Behaviour genetics: an unsuitable model for fertility theory

Atam Vetta and Daniel Courgeau

Dr Burch asks the question first put by Rupert Vance 50 years ago, namely, "Is theory for demographers?" He notes, "There is no systematic account of theory development in demography". Perhaps, demography, as *the science of population statistics* does not need one. It can use the statistical and computational theories as demographers have done so competently. To study fertility, however, they need to broaden horizons and look to genetics and evolution. It would, however, be a retrograde step if the new ideas were to be based on the unscientific methodology of Quantitative Genetics, Behaviour Genetics and Neo-Darwinism as recommended by the participants in the Workshop organised by the US Committee on Population in 2002. This is a Committee of the US National Research Council (NRC) that was set up in 1916. NRC is the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering. Its remit includes "furthering knowledge and advising the federal government" (www.national-academies.org). The UK scientific establishment was 'represented' at this workshop by Dr Michael Rutter; a Trustee of the Nuffield Council on Bioethics and Fellow of the Royal Society. The proceedings of the Workshop were published in the book "*OFFSPRING: Human Fertility Behaviour in Biodemographic Perspective*". The recommendations of the Workshop could become the template for fertility researchers. It is important to evaluate them critically. We, however, restrict ourselves the use of the behaviour genetics methodology

First we state our position clearly. Dr Jane Meneken, Chair of the US Committee on Population, said, 'It (the book *OFFSPRING*) suggests that many fertility behaviours that concern demographers may follow biodemographic templates, are influenced by genetic endowment, …"(p.vii). We would go further and assert that fertility and fertility behaviours are *determined* by genetic endowment *in an environment*. The *only* purpose of the existence of a species, including Homos, is to reproduce. Everything else revolves around it. Each species has evolved its own specialised way of reproducing and rearing young. A normal individual of a species is endowed with the genetic *ability* to reproduce, whether one does depends on one's whim and circumstance.

Historical Background:

Neo-Darwinism, Quantitative Genetics (QG) and Behaviour Genetics (BG) are based, primarily, on Fisher (1918) and on his book *The Genetical Theory of Natural selection* (*GTNS*, 1930). The noted neo-Darwinian, Richard Dawkins (1991) described R A Fisher as the "founder of neo-Darwinism" (p. 337) and said "Darwinism post-Fisher is called neo-Darwinism" (p. 115). This does not belittle the contribution of researchers like Sewell Wright and JBS Haldane but describes the unique role of R A Fisher. Behaviour geneticists, in addition regard Jinks and Fulker (1970) as the 'foundation stone' of BG.

R A Fisher is difficult to read and almost impossible to understand. However, Vetta (1976) found that Fisher's (1918) kinship correlation formulae are wrong [see also Vetta & Courgeau (2003)]. Vetta also found that there was an algebraic error in Jinks and Fulker (1970). This error diminishes it value immeasurably (Hirsch 1980, Capron et al 1999).

BG is not a science. The following points support this view:

1. QG and BG are based on the assumption that a trait is determined by a large number of factors (polygene) each having a small summary (additive) effect. The normality of the distribution of a polygenic trait follows from this assumptiom.

2. QG and BG are based on the false assumption that gene segregate *independently*. They do not. Chromosome do and normally all genes on a chromosome segregate together. Their mathematical model is not applicable to human genetics.

3. QG & BG are based on Galton's *false* assumption that effects of genes (G) and environment (E) on a trait can be separated. This is not possible. Our ancestors tried hard to fit to the *long lost environment* and we are the progeny of those who succeeded. R A Fisher himself said, the environmental variance could become a part of the genetic variance (Bennett 1983 p. 228). This is the real neo-Darwinism.

4. To separate G & E effects one would have to conduct experiments where random genotypes are brought up in random environment.

5. Galton's Twin Method is widely used in BG. It assumes that the difference between monozygotic (MZ) twin and dizygotic (DZ) twin correlations on a trait represents the genetic component of the variance on the trait. *False*. Before and after the WWII it was noticed that proportionally more MZ twins than DZ twins had tuberculosis (concordance of MZ twins was higher than DZ twins), therefore, we were told that tuberculosis is genetic! We know this is not true. Now we are told that "years of tertiary education" has a genetic component (Kohler & Rodgers 2003).

6. There is a tradition of using wrong formulae in BG model fitting that goes back to its "foundation" paper Jinks & Fulker (1970). Whenever BGcists fit realistic models involving assortative mating they invariably use incorrect formulae.

7. Only fertility is directly inherited. Any other trait would be inherited only if it has positive correlation with fertility (Falconer 1972). Thus, "No progeny, your genes are dead" (Vetta (2002). BGcists should use formulae of the type given by Capron & Vetta (2001) in model fitting. Neo-Darwinians also need to understand this fact.

8. Our concept of a gene is different from Fisher's concept. There are different types of genes, some make enzymes, some carry instructions, some regulate bodily mechanisms and some are control genes (master switches) that tell other to turn 'on' and 'off'. Fisherian QG and BG cannot take account of these different types of genes. It also cannot take account of mitochondria.

Our message is simple: Darwin and Fisher were great but it is time to move to new pastures.

We discuss Koher & Rodgers' (OFFSPRING, Chapter 3) contribution. Our comments are based on Capron et al (1999), Capron & Vetta (2001) and Vetta & Courgeau (2003).

2. Discussion of Kohler & Rodgers (*Offspring* 2003, chapter 3):

Regrettably, No behavioural trait has been shown to be polygenic. BGcists believe that Bouchard and McGue (1981) proved that IQ is polygenic. False. Almost every genetic test they used on their data, failed and they pleaded with readers "*not to hastily discount*" genetic factors (italic added). But a few lines later they said, "That the data support the inference of partial genetic determination of IQ is indisputable". This is BG!

As noted earlier, Kohler & Rodgers team commend the use of BG and they have published a few papers based on their sample of Danish twins. The research design they used is; (1) select a sample of MZ and DZ twins, (2) send a questionnaire (about 50% return), (3) find correlation or regression coefficient using their responses (4) equate correlation or regression coefficients to heritability and the complex problem of inheritance of a trait is resolved.

Vetta & Courgeau (2003) commented critically on Kohler et al (1999) and Rodgers et al (2001). Kohler & Rodgers team were also aware of Capron et al (1999) and Capron & Vetta (2001). Many of our previous criticisms apply to Kohler & Rogers (2003). These comments relate to this paper.

2.1 "Years of tertiary education" has no genetic component:

Kohler & Rogers (2003) asked MZ and DZ twin cohorts about the number of children born to them until end of 1998 and the years of tertiary education. They claim that heritability of the trait "years of tertiary education", is $h^2 = 0.33$. We are not convinced that this trait has a genetic component. Actually, it depends upon the political & social conditions, the economic viability of the family and, in some countries, on the sex of the child. For example, most western democracies have compulsory education. In England the 1944 Education Act introduced compulsory education up till 15 (now increased to 16). Children of Pakistani origin in Denmark as well as in England are subject to compulsory education laws. Their cousins in Pakistani villages would be lucky to go to a primary school. Poverty has led about 1 million Pakistani children to attend *Madrasas* (free religious schools) where they are fed, learn the Koran by heart and are 'educated' to become jehadis. Even this facility is denied to girls. Some girls school buildings in border areas of Pakistan and Afghanistan have been burnt down by religious fanatics. It would be absurd to argue that "years of tertiary education" is inherited in the West but not elsewhere. This trait has a 'political' inheritance and its genetic component is questionable.

Hindus established schools about 3000 years ago. These were called *gurukuls* (teachers' residence). They were boarding school. Parents and the society in general paid for them. Thus, the genes for "years of tertiary education" could not be very old. Perhaps, K&R will tell us how did they arise and why did they spread in western democracies alone.

2.2 With their limited data no solution to ACE model is possible:

Kohler & Rogers (2003 p. 65) said, "The starting point for most biometrical analyses using behaviour genetics designs is the ACE model". Actually, few BGcists use it. In the ACE model, A= additive, C= Common environment (of twins) and E= random environment. Thus the model assumes no dominance, no interaction or covariance of any kind and random mating. Here environment is divided into two components, common and random. The common or shared environmental variance is the fancy name given to "between groups variance" in the analysis of variance for twin data (see Neale & Cardon 1992, p. 99).

The ACE model has three parameters and three correlations (covariances) are needed to find their estimates. Kohler & Rogers (2003) had only two, MZ and DZ twin correlations. Therefore, the values of the three components of ACE cannot be estimated. It is not clear whether or not they realised this fact. They suspected the presence of dominance or epistasis and said "Detailed analysis of these effects, however, is beyond the scope of this chapter" (p.65). Actually, the ACE model assumes their absence. They said, "in the context of this chapter, the most interesting and valuable extension of the basic ACE model is the bivariate or multivariate model, in which overlapping sources of variation are evaluated". If so, there will then be at least 6 ACE parameters (three for 3 for fertility and 3 for education) plus some interaction parameters. They do not have sufficient information for any genetic model. They used Cholesky decomposition and the package Mx to find estimates. We are not convinced of the genetical validity of their analysis. We show how similar results can be obtained from their data by reducing the worthless ACE model to a worthless two variable model.

2.3 Recalculation of Kohler & Rogers' (2003) results using reduced ACE model:

The ACE model assumes, phenotypic variance Vp = Additive variance Va + Common environment variance Vc + Environmental variance Ve [Vp = Va + Vc + Ve]. Assuming that all twins in their sample were reared together and making the standard assumption of BG model (Vetta & Courgeau 2003, Capron et al 1999), we can write the complete ACE model as:

$$Vp = Va + Vc + Ve$$

$$\text{Cov MZ twins} = Va + Vc$$

$$\text{Cov DZ twins} = 0.5Va + Vc.$$

The model has 3 parameters and three equations. But Kohler & Rogers (2003) have only MZ and DZ correlations. The values of the three parameters, therefore, cannot be found. If we assume that there are no environmental effects i.e. Ve = 0, then we have

$$\text{Corr MZ twins} = Va + Vc$$

$$\text{Corr DZ twins} = 0.5Va + Vc.$$

Note that we are *also* assuming that Vp = Cov MZ = Va + Vc. We have changed covariance to correlations therefore variances on the right hand side are fractions of 1. Substituting corr. MZ twins = 0.3, corr. DZ twins = 0.17 and solving the equations gives, Va = 0.26 and Vc = 0.04 for males. These are similar to Kohler & Rogers' (2003) estimates of 0.25 and 0.05 respectively. For females corr. MZ twins = 0.38 and corr. DZ twins = 0.16. Solving the equations using these values, we get, and Va= 0.44 and Va = -0.06 for females. These differ from their values of 0.35 and 0.02 respectively. Indeed, our estimate of –0.06, being negative, suggests that something is remiss.

2.4 Heritability of a trait depends upon the covariances used in the model:

Dr Lush invented the concept of heritability in 1936 (Bell 1977). There are two types of heritabilities. Narrow heritability h^2 = (additive variance)/ (phenotypic variance) and broad heritability H^2 = (genetic variance)/phenotypic variance). They cannot be calculated directly because additive values and genetic values are hypothetical concepts (Fisher 1918) and their values are not known. QGcists and BGcists have devised numerous methods for estimating heritabilites. Capron et al (1999) claim that estimates of heritability of a trait are not robust and depend on the kinship covariances (correlations) used in the model. The estimates of male and female heritability 0.26 and 0.44 based on Kohler & Rogers' (2003) data differ because they are based on different correlations. This supports the Capron et al's (1999) claim that estimates of heritability are not robust and depend on the correlations used.

Please note that the current molecular and genomic researchers provide not support to the hypothesis that polygenes exit. If so, the concept of heritability can serve no useful purpose.

2.5 Changes in heritabilities across cohorts?

Kohler et al (1999, 2002) noted an increase in heritabilities for female fertility in younger cohorts. Heritability is a population concept and cannot be applied to an un-isolated part of a population. The reason is that we cannot know the genetic relationship of an un-isolated group to the genetic composition of the population. The researchers who discuss increase or decrease of heritability of an un-isolated section of a population exhibit a lack of understanding of quantitative genetics. Kohler & Rogers (2003) hypothesise that this is due to the increased education for females. We do not believe that the increase in the "number of years of education" can change the genetic constitution of a population in such a short time. It could delay having children and also affect the average number of children (section 2.7). As they ignore Ve, their h^2 = Va/(Va+Vc) and if Va is constant, then Vc must decrease if h^2 is to increase. This is an algebraic deduction and has nothing to do with genetics.

2.6 Consequence of negative correlation with fitness (fertility):

It is not generally realised that Fisher's model relates to fitness (fertility) genes only. Fisher should not have his model to study the inheritance of height but then it was his first major paper in genetics. The reason, as Falconer (1972) pointed out, is that only fitness is inherited directly. Vetta (2002) said, "No progeny, your genes are dead". Capron & Vetta (2001) state Falconer's (1972) formula for the heritability of a

trait correlated with fitness in a simpler form; Intensity of inheritance = h^2 of fitness x h^2 of the trait x genetic correlation (fitness, trait). Behaviour geneticists should use this formulation in heritability analysis.

Figure 3-1 and 3-2 of Kohler & Rogers (2003 p. 66-67) indicate that there was a negative correlation between fertility and "years of tertiary education" in their data. If it has a genetic component, the future of the genes of 'years of tertiary education' is bleak. Each generation some of them will disappear. Eventually, none of them will be left in the human genome.

2.7 Use of difference in MZ and DZ correlations:

Concerning the use of correlations in analysis of twin data Martin et. al. (1989, p.5) said that many of the twin studies "are analyzed in no more depth than could have been achieved in 1929". They continued, "The hypothesis testing revolution in human behavior genetics sparked by Jinks and Fulker's seminal paper in 1970 has simply passed by many of the people in the field. This is not altogether surprising: to a newcomer it is difficult stuff, requiring a reasonable grasp of statistics and polygenic inheritance as well as a smattering of calculus and matrix algebra. Most difficult of all, perhaps, is the conceptual leap required in formalizing one's verbal hypothesis in falsifiable mathematical models". We hope that Kohler and Rodgers team will reflect on these comments.

2.8 What is the value of Kohler & Rogers' work for Danes?

Some "happenstance" studies could be useful and Kohler & Rogers (2003, *Offspring*. Chapter 3) believe that given the low fertility, their heritability estimate has some value. We are not convinced. Western democracies face serious population problems and estimates of heritability cannot help to resolve them. There are many causes of low fertility (Vetta & Courgeau 2003). For example, in Denmark the age of the 'first time mother' increased from 23.7 years in 1970 to 28.3 years in 2001. Age related fertility rates decreased in the 15-19 age group from 32.4 in 1970 to 6.2 in 2003 but increased in the age group 30-34 from 66 in 1970 to 121 in 2003. The proportion of single parent household is nearly 42% in 2004. These are all due to social factors. Heritability estimates cannot assist us in solving the problems that Denmark and other Western democracies face.

Another problem is the changing population 'mix'. In Denmark 5.65 % of the population were immigrants or descendent of immigrants from non-Western countries in 2003. The fertility rate among some of these groups is much higher. It is estimated that in 2050, 12.63% of the Danes will be descendents of immigrants from non-Western countries. Their proportion in Britain and France could even be higher. These estimates alone raise a number of questions for demographers. Demographers should not chase the imaginary ghost 'heritability' and study the problems that confront us.

3. Dr Rutter's contribution to the Workshop :

Dr Rutter contributed Chapter 2 of the book *OFFSPRING*. He has previously himself used behaviour genetics. The Nuffield Council on Bioethics of which he is a

trustee, set up a Working Party (WP) on *Genetics and human behaviour: the ethical contex*t in 2001. The WP issued a public consultation document. It invited people to "imagine that we can increase the IQ of an individual with a learning disability into the 'normal' range (usually stated to be between 70 and 130 IQ points) *by altering their genetic makeup*"(italics added). It also envisaged the possibility of altering the IQ of a person in the normal range and the testing of criminals to provide "corrective" treatment. Vetta submitted robust evidence and requested that a copy each should be provided to the Trustees and to individuals who contributed to the drafting of that Consultation Paper in the hope that they would tell him where he was wrong. They could not and the WP did not recommend altering the genetic make up of people

Dr Wachter in his summary of the book said, "But Rutter cautions firmly against inferring genetic determinants of differences in levels of traits from group to group and against readily ascribing changes in level of traits over time to the same factors that modulate individual differences" (p. 4-5). Dr Rutter's himself said, "Accordingly, little is to be gained by attempting to measure the overall heritability of fertility" (p. 30). Dr Rutter's comments are most welcome to Vetta as they might have been influenced by his evidence.

4. Future researches in fertility:

4.1. Social and political problems that face demographers:

As noted earlier most of the problems related to fertility are social, political or religious. While the reproduction levels in some western countries are still below the replacement level, in some other countries the population explosion is still a major cause of concern. For example, the population of Pakistan nearly tripled in the past 57 years to about 150 million and is expected to be 350 million by 2050. Many demographers are trying to find solutions to these problems.

4.2 Fertility genes must be 'fixed' by now:

Fisher (1930) discussed the chance of survival of an individual gene (p. 80-85) and showed (see also Kimura 1962) that an allele that has an advantage in fitness will takeover the population (will become 'fixed') with a certain probability that depends on the size of the advantage. As a fitness allele F has a great advantage in fitness over its non-fitness allele f, F will eventually become 'fixed' and f will disappear from the population. Thus, over the evolutionary time *all* fitness alleles will become fixed. There will then be no segregation of fitness genes and, consequently, no genetic variation in fitness. The only genetic variation in fitness will be due to the mutations (we use this term in the widest sense including the example of infertile XO female who have the second chromosome missing). A neo-Darwinian should, therefore, not look for genetic component of variance in fitness!

4.3. Fitness genes are probably regulatory genes:

As the purpose of life is to survive and reproduce, evolutionary processes must have provided each species with mechanisms for survival and reproduction. Therefore, most of the genes in a species may be involved in these two processes.

Experiments on humans are not possible. But we share genes with other species, including the garden worm C. *elegans.* Ashrafi et al (2003) used RNAi (RNA interference) to find the function of many genes in C. *elegans*. They found that 417 genes (total number of gene is approximately 16k) were involved in metabolism. 305 of these genes *reduced* body fat (- genes) and 112 increased it (+ genes). Not all genes respond to RNAi and there may be more genes involved in the C. *elegans* metabolism. Thus, about 25% of the genes of C. *elegans* are involved in metabolism. It is likely that a significant proportion of human genes is also involved in metabolism. It is reasonable to hypothesise that an appreciable proportion of human genes are involved in fertility and fertility related behaviours. But these genes are regulatory genes (+ or – genes). Behaviour genetics cannot take account of regulatory genes. It has nothing to offer to fertility researchers. The future lies in the genomic and molecular researches and not in BG.

References:

Ashrafi K, Cheng F Y, Watts J L, Fraser A G, Kamath R S, Ahringer J, Ruvkum G 2003 Genome wide RNAi analysis of Caenorhabditis elegan fat regulatory genes". *Nature,* **421**, 268-272.

Bell A E 1977 Heritability in retrospect. *The journal of heredity*, **68,** 297-300.

Bennett J H. 1983 *Natural selection, heredity and eugenics*. Clarendon Press, Oxford.

Bouchard T J Jr. & McGue M G 1981 Familial studies of intelligence, A review. *Science*, ***212***: 1055-1059

Capron C, Vetta A R, Duyme M, Vetta A 1999 Misconceptions of biometrical IQists, *Current Psychology of Cognition*, **18**, 115-285

Capron C, & Vetta A 2001 Familial studies: genetic inferences, *International Encyclopedia of the Social and Behavioral Sciences*, **8**, 5259-5265.

Dawkins R 1991 *The Blind Watchmaker.* Penguin Books, London.

Falconer D S. 1972 Genetic consequences of selection pressure. In J E Meade and A S Parkes ed *Genetic and environmental factors*. 219-232. Oliver & Boyd, Edinburgh.

Fisher R A 1918 The Correlation Between Relatives on the Supposition of Mendelian Inheritanc. *Transactions of the Royal Society of Edinburgh*, **52**, 399-433.

Fisher R A 1958 (1930) *The genetical theory of natural selection.* Clarendon Press (2nd ed, rev. 1958), Oxford. Dover Publications, Broadway.

Hirsch J 1981 To "unfrock the charltons" *SAGE Race Relations Abstracts*. **6**, 1-65. Sage Publcations, London.

Jinks J L, Fulker D W 1970 Comparison of the biometrical genetical, MAVA, and classical approaches to the analysis of human behavior, *Psychological Bulletin*, **73**, 311-349.

Kimura M 1962 On the probability of fixation of mutant genes in a population. Genetics. **47.** 713-719

Kohler H J, Rogers J L & Christensen K 1999 Is fertility behaviour in our genes? *Population and Development Review,* **25,** 253-288.

Koher H J & Rodgers J L 2003 Education, fertility, and heritability: explaining a paradox. In *OFFSPRING: Human Fertility Behaviour in Biodemographic Perspective*. The National Academic Press, Washington

Meneken J. 2003. Preface. *OFFSPRING: Human Fertility Behaviour in Biodemographic Perspective*". The national Academic Press, Washington.

National Research Council 2003 *OFFSPRING: Human Fertility Behaviour in Biodemographic Perspective*". The National Academic Press, Washington.

Neale M C & Cardon L R 1992 *Methodology for Genetic Studies of Twins and Families* Kluwer Academic Publishers, Dordrecht.

Rodgers J L, Hughes K A ,Kohler H-P, Christensen K., Doughty D, Rowe D C, miller W B 2001b Genetic influence helps explain individual differences in human fertility outcomes: evidence from recent behavioral molecular genetic studies, *Current Directions in Psychological Science*, **10**, 184-188.

Rutter M 2003 Genetic influences on fertility: strenghs and limitations of quantitative inferences. In *OFFSPRING: Human Fertility Behaviour in Biodemographic Perspective*". The National Academic Press, Washington.

Vetta A 1976a Correction to Fisher's correlations between relatives and environmental effects. *Nature*, **263**: 316-317.

Vetta A. 2002 Discussion on Statistical Modelling and Analysis of Genetic Data. *J. Roy. Statist. Soc. B.* **64**. 741-742.

Vetta A & Courgeau D 2003 Demographic behaviour and behaviour genetics. *Population E*, **58**. 401-428. (Published in French : Comportements démographiques et génétique du comportement. *Population F*, 58 : 457-488).