward for psychopathology research. Despite assiduous efforts to eliminate it, antisocial behavior is still a problem. Bureau of Justice Statistics, The World Report on Violence and Health World Health Organization, tallies the staggering burden of mortality, disease, disability, and compromised well-being brought about by perpetrators of family violence and other violent crimes. Behavioral science needs to achieve a more complete understand-ing of the causes of antisocial behavior to provide an evidence base for effectively controlling and preventing it. A new wave of intervention research in the past decade has demonstrated clear success for a number of programs designed to prevent antisocial Show Context Citation Context This pattern of nil main effects for measured genes appears to be widespread and, if this is the case, has an implication for gene hunters: Gene-to-disorder connections may be diluted across all th The neurobiological mechanisms by which childhood maltreatment heightens vulnerability to psycho-pathology remain poorly understood. This review provides a concise synopsis of those studies investigating the neurobiological and genetic factors associated with childhood maltreatment and adversity. We first provide an overview of the neuroendocrine findings, drawing from animal and human studies. These studies indicate an association between early adversity and atypical development of the hypothalamic-pituitary-adrenal HPA axis

stress response, which can predispose to psychiatric vulnerability in adulthood. We then review the neuroimaging findings of structural and functional brain differences in children and adults who have experienced childhood maltreatment. These studies offer evidence of several structural differences associated with early stress, most notably in the corpus callosum in children and the hippocampus in adults; functional studies have reported atypical activation of several brain regions, including decreased activity of the prefrontal cortex. We also briefly consider the possible role that epigenetic mechanisms might play in mediating the impact of early adversity. Finally we consider several ways in which the neurobiological and genetic research may be relevant to clinical practice and intervention. Child abuse, maltreatment, neuroscience, genetics, HPA, psychopathology, resilience, cortisol. There is a burgeoning interest in understanding how early adverse experiences impact on the developing brain e. Twin and adoption studies have demonstrated that many of the psychiatric outcomes that are associated with maltreatment, such as PTSD, depression and antisocial behaviour, are partly heritable e. Children with persistent antisocial and aggressive behavior are diagnosed as having disruptive behavior disorder. The authors review evidence that antisocial children, and especiallythose who persist with this behavior as theygrow older, have a range of neurobiological characteristics. It is argued that serotonergic functioning and stress-regulating mechanisms are important in explaining individual differences in antisocial behavior. Moreover, low fear of punishment and physiological underactivitymaypredispose antisocial individuals to seek out stimulation or take risks and mayhelp to explain poor conditioning and socialization. The authors propose a theoretical model highlighting the interplaybetween neurobiological deficits and cognitive and emotional functioning as mediators of the link between earlyadversityand antisocial behavior problems in childhood. Implications for intervention programs are discussed. Show Context Citation Context Geneâ€”environment interactions in schizophrenia: Bull , " Concern is building about high rates of schizophrenia in large cities, and among immigrants, cannabis users, and traumatized individuals, some of which likely reflects the causal influence of environmental exposures. This, in combination with very slow progress in the area of molecular genetics, has This, in combination with very slow progress in the area of molecular genetics, has generated interest in more complicated models of schizophrenia etiology that explicitly posit geneenvironment interactions EU-GEI. These include parenting and parent-child relationships, parental cognitions These include parenting and parent-child relationships, parental cognitions, parental adjustment, marital interactions, general family relationships, and adaptive child functioning within the family. The measurement of each construct is discussed, and comparative, longitudinal, and treatment outcome studies using these measures are reviewed. It is concluded that measures of treatment outcome for children with ADHD could be improved by utilizing multiple informants, developing tools with greater content and contextual validity, relying more on observational methods, and identifying those measures which are of greatest importance to families. Given the multiple pathways via which both psychosocial and pharmacological interventions exert their influence, composite measures combining multi-informant, multimethod constructs may represent more useful measures of treatment outcome than measures of primary ADHD symptoms. Key words ADHD; family; outcome measurement Problems in parent-child interactions, marital relation-ships, family functioning, and parental adjustment are Psychosocial Stress and Psychosis. Stefanis, Inez Myin-germeys, Leuvensesteenweg Kortenberg " This article presents evidence suggesting that psychosocial stress may increase risk for psychosis, especially in the case of cumulative exposure. The neurobiological substrate of sensitization may in-volve dysregulation of the hypothalamus-pituitary-adrenal axis, contributing to a hypothesized final common pathway of dopamine sensitization in mesolimbic areas and increased stress-induced striatal dopamine release. It is argued that, in order to reconcile genetic and environmental influences on the development of psychosis, gene-environment interactions may be an important mechanism in explaining between-subject differences in risk following cumulative exposure to psychosocial stress. To date, most studies suggestive of gene-stress interaction have used proxy measures for genetic vulnerability such as a family history of psychosis; studies investigating interactions between molecular genetic meas-ures and psychosocial stressors are still relatively scarce.

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Pre-liminary evidence suggests that polymorphisms within the catechol-O-methyltransferase and brain-derived neurotro-phic factor genes may interact with psychosocial stress in the development of psychosis; however, extensive further investigations are required to confirm this. The online version of this article can be found at:

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3: Van Os Jim - publications and coauthors

Jim van Os, Bart P.F. Rutten, and Richie Poulton between environmental exposure and background genetic vulnerability is environment interaction is the.

The treatment of early psychosis has been bedevilled by an entrenched pessimism, stemming from the asylum era and the Kraepelinian model of schizophrenia. More recently, however, there has been a surge of interest in preventively oriented treatmen A Preventive Approach Second Edition presents the field of early detection and early intervention in an interesting and informative format. It is undoubtedly a comprehensive source of information with many references to guide further reading and may also be a useful teaching tool for college and university courses on this topic. This book is a clear and approachable presentation of early detection and early intervention, and I recommend it strongly. McGorry and Kelly Allott; 2. Diagnosis and the staging model of psychosis Patrick D. Genetic vulnerability Daniel Weinberger and Gregor Berger; 4. Environmental vulnerability and genetic-environmental interactions Jim van Os and Richie Poulton; 5. Neurobiological endophenotypes of psychosis and schizophrenia: At Risk Mental State: At risk mental state and prediction Alison R. At risk mental state: Phillips, Jean Addington and Anthony P. Access and Reducing Delay to Treatment: Duration of untreated psychosis: Jorm and Annemarie Wright; Pathways to care and reducing treatment delay in early psychosis Ross M. Norman and Ashok K. Initial assessment and initial pharmacological treatment in the acute phase Martin Lambert; Preventive strategies in bipolar disorders: Other Psychopathology and Comorbidity: Suicide prevention in first-episode psychosis Paddy Power and Jo Robinson; Enhancing work functioning in early psychosis Ein Killackey, Henry J. Jackson, David Fowler and Keith H. Treatment resistance in first-episode psychosis Christian G. Using research and evaluation to inform the development of early psychosis service models: Zipursky, Donald Addington, Merete Nordentoft and

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4: The Recognition and Management of Early Psychosis : Henry J. Jackson :

Gene-Environment Interactions in Schizophrenia: Review of Epidemiological Findings and Future Directions Jim van Os 1,2,3, Bart PF Rutten 2, and Richie Poulton 4.

Sep 12, - Gene-Environment Interactions in Schizophrenia: This, in combination with very slow progress in the area of molecular genetics, has generated interest in more complicated models of schizophrenia etiology that explicitly posit geneenvironment interactions EU-GEI. Although findings of epidemiological gene-environment interaction G 3 E studies are suggestive of widespread gene-environment interactions in the etiology of schizophrenia, numerous challenges remain. G 3 E is a multidisciplinary exercise involving epidemiology, psychology, psychiatry, neuroscience, neuroimaging, pharmacology, biostatistics, and genetics. Epidemiological G 3 E studies using indirect measures of genetic risk in genetically sensitive designs have the advantage that they are able to model the net, albeit nonspecific, genetic load. Experimental ecogenetic approaches with randomized assignment may help to overcome some of the limitations of observational studies and allow for the additional elucidation of underlying mechanisms using a combination of functional enviromics and functional genomics. Exciting findings in other areas of psychiatry have motivated researchers to turn their attention to better understanding the complex ways in which nature interacts with nurture to produce psychosis. This genotype 3 environmental interaction hereafter: G 3 E approach differs from the linear gene-phenotype approach by positing a causal role not for either genes or environment in isolation but for their synergistic coparticipation in the cause of psychosis where the effect of one is conditional on the other. G 3 E seems a particularly suitable approach for understanding the development of psychosis because this phenotype is known to be associated with environmentally mediated risks,8,9 yet people display considerable heterogeneity in their response to those environmental exposures. The structure of this article is as follows. For permissions, please email: Most of the findings using direct molecular genetic measures of genetic risk will be reviewed elsewhere in this issue. Fourth, considerations will be given to possible underlying mechanisms followed by a discussion of future research and directions. Ecogenetics Traditional epidemiology was concerned mainly with environmental risks. Conversely, genetic researchers of complex disorders have mostly focused on molecular genetic approaches in which the environment and interaction between genes and environment were treated as a power-reducing nuisance term. Awareness has been growing, however, that direct or indirect measures of genetic variation can be considered as a conventional epidemiological risk factor in association studies10 and that epidemiological theory can be readily applied to genetically sensitive datasets. The classic problem, however, is how coparticipation between causes in nature biological synergism can be inferred from statistical manipulations with research data statistical interaction , in particular with regard to the choice of additive change in risk occurs by adding a quantity or multiplicative change in risk occurs by multiplying with a quantity models. It has been shown that the true degree of biological synergism can be better estimated fromâ€”but is not the same asâ€”the additive statistical interaction rather than the much more often used multiplicative interaction. According to the concept of genetic moderation of sensitivity to the environment, differences in genetic endowment explain why people respond differently to the same environment figure 1. Most evidence for this type of G 3 E in psychosis has come indirectly from twin and adoption studies and a variety of naturalistic designs in which nonspecific genetic contributions have been assessed. More recently, researchers have obtained information about how variation in specific measured genes interacts with specific measured environments. The revival of interest in G 3 E derives largely from 1 failures of direct genephenotype association studies to uncover genes related to susceptibility for psychiatric disorders and the realization that their multifactorial etiology likely includes many complicated interactive effects requiring more advanced approaches19,20; 2 work demonstrating the operation of G 3 E in many other branches of medicine; and 3 recent evidence of G 3 E within psychiatry. Gene 3 Environment Interaction: Genes Controlling Environmental Sensitivity. For example, a well-known

example of gene-environment interaction is the observation that among Orientals, alcohol sensitivity is strongly regulated by genetic polymorphism of the aldehyde dehydrogenase ALDH2 gene. Similarly, there is strong evidence that some polymorphisms may be involved in psychiatric disorders. Data from animal and human research indicate that 5-HTTLPR may interact with environmental adversity to cause depression, reflecting underlying developmental mechanisms that affect the structural connectivity and, as a consequence, functional interactions, within a neural circuit involved in the regulation of emotional reactivity and extinction of fear27,28,29,30,31 figure 2. Although gene-environment synergism is likely prevalent, other models of disease causation, including models that imply that there is no synergism synergism is zero , may also apply, although likely to a lesser degree. For example, an individual may get schizophrenia only if in possession of a certain type of vulnerability conferred by either genetic or environmental factors. An environmental factor could disrupt early brain development in the same fashion as a genetic mutation. In this model, synergism is zero, and the effect of genes and environment is said to be additive. Apart from genes impacting on sensitivity for environmen- tal risk factors, G 3 E in psychotic disorder may also take the form of environmental factors impacting on either the DNA sequence causing de novo mutations or DNA methylation causing altered gene expression through epimutations. The most suggestive epidemiological evidence for such mechanisms in psychosis comes from studies linking advanced paternal age to the risk of schizophrenia in the offspring. Alternatively, the mechanism underlying the paternal age effect may be genomic imprinting. Some imprinted genes are expressed from a maternally inherited chromosome and silenced on the paternal chromosome, while other imprinted genes show the opposite expression pattern and are only expressed from a paternally inherited chromosome. The inherited methylation pattern is maintained in somatic cells but is erased and reestablished late in spermatogenesis for paternally imprinted genes, a process that could become impaired as age advances. For example, early maternal behavior in animals can affect offspring stress sensitivity through altered DNA methylation of key neuronal receptor genes involved in the stress response. For further details on epigenetics in the context of G 3 E, we refer to the article by Oh and colleagues in this issue. In rGE, exposure to environmental events is not a random phenomenon but rather stems at least partly from differences in genetic makeup. For example, parents create the early childâ€”rearing environment, as well as providing genetic material to their offspring. Passive rGE occurs when parental behavior, which is partly under genetic control, influences the nature of the early childâ€”rearing environment. Thus, parental genes can exert an influence upon the child via the environment, but whose effects are independent of the child itself. Combining examples of rGE and G 3 E in one illustrative situation: Confounding of G 3 E by rGE. In studies aimed at detecting G 3 E, rGE is noise and must be ruled out. For example, does the genetic liability for schizophrenia increase the psychotogenic ef- Fig. Gene 3 Environment Correlation: Genes Controlling Environmental Exposure. Experimental paradigms see below are able to deal effectively with this problem by randomly assigning participants to the exposed and unexposed conditions. In observational designs, however, confounding by rGE is difficult to rule out but can be tested separately. An interesting example concerns urbanicity and schizophrenia. As discussed below, 4 independent studies have suggested that the urban environment may contribute to the onset of psychotic disorder in individuals at genetic risk ie, evidence for G 3 E. An alternative explanation, however, is that the genetic liability for schizophrenia increases the likelihood of moving to the big city, ie, there may be rGE. A priori this is unlikely, given the fact that the effect of urbanicity on schizophrenia is restricted to the window of childhood and adolescence Two twin studies from Australia and The Netherlands on urban mobility support this notion. However, genetic influence in the Australian study was mostly apparent in older individuals who were well past the age at risk for onset of schizophrenia; environmental factors accounted for most of the variation in younger individuals. The reason for the discrepancy in genetic contribution to urban mobility between the Australian and the Dutch study is likely related to contextual factors. More evidence of genetic influence in Australia therefore may in part be the result of the lower base rate of urbanicity. Thus, the conclusion from the Australian and Dutch twin studies is that there are likely only very few human characteristics beyond any genetic influence, including urban

mobility. However, in young adulthood, the age range during which psychotic disorder typically declares itself, environmental more than genetic factors may influence exposure to the risk environment that urbanicity represents,48 making rGE unlikely. Another important issue in rGE is that genetic effects on the outcome can be direct or indirect figure 4. For example, genes may have an effect on both the outcome and the environmental exposure, while the environment has no effect on the outcome. In this case, the observed association between the environment and the outcome is genetically confounded figure 4A. On the other hand, genes may have an effect on the environment, but no direct effect on the outcome because only the environment has a causal effect figure 4B. For example, evidence in the situation of figure 4B of an association between the gene and the outcome can only be explained if there is a true causal relationship between the environmental risk factor and the outcome. Given random assortment of genes from parents to offspring during gamete formation and conception, gene-outcome associations representing gene-causal exposure associations are not generally susceptible to the reverse causation or confounding that may plague conventional observational studies. The Environment, Experimental Ecogenetics, and Functional Enviromics The Environment and Psychosis Here, we refer to the environment broadly as all nongenetic influences that are associated with at least 2 exposure states. There are a number of environmental exposures that are associated with psychotic disorders and symptoms and for which a mechanism of gene-environment interaction has been proposed. These environmental exposures are summarized in box 1, together with an indication to what degree the evidence for an association with schizophrenia is supported by meta-analytic estimates from systematic reviews. The most solid evidence for an association with schizophrenia and related psychosis outcomes is for paternal age, migration, urbanicity, and cannabis Fig. Gene 3 Environment Correlation rGE: Environmental Measurement and Experimental Ecogenetics There are legitimate concerns about how to accurately capture the environmental risk exposure history of participants. This task is particularly challenging when measuring psychosocial risk factors whose negative effects may act cumulatively across long periods of the life course. Measuring tobacco intake is comparatively straightforward, but even this presents problems with accuracy of recall over long periods. The advent of controlled experiments with virtual-reality environments may similarly represent an important asset for the study of environmental exposures. No Meta-analytic Estimate Available Environmental variables with likely impact in fetal life: Maternal pregnancy complications, in particular fetal hypoxia and proxies for fetal folate deficiency 2. Prenatal maternal infection, prenatal maternal stress, prenatal maternal folate deficiency 3. Prenatal exposure to chemical agents eg, lead Environmental variables with likely impact in early life: Quality of early rearing environment institutional care, school, parents 6. Urban environment during development: Stressful life events Traumatic brain injury Measures of the wider social environment: Neighborhood measures of social fragmentation, social capital, and social deprivation Measures of the microenvironment in the flow of daily life: Small daily life stressors, assessed using momentary assessment technology, subtly impacting on affect, salience, and reward by momentary assessment technologies53 to contextual effects of the wider social environment such as neighborhood-type or ethnic density. These mechanisms and their underlying pathophysiological pathways need to be clarified in order to develop a priori gene-environment interaction research paradigms. Molecular genetic and functional genomic studies focusing on genes associated with dopamine neurotransmission suggest that this gene group may be useful for G 3 E studies. For example, a recent large study focusing on gene-gene interaction epistasis and functional effects suggested that a network of interacting dopaminergic polymorphisms may increase risk for schizophrenia. Recent work of this type, using a prefrontal function fMRI phenotype, similarly suggests epistasis between polymorphisms in genes that control dopamine signaling. Development of Experimental Gene 3 Environment Approaches. This well-recognized heterogeneity in response points to the operation of G 3 E. A number of studies have examined G 3 E using indirect measures of genetic risk, such as being a relative, a twin or adopted away offspring of a person with schizophrenia, or the level of psychometric psychosis proneness in a person as an expression of distributed genetic risk for psychotic disorder see below. The advantage of these studies is that

the measure of genetic risk, while nonspecific and therefore not able to capture gene-environment interactions with very specific mechanisms, is nevertheless 1 well validated and 2 represents the complete net genetic load including all gene-gene interactions. While newer studies using direct molecular genetic measures of genetic risk have the advantage of using specific measures, they are also prone to false-positive findings, given the enormous amount of molecular genetic variation that can be used for G 3 E modeling, and the absence of all other factors influencing genetic risk in the model of G 3 E using a small contribution to genetic variation in the form of a single-nucleotide polymorphism SNP. Therefore, epidemiological studies using indirect measures of genetic risk remain useful and may point the way to G 3 E studies using direct measures of genetic risk; to date, they remain the most informative. A review of these findings is presented here. First, there is widespread geographic, temporal, ethnic, and other demographic variation in the incidence of schizophrenia,89,90 reinforcing the Findings From Twin, Adoption, and Family Studies Twin and adoption studies provide strong but nonspecific evidence for the involvement of both genes and environmental factors in the etiology of schizophrenia. For example, Carter et al93 compared, in a year longitudinal study, children of schizophrenic mothers with 99 children of normal parents in terms of exposure to environmental risk ie, institutional care and family instability.

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5: - NLM Catalog Result

Risk and Vulnerability 3. Genetic vulnerability - Daniel Weinberger and Gregor Berger 4. Environmental vulnerability and genetic-environmental interactions - Jim van Os and Richie Poulton 5.

Describing a stage-specific model highlighting the risk, the clinical and biological factors present during the development of the illness, and the best treatments available for each of these stages, this new edition will guide practitioners and researchers in the adoption of carefully planned management strategies fully integrating treatment with prevention. Issues such as resistance to drugs and vocational recovery are covered, with related topics such as service organization and community education. This will be essential reading for all those involved in the care of people with early psychotic illness, or those responsible for the organization of services. McGorry and Kelly Allott; 2. Diagnosis and the staging model of psychosis Patrick D. Genetic vulnerability Daniel Weinberger and Gregor Berger; 4. Environmental vulnerability and genetic-environmental interactions Jim van Os and Richie Poulton; 5. Neurobiological endophenotypes of psychosis and schizophrenia: At Risk Mental State: At risk mental state and prediction Alison R. At risk mental state: Phillips, Jean Addington and Anthony P. Access and Reducing Delay to Treatment: Duration of untreated psychosis: Jorm and Annemarie Wright; Pathways to care and reducing treatment delay in early psychosis Ross M. Norman and Ashok K. Initial assessment and initial pharmacological treatment in the acute phase Martin Lambert; Preventive strategies in bipolar disorders: Other Psychopathology and Comorbidity: Suicide prevention in first-episode psychosis Paddy Power and Jo Robinson; Jackson, David Fowler and Keith H. Treatment resistance in first-episode psychosis Christian G. Using research and evaluation to inform the development of early psychosis service models: Phillips, Jean Addington, Anthony P. Jorm, Annemarie Wright, Ross M. Zipursky, Donald Addington, Merete Nordentoft.

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6: Developmental gene-environment interactions: A model for psychosis | EurekAlert! Science News

Attempts to discover genes that relate directly to psychotic disorder (i.e., the simple "main effects" approach) have been frustrating and often disappointing, resulting in the expression of.

Artikel bewerten This new edition describes a stage-specific model highlighting the risk, the clinical and biological factors present during the development of psychotic illness, and the best treatments available for each of these stages. Guides practitioners and researchers in the adoption of carefully planned management strategies fully integrating treatment with prevention. Psychotic illness is managed and treated with best results when it is recognized at the earliest stages of a person developing the disorder, or when that person is identified as being at high risk of doing so. Describing a stage-specific model highlighting the risk, the clinical and biological factors present during the development of the illness, and the best treatments available for each of these stages, this new edition will guide practitioners and researchers in the adoption of carefully planned management strategies fully integrating treatment with prevention. Issues such as resistance to drugs and vocational recovery are covered, with related topics such as service organization and community education. This will be essential reading for all those involved in the care of people with early psychotic illness, or those responsible for the organization of services. McGorry and Kelly Allott; 2. Diagnosis and the staging model of psychosis Patrick D. Genetic vulnerability Daniel Weinberger and Gregor Berger; 4. Environmental vulnerability and genetic-environmental interactions Jim van Os and Richie Poulton; 5. Neurobiological endophenotypes of psychosis and schizophrenia: At Risk Mental State: At risk mental state and prediction Alison R. At risk mental state: Phillips, Jean Addington and Anthony P. Access and Reducing Delay to Treatment: Duration of untreated psychosis: Jorm and Annemarie Wright; Pathways to care and reducing treatment delay in early psychosis Ross M. Norman and Ashok K. Initial assessment and initial pharmacological treatment in the acute phase Martin Lambert; Preventive strategies in bipolar disorders: Other Psychopathology and Comorbidity: Suicide prevention in first-episode psychosis Paddy Power and Jo Robinson; Enhancing work functioning in early psychosis Eoin Killackey, Henry J. Jackson, David Fowler and Keith H. Treatment resistance in first-episode psychosis Christian G. Using research and evaluation to inform the development of early psychosis service models: Zusatzinfo 41 Tables, unspecified; 5 Halftones, unspecified Verlagsort.

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