original article

Gene-environment interactions and health behaviours: Opportunities for European health psychology

Rutger C. M. E. Engels*[1] & Carmen S. van der Zwaluw[1]

[1] Radboud Universiteit Nijmegen, the Netherlands

Important theoretical models in contemporary health psychology have concentrated on environmental risk factors, such as norms and behaviours of peers and family members, to explain health behaviours. A few examples are the prototype-willingness model (Gibbons et al., 2006), the theory of planned behaviour (Ajzen, 1991), the I-change model (de Vries et al., 2003), the social learning theory (Bandura, 1986), and the transtheoretical model (Prochaska et al., 1992), which inspire many scholars in our area. Besides social norms and behaviours, another stream of research in health psychology focuses on the role of chronic and acute environmental stressors (e.g., childhood trauma, bad family relations, divorce, aggression, and bullying), and people's perceptions of these experiences, on engagement in health-threatening behaviours.

Most of the research based on these models is moving away from straight-forward approaches examining direct associations between environmental factors and behaviour, to the more complex interplay between environmental and individual factors on behaviour. In the past decade, there has been increasing attention for the interaction between individual characteristics, such as novelty seeking, extraversion, self-control, self-efficacy or habit strength on the one hand, and environmental factors on the other, in relation to health-threatening behaviours. However, less effort was made to include genetic susceptibility in designs as a key individual characteristic in explaining (transitions in) health behaviour. As such, we would like to plead for an inclusion of genetic effects in the models described above, and to focus on gene-environment interactions in health psychological research. We will first briefly elaborate on the proposed biological mechanisms underlying the link between genes and behaviour. Further, we will address several reasons for looking at gene-environment effects, and possible directions one can follow. To make our discussion as concrete as possible, we will concentrate on alcohol use and dependence as a specific type of health behaviour.

The value of genetic effects on alcohol use was already emphasized by substantial evidence from studies with behaviour-genetic designs (adoption and twin designs) showing strong effects of genetic influences on variations in alcohol use, misuse and dependence (e.g., Dick et al., 2007; Poelen et al., 2007; Rhee et al., 2003; Viken et al., 1999). Besides behavior-genetic research showing genetic effects, molecular genetic research has described a number of candidate genes that might be associated with susceptibility for alcohol consumption and dependence. In the past decades neurological dopamine systems were identified as key systems in reward and reinforcement with regard to alcohol use and dependence (Herz, 1997; Wise & Bozarth, 1984; Wise & Rompre, 1989). It is now recognized that numerous circuits in the brain, including parts of the limbic system and the prefrontal cortex, and several corresponding neurotransmitters, such as among others dopamine (DA), serotonine (5-HT), and norepinephrine (NE) are involved in the biology of reward (Pierce & Kumaresan, 2006; Robinson & Berridge, 2003). Genetic mutations (polymorphisms) may alter the functioning of (parts) of these reward systems, possibly creating inter-individual differences in alcohol use, in responses to alcohol and/ or in craving, and are as such primary candidates to investigate with regard to alcohol use and dependence. In addition, polymorphic ►

Rutger Engels
Professor
Behavioral Science Institute
Radboud Universiteit Nijmegen
The Netherlands

Carmen van der Zwaluw
PhD student
Behavioral Science Institute
Radboud Universiteit Nijmegen
The Netherlands

*Corresponding Author: Rutger Engels; email: **r.engels @ pwo.ru.nl**

original article

Gene-environment interactions and health behaviours

variations in genes may also cause different responses to environmental factors (see e.g., Jabbi et al., 2007), while stressors in turn may be associated with increased alcohol consumption (Conger, 1956; Goeders, 2003).

For more than a decade now, it is acknowledged that to understand individual differences in phenotypes like alcohol use and dependence, it is not sufficient to know to what extent genes or environment affect that behavior, but that the focus of interest should shift towards the interaction between genes and environment (see elaboration in Rutter, 2002). That is, nature and nurture do not operate independently of each other but primarily in combination, and genetic effects on behavior may exist because they affect an individual's susceptibility to adverse environments. Thus, adverse environments, consisting of, for instance, negative or inadequate parenting, traumatic childhood experiences, or other environmental stressors may pose a risk for alcohol misuse, depending on genetic susceptibility factors (Rutter & Silberg, 2002). With respect to the field of alcohol research, Heath and Nelson (2002) pointed to two main reasons for gene-environment interactions in genetic epidemiological research. First, a lack of attention to genetic effects in studies on environmental risk factors may lead to wrong conclusions about the role of specific environmental factors for alcohol use and dependence. Second, studies exclusively examining genes might underestimate the effects of specific genetic if these effects are only present or strong and consistent under specific environmental circumstances.

Although the value of gene-environment studies is thus widely emphasized, there is still a paucity in empirical research on gene-environment interactions in relation to alcohol use. The literature on environmental risk factors linked to development of drinking in adolescence, transitions from regular drinking to alcohol misuse and dependence, and the negative alcohol-related consequences, is enormous with thousands of articles published annually. In addition, in the past decade, there has also been an enormous boost in molecular epidemiological research focusing on the direct effects of candidate genes on alcohol-related phenotypes. However, when we specifically took a look at studies testing gene-environment interactions associated with alcohol use and dependence in humans – by means of systematically searching Psychinfo, Ovid Medline, and Pubmed, checking the reference lists of all identified articles, and through expert consultations - we identified only nine articles. These papers focused on a small range of stressors such as childhood abuse (Ducci et al., 2007), maltreatment (Kaufman et al., 2007; Nillson, et al., 2007), stressful life events (Nillson et al., 2005) and negative life experiences (Bau et al., 2000; Madrid et al., 2001) in interaction with specific polymorphisms. Although these studies indeed found support for gene-environment interactions effects, the strong diversity in studies published so far in terms of heterogeneity in genes, environmental risk factors, phenotypes (alcohol use and dependence measures), sample characteristics, and study designs makes it not possible to draw firm conclusions.

What we would like to stress, first, is that it is important for further development of theories in health psychology dealing with environmental risk factors, to acknowledge the interplay with genetic factors, as well as genetic effects on environment itself (see for details on the latter issue Rutter et al., 2006). Second, scholars in the field of health psychology are well trained, highly skilled and have the theoretical backup to adequately set up designs, such as matched case-control studies, longitudinal population studies and experimental studies with homogeneous samples, and measure or even manipulate environmental risk factors. As many molecular genetic-informative studies lack sufficient measurements of these environmental stressors (see also Moffitt et al., 2006), input of scholars in disciplines of health psychology as well as developmental psychology, will be of eminent value. We assume that this will be the start of a new era of research which will include both genetic and environmental factors, and their interplay in explaining behaviour, and as such cover a significant number of risk factors for, in this case, alcohol use and dependence. Besides the environmental aspects mentioned before, other environmental risk factors, such as norms and examples set by drinking family members and peers, as well as alcohol cues (e.g., Hutchison et al., 2002) may also be included in this type of studies.

We feel that gene-environment interactions should be a focus of future studies in health psychology. In conclusion we will briefly explore some innovative, new views on gene-environment research. It has been proposed that clinically defined phenotypes such as alcoholism are too heterogeneous in their clinical presentation to be reliably associated with both certain genes or environmental factors (van der Zwaluw et al., 2007). Perhaps, then, should we concentrate on distinct aspects of alcoholism, such ►

original article

Gene-environment interactions and health behaviours

as withdrawal or tolerance, include co-morbid disorders, such as depression or ADHD in our phenotypes, or focus on mediating traits, so called endophenotypes (Gottesman & Gould, 2003) such as craving (Hutchison et al., 2002) or brain waves (Porjesz et al., 2005), to represent phenotypes that might be more closely related to specific genetic factors and perhaps also to environmental ones. In addition, besides the fact that genes may interact with each other (epistasis) and in this way change or conceal the measured effects of one locus or gene (Cordell, 2002), there may also be environment-environment interactions. For example, a traumatic life event, in combination with the presence of an alcohol-dependent partner - *and* a genetic susceptibility - may cause a person to start consuming large amounts of alcohol. Although we recognize that gene-environment research has many difficulties to overcome, we are convinced of the importance of gene-environment studies in an attempt to better explain health behaviours in humans ■

References

Ajzen, I. (1991). The Theory of Planned Behavior. *Organizational Behavior and Human Decision Processes, 50*, 179-211.

Bandura, A. (1986). *Social Foundations of Thought and Action: A Social Cognitive Theory*. Englewood Cliffs, NJ: Prentice-Hall.

Bau, C. H. D., Almeida, S., Hutz, M. H. (2000). The Taq1 A1 allele of the dopamine D2 receptor gene and alcoholism in Brazil. *American Journal of Medical Genetics (Neuropsychiatric Genetics), 96,* 302-306.

Cordell, H. J. (2002). Epistasis, what it means, what it doesn't mean, and statistical methods to detect it in humans. *Human Molecular Genetics, 11*, 2463-2468.

Conger, J. (1956). Reinforcement theory and the dynamics of alcoholism. *Quarterly Journal of Studies on Alcohol, 17*, 296-305.

De Vries, H., Mudde, A., Leijs, I., Charlton, A., Vartiainen, E., Buijs, G., Clemente, M. P., Storm, H., Gonzalez Navarro, A., Nebot, M., Prins, T., & Kremers, S. (2003). The European Smoking Prevention Framework Approach (EFSA): An example of integral prevention. *Health Education Research, 18*, 611-626.

Dick, D. M., Pagan, J. L., Viken, R., Purcell, S., Kaprio, J., Pulkkinen, L., et al. (2007). Changing environmental influences on substance use across development. *Twin Research and Human Genetics, 10*, 315-326.

Ducci, F., Enoch, M, Hodgkinson, C., Xu, K., Catena, M., Robin, R. W., Goldman, D. (2007). Interaction between a functional MAOA locus and childhood sexual abuse predicts alcoholism and antisocial personality disorder in adult women. *Molecular Psychiatry, 1*, 1-14.

Gibbons, F. X., Gerrard, M., Reimer, R. A., & Pomery, E. A. (2006). Unintentional behavior: A subrational approach to health risk. In: de Ridder, D. T. D. & de Wit, J. B. F. (Eds.), *Self-regulation in Health Behavior* (pp. 45-70). Chichester, UK: John Wiley & Sons, Ltd.

Goeders, N. E. (2003). The impact of stress on addiction. *European Neuropsychopharmacology, 13*, 435-441.

Gottesman, I. I., & Gould, T. D. (2003). The endophenotype concept in psychiatry: Etymology and strategic intentions. *American Psychiatry, 160*, 636-645.

Heath, A. C., & Nelson, E. C. (2002). Effects of the interaction between genotype and environment: Research into genetic epidemiology of alcohol dependence. *Alcohol Health and Research World, 26,* 193-201.

Herz, A. (1997). Endogenous opioid systems and alcohol addiction. *Psychopharmacology, 129*, 99-111.

Hutchison, K. E., La Chance, H., Naiura, R., Bryan, A., & Smolen, A. (2002). The DRD4 VNTR polymorphism moderates craving after alcohol consumption. *Journal of Abnormal Psychology, 111*, 134-143.

Jabbi, M., Korf, J., Kema, I. P., Hartman, C., Van der Pompe, G., Minderaa, R. B., Ormel, J., & Den Boer, J. A. (2007). Convergent genetic modulation of the endocrine stress response involves polymorphic variations of 5-HTT, COMT and MAOA. *Molecular Psychiatry, 12*, 483-490.

Kaufman, J., Yang, B. Douglas-Palumber, H., Crouse-Artus, M., Lipschitz, D., Krystal, J. H., & Gelernter, J. (2007). Genetic and environmental predictors of early alcohol use. *Biological Psychiatry, 61,* 1228-1234.

Madrid, G. A., MacMurray, J., Lee, J. W., Anderson, B. A., & Comings, D. E. (2001). Stress as a mediating factor in the association between the DRD2 taq1 polymorphism and alcoholism. *Alcohol, 23,* 117-122.

Moffitt, T. E. (2005). The new look of behavioral genetics in developmental psychopathology: Gene-environment interplay in antisocial behaviors. *Psychological Bulletin, 131,* 533-554.

Moffitt, T. E., Caspi, A., & Rutter, M. (2006). Measured gene-environment interactions in psychopathology. *Perspectives on Psychological Science, 1,* 5-27.

Nilsson, K. W., Sjöberg, R. L., Damberg, M., Alm, P., Öhrvik, J., Leppert, J., Lindström, L., & Oreland, L. (2005). Role of serotonin transporter gene and family function in adolescent alcohol consumption. *Alcoholism: Clinical and Experimental Research, 29,* 564-570.

Nilsson, K. W., Sjöberg, R. L., Wargelius, H., Leppert, J., Lindström, L., Oreland, L. (2007). The monoamine oxidase A (MAO-A) gene, family function and maltreatment as predictors of destructive behavior during male adolescent alcohol consumption. *Addiction, 102,* 389-398.

Pierce, R. C. & Kumaresan, V. (2006). The mesolimbic dopamine system: The final common pathway for the reinforcing effect of drugs on abuse? *Neuroscience and Biobehavioral Reviews, 30*, 215-238.

Poelen, E. A. P., Derks, E. M., Engels, R. C. M. E., Van Leeuwe, J., Scholte, R., Willemsen, G., & Boomsma, D. I. (2007). The relative contribution of genes and environment to alcohol use in early adolescents: Are similar factors related to initiation of alcohol use and frequency of drinking? *Under review.*

Porjesz, B., Rangaswamy, M., Kamarajan, C., Jones, K. A., Padmanabhapillai, A., & Begleiter, H. (2005). The utility of neurophysiological markers in the study of alcoholism. *Clinical Neurophysiology, 116*, 993-1018.

Prochaska J.O., DiClemente C.C., & Norcross J.C. (1992). In search of how people change: Applications to addictive behaviors. *American Psychologist, 47*, 1102-1114.

Rhee, S. H., Hewitt, J. K., Young, S. E., Corley, R. P., Crowley, T. J., & Stallings, M. C. (2003). Genetic and environmental influences on substance initiation, use, and problem use in adolescents. *Archives of General Psychiatry, 60*, 1256-1264.

Robinson, T. E. & Berridge, K. C. (2003). Addiction. *Annual Review of Psychology, 54,* 25-53.

Rose, R. J., & Dick, D. M. (2005). Gene-environment interplay in adolescent drinking behavior. *Alcohol Research and Health, 28*, 222-229.

Rutter, M. (2002). The interplay of nature, nurture, and developmental influences: The challenge ahead for mental health. *Archives of General Psychiatry, 59,* 996-1000.

Rutter, M., & Silberg, J. (2002). Gene-environment interplay in relation to emotional and behavioral disturbance. *Annual Review of Psychology, 53*, 463-490.

Rutter, M., Moffitt, T. E., & Caspi, A. (2006). Gene-environment interplay and psychopathology: Multiple varieties but real effects. *Journal of Child Psychology and Psychiatry, 47,* 226-261.

Van der Zwaluw, C. S., van den Wildenberg, E., Wiers, R. W., Franke, B., Buitelaar, J., Scholte, R. H. J., & Engels, R. C. M. E. (2007). Polymorphisms in the mu-opioid receptor gene (*OPRM1*) and the implications for alcohol dependence in humans. *Pharmacogenomics, 8*, 1427-1436.

Viken, R. J., Kaprio, J., Koskenvuo, M., & Rose, R. J. (1999). Longitudinal analyses of the determinants of drinking and of drinking to intoxication in adolescent twins. *Behavior Genetics, 29*, 455-461.

Wise, R. A., & Bozarth, M. A. (1984). Brain reward circuitry: Four circuit elements "wired" in apparent series. *Brain Research Bulletin, 12,* 203-208.

Wise, R. A., & Rompre, P. P. (1989). Brain dopamine and reward. *Annual Review of Psychology, 40*, 191-225.