BJPsych | The British Journal of Psychiatry (2011) 198, 73–75

Correspondence

Edited by Kiriakos Xenitidis and Colin Campbell

Contents

Depression and smoking

In their study of a birth cohort ($n = 1265$) in Christchurch, New Zealand, Boden *et al*[1] found that cigarette smoking increased the risk of depression. The cohort was 'studied' at birth, 4 months, 1 year, then annually to age 16 years, and at age 18, 21 and 25 years. At the last three assessments, the study participants were interviewed and data on depression and smoking were collected. The Composite International Diagnostic Interview (CIDI) was used to ascertain the symptoms of major depression and data on the number of cigarettes smoked and the symptoms of nicotine dependence were recorded. The authors used a variety of regression analyses to determine the causal relationship between depression and smoking, adjusted for covariates.

No matter how sophisticated the analyses are, the results of the study reflect the quality of data. The data for this study were incomplete and flawed. The data on depression and smoking were for three 12-month periods and three 1-month periods prior to the interviews. Consequently, the data on the prevalence of depression before age 17 and from age 18 to 20 and age 21 to 24 were missing. Except for three 1-month periods between age 18 and 25, all data on smoking and nicotine dependence were also missing. It is possible that some teenagers experienced depression and smoked cigarettes before age 17. It is also possible that the study participants started and quit smoking or recovered from depression between age 18 and 20, and between age 21 and 24, periods for which data were not collected. In effect, the data collected at age 18, 21 and 25 were almost cross-sectional, which cannot provide evidence for the direction of the association. If a study participant reported smoking at the age-18 interview and gave history of depression prevalent in the year prior to age 21, the authors would conclude that smoking caused depression because, according to their data, smoking preceded depression. But the authors did not know that this participant had quit smoking before the onset of depression at age 19 because they did not obtain the data for the 2 years prior to age 20. In fact, this participant's depression had been caused by smoking cessation, not by smoking.

As Munafò & Araya remarked in their editorial,[2] the CIDI uses symptoms to determine the diagnosis of depression, not its severity. The number of cigarettes smoked is an appropriate measure of exposure to tobacco smoke, not the number of symptoms of nicotine dependence. Consequently, an association between the number of symptoms of depression and those of nicotine dependence is meaningless.

Given that tobacco smoke has anti-anxiety and antidepressant properties[2,3] and that attempted or successful smoking cessation results in depression regardless of prophylactic nicotine replacement or antidepressant therapy,[4,5] smoking cannot cause depression. If smoking causes depression, smoking cessation would relieve depression. The authors neglected to describe data on smokers developing depression when they quit smoking and data on antidepressant therapy during the observation period. Any study that does not use data on depression following reduction in or cessation, even transient, of tobacco smoking and data on pharmacotherapy cannot reliably determine the direction of the cause–effect relationship between smoking and depression.

1 Boden JM, Fergusson DM, Horwood LJ. Cigarette smoking and depression: tests of causal linkages using a longitudinal birth cohort. *Br J Psychiatry* 2010; **196**: 440–6.

2 Munafò MR, Araya R. Cigarette smoking and depression: a question of causation. *Br J Psychiatry* 2010; **196**: 425–6.

3 Balfour DJ, Ridley DL. The effects of nicotine on neural pathways implicated in depression: a factor in nicotine addiction? *Pharmacol Biochem Behav* 2000; **66**: 79–85.

4 Wilhelm K, Wedgwood L, Niven H, Kay-Lambkin F. Smoking cessation and depression: current knowledge and future directions. *Drug Alcohol Rev* 2006; **25**: 97–107.

5 Glassman AH, Covey LS, Stetner F, Rivelli S. Smoking cessation and the course of major depression: a follow-up study. *Lancet* 2001; **357**: 1929–32.

Kazim Sheikh, Physician, University of Kansas School of Medicine, USA. Email: kazim.sheikh@cms.hhs.gov

doi: 10.1192/bjp.198.1.73

Authors' reply: Dr Sheikh notes that 'It is possible that some teenagers experienced depression and smoked cigarettes before age 17'. In response we would point out that the purpose of the study was not to measure or compare the onset or first cause of either depression or cigarette smoking, but rather to examine the dynamic interplay between cigarette smoking and symptoms of depression during early adulthood, and the extent to which either cigarette smoking or depression played a causal role in the maintenance of this association across time.

He also asserts that 'the data collected . . . were almost cross-sectional'. This is not true. The data were discrete longitudinal data, in which both smoking and depression were assessed over several time periods. The separation of these assessments by unobserved periods was not sufficient to render the data cross-sectional.

It is also not strictly true to suggest that data observed at the same time periods could not be used to model causality. Given the availability of data observed at multiple points in time, it proves possible to fit structural equation models of the time-dynamic associations between two variables (such as cigarette smoking and depression) across time, comparing the relative fit of models that posit: (a) a reciprocal causal effect between smoking and depression; (b) a unidirectional causal effect from smoking to depression; and (c) a unidirectional causal effect from depression to smoking. Our data clearly show that the most parsimonious model is one in which there is a unidirectional causal effect from smoking to depression. This same approach has been used to examine the causal associations between numerous variables using the Christchurch Health and Development Study (CHDS) data.[1,2]

Dr Sheikh argues that measures other than nicotine dependence might have led to differing results. We have in fact conducted several additional analyses using a range of measures of both cigarette smoking and depression, including: measures of smoking frequency; measures of the number of cigarettes smoked; and whether participants met criteria for DSM–IV nicotine dependence and major depression. In all cases the analyses were consistent with those reported in the original study; measures of smoking and measures of depression demonstrated significant ($P < 0.05$) associations using fixed-effects regression models; and the results of structural equation modelling showed

that the best-fitting model was one in which cigarette smoking (or nicotine dependence) predicted depression. In the original study, we reported on analyses of nicotine dependence symptoms and symptoms of depression in order to maintain a focus on measures germane to psychiatry, in view of the scope of this *Journal*.

Finally, Dr Sheikh argues that depression must be caused by nicotine withdrawal rather than smoking. However, Benowitz[3] has shown that active smokers go through several withdrawal phases during each day, and that these withdrawal phases are one of the factors that causes self-administration of nicotine. Therefore, it could also be argued that depressive symptomatology may be increased among active smokers because of this continual cycle of withdrawal and satiety.

1 Fergusson DM, Horwood LJ, Ridder EM. Tests of causal linkages between cannabis use and psychotic symptoms. *Addiction* 2005; **100**: 354–66.

2 Fergusson DM, Boden JM, Horwood LJ. Structural models of the comorbidity of internalising disorders and substance use disorders in a longitudinal birth cohort. *Soc Psychiatry Psychiatr Epidemiol* in press.

3 Benowitz NL. Nicotine addiction. *New Engl J Med* 2010; **362**: 2295–303.

Joseph M. Boden, **David M. Fergusson**, University of Otago, Christchurch, New Zealand. Email: joseph.boden@otago.ac.nz

doi: 10.1192/bjp.198.1.73a

Evolution and non-clinical psychotic symptoms

In their recent editorial, Kelleher *et al*[1] emphasised the importance of evolutionary theory for explaining the persistence of psychotic symptoms, depression and anxiety in humans. The authors did not mention the difference between proximate and ultimate explanations, in other words between 'how' and 'why' explanations,[2] and this could make their argument for using evolutionary theory in psychiatric research more specific. In the development of treatments one needs an explanation at the proximate level, whereas the ultimate level can be necessary for generating hypotheses.

In evolutionary-based research the challenge is to find not which behaviour is beneficial now, but which behaviour has been advantageous for the procreation of ancestors in the past. This is the ultimate-level explanation. We know very little about our human ancestors and hypotheses can easily become 'just-so' stories with limited predictive value. Therefore rigorous testing at the how level is required.[3] Furthermore, there are complicating factors such as cliff-edged fitness,[4] whereby a limited number of traits is beneficial but too many are detrimental.

The possible theories for psychosis or schizophrenia mentioned by Kelleher *et al* vary enormously. It might have something to do with language development, complex social cognition, hypervigilance or with something completely different. However, all these theories need to be further developed to generate hypotheses at the how level, for example how language/hypervigilance/social cognition skills differ in humans with genes associated with schizophrenia or in family members of people with schizophrenia. The aim is to explain psychotic disorders at the proximate level, because that is needed to find the best possible treatment.

1 Kelleher I, Jenner JA, Cannon M. Psychotic symptoms in the general population – an evolutionary perspective. *Br J Psychiatry* 2010; **197**: 167–9.

2 Mayr E. Cause and effect in biology. *Science* 1961; **134**: 1501–6.

3 DeBruine L. Beyond 'just-so stories'. *Psychologist* 2009; **22**: 930–3.

4 Nesse RM. Cliff-edged fitness functions and the persistence of schizophrenia. *Behav Brain Sci* 2004; **27**: 862–3.

Dieneke Hubbeling, Consultant Psychiatrist, Wandsworth Crisis and Home Treatment Team, London, UK. Email: dieneke@doctors.org.uk

doi: 10.1192/bjp.198.1.74

Kelleher *et al*[1] argue that evolutionary theories of psychosis provide a valuable theoretical framework for the investigation of non-clinical psychotic phenomena and that the findings of such research would generate new insights into the aetiology, nosology and treatment of psychosis. They rely mostly on Nesse's ideas of cliff-edged fitness[2] and Dodgson & Gordon's work on hypervigilance hallucinations[3] and think that there must be an evolutionary advantage to non-clinical psychotic symptoms – why would they otherwise be so prevalent in the population?

I would like to add two further possible explanations. The first is that non-clinical psychotic symptoms are neither advantageous nor disadvantageous and may have been passed on alongside other fitness enhancing phenotypes. The second is that non-clinical psychotic symptoms are disadvantageous but their negative effects are diminished by being coupled to advantageous phenotypes. Fodor & Piattelli-Palmarini[4] call this free-riding and argue that this is a counterexample to natural selection as proposed by Darwin (although Darwin was very well aware that non-adaptive processes play an important role in evolution).

Evidence to support one or the other evolutionary theory of mental illness will be hard to come by – I have argued elsewhere that, owing to its necessarily historical nature, it will be difficult to arrive at credible causal explanations.[5]

Even if evidence were available, there remains a considerable explanatory gap – why do some (young) people who experience non-clinical psychotic symptoms develop a full-blown psychotic illness with significant functional impairment? One of the aims of evolutionary psychiatry is to define mental disorder in value-free terms. However, when assessing a patient's ability to function, values do come into play, as has been shown by Fulford.[6] I think that whichever way one might argue the case, arriving at a psychiatric diagnosis is unlikely ever to make do without a notion of dysfunction.

As for the direct clinical utility of an evolutionary theory, I cannot see how knowing that psychotic symptoms might have been advantageous in times long gone is of huge benefit to patients or, for that matter, clinicians, and I think that current and possibly future treatment strategies work just as well without taking recourse to an evolutionary perspective.

I would like to thank Professor Ebmeier for his helpful suggestions and thoughts on evolutionary psychiatry.

1 Kelleher I, Jenner JA, Cannon M. Psychotic symptoms in the general population – an evolutionary perspective. *Br J Psychiatry* 2010; **197**: 167–9.

2 Nesse RM. Evolution at 150: time for truly biological psychiatry. *Br J Psychiatry* 2009; **195**: 471–2.

3 Dodgson G, Gordon S. Avoiding false negatives: are some auditory hallucinations an evolved design flaw? *Behav Cogn Psychother* 2009; **37**: 325–34.

4 Fodor JA, Piattelli-Palmarini M. *What Darwin Got Wrong*. Farrar, Strauss and Giroux, 2010.

5 Treffurth Y. Evolution and psychiatry. *Br J Psychiatry* 2010; **196**: 247.

6 Fulford KWM. *Moral Theory and Medical Practice*. Cambridge University Press, 1989.

Yvonne Treffurth, ST6 Child and Adolescent Psychiatry, Child and Adolescent Mental Health Learning Disability Team, The Phoenix Centre, Cambridge, UK. Email: yvonne.treffurth@gmail.com

doi: 10.1192/bjp.198.1.74a

I found the editorial by Kelleher *et al*[1] both stimulating and thought provoking. However, it is important to bear in mind that a given characteristic must either promote or hinder an individual's chances of survival and procreation if it is going to have an impact on natural selection. Even if the presence of a