quantity of heroin and purity of heroin are similar risk factors in that both mediate their effects by exceeding the tolerance of the user, the controversial intervention of prescribed injectable heroin could also be considered.

To conclude, an entirely different methodology has been utilized to re-affirm the currency of the risk posed by concomitant ingestion of benzodiazepines and alcohol among heroin users and reminds us that this message continues to be relevant for drug users and those who work in the field alike. What is newer, and probably long suspected by users and others, is the evidence presented now, of a dose–response relationship between heroin and subsequent overdose.

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CANNABIS-RELATED PSYCHOSIS AND THE GENE–ENVIRONMENT INTERACTION: COMMENTS ON FERDINAND *ET AL.* 2005

The results of this impressive study [1] confirm the results by Henquet *et al*. [2], who first tested the hypothesis that psychotic experiences at baseline (assessed with the Symptom Checklist Psychoticism and Paranoid Ideation scales) predict future cannabis use. Henquet and colleagues reported an OR of 1.42 (95% CI: 0.88, 2.31) for the risk of developing cannabis use in those who 3–4 years earlier had displayed psychotic experiences and had not used cannabis before. While not statistically significant, this OR indicates a 42% excess risk to start using cannabis and the 95% CI is biased to values greater than unity. Therefore, the findings reported by Ferdinand and colleagues are of great value, as they yield a statistically conclusive result of the hypothesis that (the liability to) psychosis may also predispose to cannabis use.

The main effects of cannabis on psychosis and vice versa reported by Ferdinand and colleagues probably do not represent the complete model of the relationship(s) between cannabis and psychosis, as several studies have suggested that the effects of cannabis on psychosis outcomes such as schizophrenia and psychotic symptoms is modified by prior expression of (genetic) psychosis liability [2–4]. The wider implication of the findings, therefore, is that the genetic factors that influence the sensitivity to the psychosis-increasing effects of cannabis may also influence the probability that individuals will start using cannabis in the first place. The first mechanism (genetic control of sensitivity to an environmental risk factor) is referred to as gene–environment interaction, the second (genetic control of exposure to an environmental risk factor) is referred to as gene–environment correlation [5,6].

In fact, it is not uncommon for the same genetic risk factor to show, in relation to a particular environmental exposure, not only gene–environment interaction, but also gene–environment correlation. For example, it has been shown that the genetic liability for depression acts in part by increasing the sensitivity to stressful life events [7]. However, the same genes also influence the probability that individuals will experience life events in the first place [8]. The same may hold for perinatal adversity in relation to later risk for schizophrenia: the genes predisposing for schizophrenia may not only render an individual more sensitive to the risk-increasing effect of perinatal adversity, but may also increase the risk for perinatal adversity itself [9].

In conclusion, therefore, the commonly reported simultaneous existence of not only gene–environment interaction but also gene–environment correlation in the causation of psychiatric phenotypes may apply similarly to the relationship between cannabis and psychosis.

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