TURUN YLIOPISTON JULKAISUJA
ANNALES UNIVERSITATIS TURKUENSIS

SARJA - SER. AII OSA - TOM. 223

BIOLOGICA - GEOGRAPHICA - GEOLOGICA

PHENOTYPIC AND GENETIC VARIANCE AND COVARIANCE IN LIFE-HISTORY TRAITS IN PRE-INDUSTRIAL HUMAN POPULATIONS

by

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TURUN YLIOPISTO
Turku 2008

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ISBN 978-951-29-3545-1 (PRINT)
ISBN 978-951-29-3546-8 (PDF)
ISSN 0082-6979
Painosalama Oy – Turku, Finland 2008

"A mind is like a parachute. It doesn't work if it's not open."

Frank Zappa

LIST OF ORIGINAL PAPERS

This thesis is based on the following articles which will be referred in the text by their Roman numerals:

I Jenni E. Pettay, Loeske E. B. Kruuk, Jukka Jokela, and Virpi Lummaa 2005. Heritability and genetic constraints of life-history trait evolution in pre-industrial humans.
- *Proceedings of the National Academy of Science USA* 102: 2838-2843

II Jenni E. Pettay, Anne Charmantier, Alastair J. Wilson, and Virpi Lummaa. Age-specific genetic and maternal effects in fecundity of pre-industrial Finnish women.
-*Evolution, in press*

III Jenni E. Pettay, Jukka Jokela, and Virpi Lummaa. Two generations of local mating increased offspring mortality in humans.
-*Manuscript*

IV Virpi Lummaa, Jenni E. Pettay, and Andrew F. Russell 2007. Male twins reduce fitness of female co-twins in humans.
-*Proceedings of the National academy of Science USA* 104: 10915-10920

V Jenni E. Pettay, Samuli Helle, Jukka Jokela, and Virpi Lummaa 2007. Natural selection on female life-history traits in relation to socio-economic class in pre-industrial human populations.
-*PLoS ONE 2: e606*

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CONTENTS

1. INTRODUCTION 7

1.1. Evolution of life-histories 7
1.2. Human life-history evolution 7
1.3. Variation in traits caused by genetic factors...9
1.4. Variation in traits caused by age 10
1.5. Variation in traits caused by inbreeding depression.....................................11
1.6. Variation in traits caused by pre-natal environmental conditions...................12
1.7. Variation in traits caused by post-natal environmental conditions 13
1.8. Phenotypic and genetic correlations between life-history traits 13
1.9. Aims of the thesis...14

2. MATERIALS AND METHODS...15

2.1. The demographic data..15
    2.1.1. The Family of Sursill 15
    2.1.2. Parish-record data on five populations of Finns...................................16
2.2. Studied life-history traits..17
2.3. Data Analysis 18
    2.3.1. Pedigree analysis...18
    2.3.2. Survival analysis 19
    2.3.3. Measuring fitness and natural selection 19
    2.3.4. General comments on long-term fitness 20

3. RESULTS AND DISCUSSION...21

3.1. Variation in traits caused by genetic factors...21
3.2. Variation in traits caused by age 22
3.3. Variation in traits caused by inbreeding depression..22
3.4. Variation caused by pre-natal conditions 23
3.5. Variation caused by post-natal environmental conditions................................23
3.6. Phenotypic and genetic correlations between life-history traits 24

4. CONCLUSIONS AND FUTURE PROSPECTS..25

5. ACKNOWLEDGEMENTS 27

6. REFERENCES 29

ORIGINAL PUBLICATIONS...35

1. INTRODUCTION

1.1. Evolution of life-histories

For evolution, we need two processes (Darwin 1859, Fisher 1930). First, there must be differential reproductive success between individuals. For example, an individual can fail to have offspring at all, because it did not survive to breeding age, or did not find a mate, or it can have fewer offspring than another because of being in poorer body condition or breeding in poor circumstances. The second requirement for evolution is that a trait is genetically determined and genetic variation in that trait exists between individuals. Evolution constitutes changes in gene frequencies caused by natural selection (or by other forces such as random drift) in a population.

Given that individuals which spread the most genes through a population will be favoured by natural selection (i.e. will be most fit), the question is how should individuals accomplish maximum fitness? Life-history theory (reviewed in Roff 1992, Stearns 1992) attempts to answer this question by investigating: How fast should an individual grow and mature? How many offspring, what size and sex should one produce? When to reproduce? How long to continue reproducing? When to senescence and die? These questions are not only important to understanding how individuals attempt to maximise fitness, but also because life-history traits such as maturation age, fecundity and longevity may be negatively correlated with each others (“trade-offs”) due to inevitable limits of time and energy available to individuals. Hence, individuals have to allocate their limited resources to growth, maintenance and reproduction, and life-history theory assumes that an optimal combination of such life-history traits exists to maximize fitness (Cole 1954, Gadgil & Bossert 1970, Schaffer 1974, Williams 1957, reviewed in Roff 1992, Stearns 1992).

Variation in life-history traits, reproductive success and fitness observed in nature may be attributed to two sources. The g*enotype* of an individual refers to the genetic construction of an individual. However, it is the *phenotype* of an individual that we observe, and this phenotype is a result of an interaction between and an individual’s genotype and its environment. Thus, the variation between individuals in morphological features, life-history traits, and in the end fitness is the end-product of both variation in the genes and variation in the environment.

1.2. Human life-history evolution

Major shifts in human speciation and life history evolution have been suggested to take place in the Pleistocene (~1.8 million to 10,000 years ago), a time period preceding agriculture when humans were hunter-gatherers (Hrdy 2000). However, the environment has gone through massive changes during this period, including significant ice-ages. More recently, the development of agriculture approximately 10,000 years ago emerged at the same time as larger permanent population settlements of humans (Lewin 1998). Larger and denser populations probably affected the strength and direction of selection; especially with respect to susceptibility to infectious diseases, which became the new main cause of death (Kallioinen 2005). In those 10,000 years since the invention of agriculture, there have been approximately 400 human generations, giving rise to 400 chances of selection to have an impact on populations, which is enough for allele frequencies to change considerably (Hrdy 2000). One example of how such changing environmental conditions can cause rapid changes in gene frequencies is the evolution of the lactase gene. In most human populations, the ability to digest lactose in milk usually disappears in childhood, but in European-derived populations, lactase activity persists into adulthood (Scrimshaw & Murray 1988). Studies based on population and molecular genetics suggest that strong selection occurred in Europe between the last 5,000-10,000 years on the ability to utilise milk as an important part of the diet, consistent with an advantage to lactase persistence in areas of dairy farming (Bersaglieri et al. 2004). This is perhaps the clearest example of how human cultural evolution can also affect biological evolution.

Human life-history evolution has attracted considerable attention (Hill & Kaplan 1999, Kaplan et al. 2000, Mace 2000). This is both because of its obvious wide-reaching relevance and also because human life-history is unusual, with late age at first reproduction, the production of relative large offspring and female menopause (Robson et al. 2006). Despite this, life-history studies have typically investigated human evolution from a phenotypic perspective (Lummaa 2007). However, the evolution of human life-history traits, as those of any species, is not only a consequence of phenotypic selection, but also depends on the level of heritability. Despite this, this latter area of human life-history evolution has been almost wholly devoid of attention from a life-history perspective. A lack of information on the heritability and genetic correlations of reproductive traits in human populations has resulted in a limited understanding of whether the documented phenotypic selection could lead to evolutionary changes over time. Moreover, although considerable interest has been paid among anthropologists on the effects of large-scale environmental changes on human evolution (see above), very little is known concerning how: the environmental conditions prevailing during the early development and breeding age of individuals modify the expression of human life-history traits; how it affects the trade-offs between them; or impact the potential for evolutionary change over generations as a result of the documented phenotypic selection. Finally, due to the fact that human populations are commonly characterised by small local population sizes isolated by distance, an additional factor potentially affecting life-history trait variation in many populations is inbreeding. Yet, little is currently known concerning what effects this may have on life-history traits and reproductive success over generations.

1.3. Variation in traits caused by genetic factors

Selection on, and genetic variation in, traits are the basic premises for evolution to take place. Often life-history studies show selection on a studied trait, but they cannot confirm whether the trait is exhibiting additive genetic variation (heritability), even though this is a prerequisite for evolution to occur (Roff 1997). Because heritability measures the proportion of variation in a trait that is heritable, in stochastic environments, random variation is more likely to explain a larger proportion of overall variation in a trait than in constant environments, where heritability can be more profound while environmental variation is smaller (Houle 1992, Kruuk et al. 2000, Wilson et al. 2006). This means that populations that experience less stochastic environmental variation, heritability can be larger, and thus response to selection can be more rapid than in populations with more environmental variation.

In theory, direct selection on a trait would erode additive genetic variation, and so life-history traits that are under strong selection are assumed to have little genetic variation (Fisher 1930, Falconer & Mackay 1996). However, there are many examples that show heritable genetic variation in life-history traits in wild animal population (reviewed in: Fisher 1930, Falconer & Mackay 1996, Roff 1997). There are several possible mechanisms that could preserve genetic variability. I list these possibilities (by Roff 1997) and refer to papers included in this theses in parenthesis where I discuss this possibility: (1) *Stabilizing selection* where selection favours intermediate phenotypes over extreme ones; (2) *disruptive selection* where extreme types are selected; (3) *mutation-selection balance*, where mutations are assumed to 'replace' erosion caused by selection; (4) *heterozygote advantage* (**III**), idea that heterozygotes have higher fitness than homozygotes; (5) *Antagonistic pleiotropy* **(I)**, a concept that traits that have beneficial effects early in life (e.g. fast growth or fecundity) can be correlated with effects that have negative effects late in life; (6) *Frequency-dependent selection*, where the fitness of a phenotype or a genotype varies with the phenotypic or genotypic composition of the population; and (7) *Environmental heterogeneity*, where environmental variation could favour various kind of genotypes **(IV,V).** Furthermore, life-history traits show great plasticity, the same genotype can adjust its behaviour and expression of traits according of its environment (Roff 2002). This is very important in long-living animal such as humans.

The heritability of a trait is usually estimated by regression between relatives, e.g. between parents and offspring. The problem with estimating heritability in humans arises because individuals cannot be cross-bred and fostered in standard environments (as is the case in many animals) and so the inevitable shared environment, which human relatives occur in can lead to an overestimation of heritability. One source for heritability estimates of humans are twin-studies (Kaprio et al. 1990, Kaprio et al. 2002). For example, Kirk et al. (2001) took advantage of twin data from contemporary Australian women to estimate heritability of age at menarche and first and last reproduction to find these life history traits to have heritable basis. Herskind et al. (1996) used historical records of Danish twin pairs to estimate heritability of lifespan to be ~ 0.25. However, twin studies have limitations; twinning is rare in humans and data are hard to obtain, especially from non-industrialized conditions. Yet more information on heritability of human life-history traits is needed in different and also from non-industrialized populations to draw any conclusions concerning the general patterns.

1.4. Variation in traits caused by age

Variation in life-history traits may also be affected by age. Evolutionary theories of senescence predict that the additive genetic variance in fitness traits is age-dependent. For example, the ‘mutation accumulation’ hypothesis (Medawar 1952) predicts that the additive genetic variance, dominance variance and inbreeding depression of traits increase with age (Charlesworth 1990; Charlesworth & Hughes 1996). This is due to the declining force of natural selection with age, whereby selection is unable to remove harmful mutations expressed after reproduction. Similarly the ‘antagonistic pleiotropy’ hypothesis predicts that natural selection favours genes that have beneficial early-life effects even though they may have harmful late-life effects (Williams 1957), leading to an age-specific increase in additive genetic variance and negative genetic covariances between early and late life-history traits (Rose 1991). Although selection may be strong earlier in an individual’s life there might be little genetic variation that can lead to evolutionary change, while later in life selection can be weaker but genetic potential for evolutionary change may be higher as genetic variation increases.

Such age-dependent variation in genetic variance has the potential to be of particular importance in human female life-history traits, because female fertility in humans also shows clear changes with age. First, in young women, maternal effects may be important for successful reproduction, such as wealth of the parents that correlates both with female body condition and thus their age at menarche (reviewed in Voland 1998) and marital success (Voland 1990). Furthermore, family help, such as the presence of grandmothers, may be an important determinant of female reproductive rate: daughters enjoying help from their post-reproductive mothers show reduced inter-birth intervals (Lahdenperä *et al.* 2004, Voland & Beise 2002) and increased breeding probability (Sear *et al.* 2003). Second, female fertility also shows senescence with age: the natural conception rate falls rapidly already from mid-30s onwards (Sievert 2001), and the risk of unsuccessful pregnancy (miscarriage) increases with age while the quality of offspring, in terms of developmental and genetic problems, may decrease (Holman & Wood 2001). Despite this, little is known about the role of age-dependent changes in heritability in affecting the evolutionary potential of traits in long-lived animals (see Réale et al. 1999 and Charmantier et al. 2006 for recent exceptions suggesting that such effects may be important in wild populations of animals), and no previous studies have been conducted on humans to my knowledge.

1.5. Variation in traits caused by inbreeding depression

Inbreeding depression is simply the reduction of fitness traits of inbred offspring in comparison to outbred offspring (Wright 1977, Charlesworth & Charlesworth 1987, Keller 2002). Outbred and thus more heterozygotic individuals often have higher vigour and better reproductive performance (Charlesworth & Charlesworth 1987, Thornhill 1993, Keller 2002). The better performance of outbred individuals is a result of masking harmful recessive alleles, often called ‘the partial dominance’, or an advantage of heterozygosity itself which is called ‘heterosis’ or ‘overdominance’ (Charlesworth & Charlesworth 1987). However, crossing individuals of different species or from genetically differentiated population can lead to ‘outbreeding depression’, worse performance of hybrids (Falconer & Mackay 1996). This can result when either allopatric, differentiated populations are locally adapted and hybrids are not fit to either of the parental environments, or when high fitness is a result of co-adapted gene complexes, which are broken when hybridization occurs. Sometimes the first generation hybrids (F_1) benefit from heterosis, but the breaking of co-adapted gene-complexes starts in the second generation of offspring (F_2) after recombination, leading to reduced fitness in that generation (Lynch & Walsh 1998). For this reason, it is important to study more than just one generation of crosses, but studies of multiple succeeding generations of individuals are rare in wild living animals (but see Edmands 1999, Kruuk et al. 2002, Marr et. al. 2002, Meagher et al. 1999, Slate et al. 2000 for exceptions).

In contrast, how much humans are affected by inbreeding depression is an extensively studied question, but the results obtained are inconsistent. Some studies have shown negative effects of consanguineous mating in humans on traits such as height and IQ score (Falconer & Mackay 1996). However, most studies to date have generally reported no significant difference in numbers of surviving children in consanguineous versus unrelated families (Bittles et. al. 2002 and refs therein), but some report higher childhood mortality for consanguineous couples (Bittles et. al. 1991, Dorsten et al. 1999, Fuster 2003). An alternative is to assume that small populations have higher levels of inbreeding (i.e. reduced genetic variation within breeding units) than large populations, even though consanguineous marriages are rare. In other words, in small populations people are more likely to marry a person, with who they share a common ancestry with, without knowing it. This can to lead inbreeding depression in offspring.

1.6. Variation in traits caused by pre-natal environmental conditions

The environment often sets limits for fitness and evolution of life-history traits (Roff 1992, Stearns 1992). There is increasing evidence that conditions experienced before birth can have profound effects on life-history trait variation (Barker 1994, Lindström 1999, Lummaa & Clutton-Brock 2002). For example, long-term studies on several wild mammal populations show that pre-natal growth rates of individuals are commonly influenced by current environmental conditions, and that these can have substantial effects on the subsequent growth, breeding success and longevity of those individuals (Clutton-Brock 1991, Lindstrom 1999, Metcalfe and Monaghan 2001). Similarly, in humans, the quality and quantity of nutrition received *in utero* and/or the timing of birth have been shown to predict post-natal growth rates (Weber et al. 1998), the onset of chronic diseases in adulthood (Barker 1994), longevity (Doblhammer & Vaupel 2001) and reproductive success or fitness (Lummaa & Tremblay 2003, Huber et al. 2004).

Another, but less considered, aspect of the early environment that can impose variation in life-history traits is the amount of sex hormones (testosterones and oestrogens) to which developing young are exposed. For example, the pre-natal acquisition of hormones from developing neighbours in viviparous animals has been shown to have significant consequences for adulthood morphology, physiology and behavior both in mammals (Ryan & Vandenbergh 2002, Even et al. 1992, Clark & Bennett 1995) as well as in viviparous lizards (Uller at al. 2004). In rodents, female fetuses positioned between two males have higher levels of testosterone than those from the same litter positioned between females (Ryan & Vandenbergh 2002). Furthermore, such females commonly have greater (i.e., more male-like) anogenital distances and often show more aggression, delayed maturation, longer oestrus cycles, reduced sexual attractiveness to males, and shorter reproductive lifespans (Ryan & Vandenbergh 2002). Given that testosterone is lipid-soluble, there is no basis for assuming that interfoetal transfer of testosterone, unequivocally demonstrated in rodents, will not occur in any multiparous mammal. Thus, in humans, sex hormones are also likely to diffuse across foetal membranes and amniotic fluid, leading to the likelihood that human twins also can be influenced hormonally by the presence of a co-twin (Miller 1994). Because mammal fetuses are exposed to maternal estrogens, males with an opposite-sex co-twin may be exposed to similar levels of estrogens as males with a same-sex co-twin, but females with an opposite-sex co-twin may be exposed to elevated levels of testosterone compared with females with a same-sex co-twin (vom Saal 1989). In accordance, human twin studies have shown that having a male co-twin can be associated with increased female growth *in utero* (Blumrosen et al. 2002, Glinianaia et al. 1998) and masculinisation of sexually dimorphic anatomical traits known to be sensitive to testosterone concentrations during foetal development, including second- to fourth-digit finger ratio (van Anders et al. 2006), auditory system (MacFadden 1993), craniofacial growth (Boklage 1985), visual acuity (Miller 1995), and canine size (Dempsey et al. 1999). In addition, such females commonly show more male-like behaviours and attitudes after birth (Cohen-Bendahan et al. 2005). However, we do not yet know how this affects reproductive success and long-term fitness in humans.

1.7. Variation in traits caused by post-natal environmental conditions

Some life-history combinations can be optimal in one environment, but not in others. Because environments are rarely constant, variation in environments can also preserve genetic variation (Roff 1997). Plasticity of behaviour and life-history trait expression is important for long-living animals such as humans, who can experience different environment during their lifespan. Resources that individual possess are important for fitness and expression on life-history traits. Individuals with limited resources might face trade-offs between different life-history traits e.g. between reproduction and maintenance, while individuals with plentiful resources can allocate to both maintenance and reproduction (Noorwijk 1986). In humans, socio-economic status is a good indicator of the amount of resources available to individuals, and has been shown to affect family size in historical populations (Low 1991, Voland 1990) and contemporary pastoralists (Cronk 1991, Borgerhoff Mulder 1987), and on health even in modern developed countries (Lahelma & Valkonen 1991, Martikainen 1995). However, we currently do not know how resource availability affects the strength and direction of selection on life-history traits and long-term fitness.

1.8. Phenotypic and genetic correlations between life-history traits

Not only variation in traits *per se* is important, but also the interactions between them. Selection can target traits both directly and indirectly, through other traits, and correlations between traits can be positive or negative. For example, if two traits are correlated negatively, positive selection on one trait will lead to negative indirect selection on the other trait, and can thus impact the evolution of that trait. Yet, little is known about how phenotypic interactions between different life-history traits translate into genetic interactions, and how they are affected by the resources available to individuals. Such information would be important because current knowledge of trade-offs between human life-history traits are mainly based on correlations between trait pairs, while interactions between traits are probably much more complex involving many traits at different hierarchical levels (Lande & Arnold 1983). Furthermore, our knowledge of trade-offs between traits are based on phenotypic correlations, but we know very little about the underlying genetic correlations. For example, Helle et al. (2005) showed, than in a historical northern Finnish population, Sami, the most important component of female fitness (i.e., the phenotypic trait with the highest selection differential) was the number of delivered offspring, but women also gained higher fitness (larger total number of offspring raised to adulthood over lifetime) if they began reproducing earlier, had shorter interbirth intervals, and continued reproducing later. Phenotypic covariation between female life-history traits indicated that interbirth intervals were independent both of ages at first and last reproduction, whereas women who started to reproduce early also ceased reproduction young (Helle et al. 2005). Borgerhoff Mulder (1989) could demonstrate that age at maturation and lifetime reproductive success are correlated in Kipsigis, who are pastoralists living in Kenya. But because heritability of these traits could not be tested, the evolutionary significance of these correlations are unclear.

1.9. Aims of the thesis

The aim of this thesis was to investigate factors affecting the evolution of human life-history traits. In particular, I aimed to estimate the heritability of human life-history traits. Heritability of life-history traits is crucial for evolution, yet this area of human-life history evolution is lacking attention. First, in article **I**, I investigated the amount of heritable variation and maternal effects in human life history traits. Second, in paper **II**, I investigated heritability changes over lifespan, since senescence theories suggest that heritability should increase with age. This can have important evolutionary implications especially in humans where survival to late ages is high compared to other animals. Third, in paper **III**, I investigated the consequences of inbreeding and outbreeding for life-history trait variation and reproductive success by studying cumulative effects of local vs. nonlocal mating in succeeding generations of humans. In paper **IV,** I investigated the role of prenatal environmental conditions in affecting an individual's life-history traits and reproductive success in adulthood, while in paper **V** I studied the effects of post-natal environmental conditions, in terms of resources available to individuals, on life-history trait variation, trade-offs and strength of natural selection. To answer these questions, I analysed demographic pedigree data collected from church records of pre-industrial (1700-1900) Finland.

2. MATERIALS AND METHODS

2.1. The demographic data

Accurate Finnish church book records are the basis of this study. The Lutheran Church has kept census, birth/baptism, marriage and death/burial registers of each parish in the country since the 17th century (Pitkänen 1988, Luther 1993). These records provide information for each individual from birth to death. Following succeeding generations, child numbers and lifetime reproductive success can be collected at the individual level and linked with the socioeconomic status of each family.

The study period (1730-1860) ends before industrialism and so before more liberal economics, healthcare improvements and modern birth-control methods had significant effects on survivorship and standard of living in Finland. Especially child mortality was high; almost half of all children born died before adulthood (age 15 years), with infectious diseases, such as smallpox, measles, typhus and pulmonary tuberculosis being the main cause of death in children in Finland during the study period (Turpeinen 1978). This is similar to child mortality detected in contemporary hunter-gatherer population (Gurven & Kaplan 2006). In my studies, I used two separate datasets; the genealogical database for the family of Sursill, and parish record data of Kustavi, Hiittinen, Rymättylä, Ikaalinen and Pulkkila.

During the study era, inheritance in Finland usually favoured the eldest son, and the predominant household contained both parents and the family of one or more children, whereas the other siblings usually lived close by (Moring 2003). Furthermore, 95% married within same village (Nevanlinna 1973). The mating system was monogamous and extramarital affairs were a strict taboo of the Lutheran church and punishable. The rate of extra-pair paternity (EPP) was probably around 1.7–3.3% suggested for modern populations with high paternity confidence, or at least substantially lower than the median worldwide extra-pair paternity rate of 9% (Anderson 2006). Such EPP rates detected in humans are insufficient to trigger significant biases in heritability estimates (Charmantier & Reale 2005).

2.1.1. The Family of Sursill

The Family of Sursill is a large database containing approximately 200,000 individuals (Kojonen 1971; Genealogia Sursilliana CD-2000 database, I. B. Voipio, personal communication). The starting person of this family tree lived in 15th century Sweden while the subsequent generations inhabited various parishes in Finland. This database includes more Finnish clerks and other officials who were mainly Swedish speaking in 18th and 19th centuries, than would be expected by random chance.

To achieve an analysable representative random sample, I chose a birth cohort from 1745 to 1765 from four parishes (Oulu, Kokkola, Kaarlela and Kuusamo) with the largest numbers of individuals present in the database. The data-set includes 194 base individuals, and all of their descendants to great-grandchildren level, as well as the spouses of all married individuals. Complete individual life-histories (birth, death, and all reproductive events) were recorded for three generations, resulting in a total of 1894 individuals. This data was used in works (I, II, III). Studies on vertebrates recording reproductive performance of recognisable individuals over the whole lifespan are rare (Clutton-Brock 1988) and data sets allowing assessment of reproductive success and its components over generations in a given maternal or paternal line are even more exceptional, often involving geographically very isolated populations (e.g. collared flycatchers of Gotland (Merilä & Sheldon 2000); red deer of Isle of Rum (Kruuk et al. 2000), soay sheep of St Kilda (Clutton-Brock 1996)).

2.1.2. Parish-record data on five populations of Finns

The second data set used in this thesis is a large (n=15,000 people), individual-based data set collected using the historical church records. The data set covers the full life-history of three complete generations of pre-industrial Finns living in two ecologically different areas (archipelago vs. inland areas) between 1720 and 1900. In inland areas, agriculture was the major source of livelihood, while in archipelago fishing provided an important resource (Heervä & Joutsamo 1983). This data set is also multigenerational, and allows following each maternal line up to the grand-offspring level. These demographic data have been combined with information on wealth and social class of each family, with reasons of death, and with data on annual local population size and structure, sex-specific intra- and inter-parish migration, as well as fertility and mortality rates. Inland populations often lived under food-restricted conditions and famines were common throughout the study period (Jutikkala & Kaukiainen 1980), whereas the seasonal variation in food conditions and mortality was lower in south-west Finland. I also classified individuals according to their socio-economic status. Because there was no direct knowledge of the actual wealth of the families, such as taxes paid or farm size, available to me, and since women in our study period rarely had an occupation of their own, I used a husband's occupation as a reference to wealth and social status of women. I divided individuals into three wealth classes; rich, middle-class, and poor. The rich class included noblemen, priests and free farmers, the middle-class included mainly tenant farmers and craftsmen, while the poor included servants and dependent lodgers. This categorisation was based on the historical studies of Finnish populations (Hiltunen et al. 1996, Saari et al. 2000). This data was used in works IV and V.

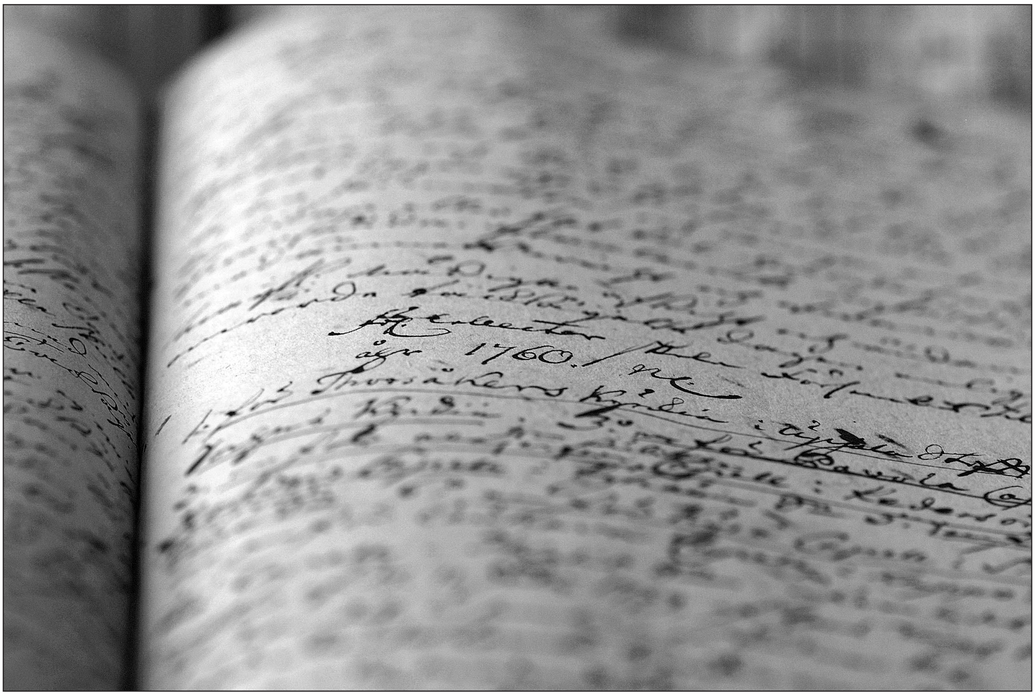

Figure 1. Old church books were written by old Swedish handwriting, and the data collection from them was conducted by genealogists. Photo by Esko Pettay.

2.2. Studied life-history traits

Certain central life-history traits reappear in works included in this thesis. The following list describes them and their importance in terms of fitness and thus evolution. In this thesis the main fitness measure was lifetime reproductive success.

(i) Lifetime reproductive success was measured as the total number of children produced in a lifetime that survived to adolescence, here to an age of fifteen years. Lifetime reproductive success was used as fitness measure in works I, III, IV and V.

(*ii*) *Individual lambda* λ (calculated after McGraw & Caswell 1996), is an age-dependent measure of lifetime reproductive success, which considers at the same time both the timing of reproduction and the number of children raised to adulthood (age 15). LRS and λ may rank individuals differently according to their fitness, since (with λ) children produced at early ages contribute more to the fitness than children produced at later ages. Rate sensitive λ allows for more accurate estimation of individual fitness in humans, even though overall lifetime reproductive success explains more than 90% of variation in λ (Käär & Jokela 1998). Individual lambda was used as a fitness measure in work I.

(iii) Fecundity is the number of children produced in a lifetime, irrespective of their survival.

(iv) Age at first reproduction is the age in years when a woman gave birth to her first child or a man fathered his first child.

(v) Mean inter-birth interval is the average time in months between successive births.

(vi) Offspring survival. Survival percentage of children born that survived to adulthood (lifetime reproductive success/fecundity).

(vii) *Age at last reproduction* was defined as the age in years when a woman gave birth to her last child.

(viii) Adult longevity is the age in years at death of individuals that survived past fifteen years of age.

(iv) Number of grandchildren is the number of grand offspring 'born' to an individual.

2.3. Data Analysis

I used many statistical methods to test predictions using the data available. To make scientifically valid conclusions from correlative data (without the possibility to conduct experiments) is challenging. Here I describe briefly the statistical methods used in the works of this thesis, more detailed information is offered in the methods of works of this thesis and in the references cited.

2.3.1. Pedigree analysis

In humans, estimating heritability is problematic, because cultural transmission makes it difficult to distinguish between genetic and non-genetic similarity between close relatives such as parents and offspring. In this thesis I adopt an "animal model" approach, which is a method adopted from animal breeders, and helps to overcome, at least partly, problems associated with traditional regression between relatives to estimate heritability for human life-history traits. Animal model takes into account all relationships in the pedigree, and because more distant relatives are less likely to share the same environment, this helps to overcome the problem of shared environment. In works I and II, variance components and heritability values for life-history traits were estimated using a multivariate restricted maximum likelihood mixed model procedure (REML). An Animal Model was fitted, in which, for a given trait, the phenotype of each individual was broken down into its components of additive genetic value and other random and fixed effects (Lynch & Walsh 1998; Kruuk 2004). The total phenotypic variance (V_P) was parted as: $V_P = V_A + V_M + V_R$, with V_A, additive genetic variance; V_M, maternal effect variance, and V_R, residual variance. Variance components were constrained to positive values, resulting in a narrow sense heritability ($h^2 = V_A/V_P$) varying between 0 and 1.

2.3.2. Survival analysis

In works III, IV, and V Cox-regression was used to analyse individual age specific survival probabilities (Allison 1995, Collett 2003). Cox-regression is well suited for analysing data in the form of time from a well defined time origin (birth) until the occurrence of some particular event or end-point (death) (Collett 2003). Survival data have two features that are difficult to handle with conventional statistical methods: censoring and time-dependent covariates (Allison 1995). In our data censoring refers to a case where the death date of a person is not known, but we know for example age at last reproduction, so that we know that person was a live at a particular time. Some covariates can change during lifespan and be time-dependent, which means that effect can differ during lifespan/follow-up period (Allison 1995).

2.3.3. Measuring fitness and natural selection

The use of multivariate statistics, which allow one to control for the many potential confounding influences is essential when studying the life-history evolution of humans, given that an experimental approach is not possible. Generalised linear mixed models (McCulloch & Searle 2001) were used in works III and IV. This method allows fitting fixed effects (e.g. study parish and birth cohort) and random effects (e.g. family line or mother identity), which helps to taking into account possible confounding factors.

Because selection acts simultaneously on several life-history traits, and both positive and negative (i.e., trade-offs) correlations between the traits may exist, it is crucial to consider selection on several life-history traits simultaneously (Lande & Arnold 1983). I thus take an advantage of path analysis to model and estimate the strength of natural selection on complex female life history in work V (Scheiner at al. 2000, Hatcher 1994, Tomer & Pugesek 2003). The estimated selection differential is the sum of direct and indirect selection on a trait relating to fitness. Direct selection on a trait is estimated by its direct effect and effects through intermediate steps on fitness, whereas indirect selection on a focal trait is estimated by its effects via correlations with other traits related to fitness in the model (Scheiner at al. 2000).

2.3.4. General comments on long-term fitness

Arguably, one of the most reflective fitness measures available is the number of great-grandchildren produced. Using data collected from the *Sursill,* it is also possible to investigate factors that affect probability for an individual (who have reproduced him/herself) to have descendants at the F_3 level (great grandchildren), and also to have a hint of the distribution of F_3 descendants. Of the 87 individuals in the parental generation (born 1745-1765), who had at least one child in their lifetime, 66 had at least one great grandchild, while 21 “family lines” out of 87 went extinct. This distribution is interesting; less than ten percent of parental individuals contributed almost half (45%) of the F_3 generation, and the greatest number of great grandchildren for one person was 231. While these numbers are probably underestimates, because of failures to follow-up of all individuals, they do suggest that people are descendants of a relatively small number of individuals, while many individuals fail to have long-term fitness. An analysis with generalized linear mixed model shows that lifetime reproductive success explains significantly the probability of having F_3 offspring at all ($\chi^2=11.62$, $P=0.0007$), with a 4% increase in the probability of having F_3 offspring with each additional child raised to adulthood. This suggests that lifetime reproductive success is a reliable measure of actual fitness.

3. RESULTS AND DISCUSSION

3.1. Variation in traits caused by genetic factors

Most studies of human life-history evolution are based on phenotypic selection without knowledge of the underlying genetic variation. In order to show that selection can lead to an evolutionary change the trait has to have a genetic basis. In work (I) I show that most female life-history traits were heritable (fitness, fecundity, age at last reproduction, mean inter-birth intervals and longevity), and that maternal and/or family effects were important for the starting age of reproduction. In males, lifespan was found to be the only life-history trait with significant heritability. The most plausible explanation for this difference between the sexes is that in monogamous society reproduction is under physiological control of the female (e.g. pregnancy, lactation), and therefore we might not expect to see a correlation between reproductive traits among male relatives. The results found in females are in accordance with previous findings on heritability estimates for these traits. For example a twin study on contemporary Australian women suggests that heritability for menopause is 0.44, while I found heritability for age at last reproduction to be close to that value (0.42). Also, my estimate for heritability of adult lifespan (~0.17) was only a little lower than estimates provided by twin studies ranging from 0.20 to 0.30 (Finzh & Tanzi 1997, Herskind et al. 1996, Hjelmborg et al. 2006). A slightly lower estimate for adult lifespan can be due to a different estimation method, or a more stochastic environment experienced by historical Finns compared to more contemporary populations.

As in all studies of heritability of human life-history traits, or behavioural traits, the possibility of cultural transmission have to be taken into account. Even though animal model is less prone to inflation of heritability estimates due to shared environment than the traditional parent-offspring regression approach, I cannot claim that using animal model would remove effects of cultural transmission entirely, since effects can be cross-generational. However, in a case that heritability estimates would be affected by cultural transmission we would expect the effect to be present in both sexes. In this study, females showed surprisingly strong heritability in almost all studied traits and men did not, which is suggesting that inflation due to cultural transmission is probably not severe. Animal model also assumes that the base population has not been subject of selection, but this cannot be true in any natural population.

This study (I) is the first that investigates heritability of many human life-history traits simultaneously and to compare female and male values. I demonstrate that most female life-history traits had considerable amounts of heritable genetic variation. This suggests that selection on phenotypic values had the potential to lead to an evolutionary change in historical Finnish women, and possibly in other populations as well.

3.2. Variation in traits caused by age

In work II, my aim was to investigate the quantitative genetic composition of female fecundity in more detail by exploring variation in heritability estimates with the age of the individuals. Consequently, I split fecundity into early and late age fecundity (i.e., the numbers of children produced before and after, respectively, the mean and median reproductive age of 31) and estimated the magnitude of heritability and maternal effects for both traits separately. My results suggest that for early life fecundity, family effects were significant, while heritability was not. For late age fecundity the opposite was true. Selection may deplete additive genetic variation of traits that are closely associated with fitness (Falconer and Mackay 1996), which could explain the lack of heritability in early age fecundity. In addition, a more relaxed selection in later age would lead to the accumulation of deleterious mutations resulting in an increase of additive genetic variation (Medawar 1952). The result of this work is interesting, since contrary to many other animals, women have high survival also in late ages, and selection for later age reproductive events is high, for example in historical Sami women (Helle et al. 2005). This study confirms that early and late life reproductive events can have differing potential to evolve under natural selection.

3.3. Variation in traits caused by inbreeding depression

Inbreeding depression can affect reproductive success especially in small populations. Because Finland is a geographically large country, and the population density was historically low, people used to marry within populations of a few hundreds of people; often the spouse was found in an individual's own natal village (Nevanlinna 1973). Also founder effects were strong in areas where settlers migrated (Norio 2000). Since in small breeding units, individuals often have a common ancestor, so that offspring can inherit recessive genes from both of their parents. These effects have been seen as endemic recessive genetic diseases (Norio 2000). I showed negative effects of local mating on female, but not male, fitness in work III. Females of locally married parents had lower fitness than females of non-locally married parents. Lower fitness was due to high offspring mortality of females of locally married parents, who themselves married also locally. Why were females, but not males, negatively affected by local mating? One possibility is lower maternal qualities of inbred women. Maternal qualities are believed to be among the most sensitive characters to inbreeding depression (Falconer & Mackay 1996). For example, Richardson et al. (2004) found lower offspring survival of less heterozygous mothers in Seychelles warblers, and in humans, Ober et al. (1999) found reduced fertility among more inbred Hutterite women, suggesting the presence of recessive alleles that have negative effects either at conception or peri-implantation. As show by my study, local mating in small populations may have complex outcomes where inbreeding history, gender and importance of maternal effects on focal traits may all have important effects on offspring fitness.

3.4. Variation caused by pre-natal conditions

Pre-natal conditions can have an impact on an individual's development, reproduction and survival. One aspect of the pre-natal environment is the sex-hormones (testosterones and oestrogens) to which developing young are exposed. Work IV shows that females who had a male co-twin had reduced lifetime reproductive success compared to females with a female co-twin. This effect arose because a female that had a male co-twin had both reduced probability of marrying and reduced fecundity compared to females born with female co-twin. Moreover, these results show that as a consequence of these effects, mothers who produced opposite-sex twins had fewer grandchildren (and hence lower evolutionary fitness) than mothers who produced same-sex twins. These results provide the first evidence that sex-ratio adjustment itself influences offspring fitness due to sex-specific interactions between offspring pre-birth, and have significant implications for understanding the nature of sex ratios in mammals. Selection might be favouring same-sex twin pairs over male-female pairs (Uller et al. 2006). In other words, natural selection would favour variance of sex-ratios rather than its mean. Furthermore, this study suggests that fitness of average twin would be ~13% less than average singleton due to purely male-co twin effect. This effect together with the lower survival of twins in general (Guo & Grummer-Strawn 1993, Lummaa et al. 2001) show trade-off between quantity and quality of offspring in humans, and might explain the rarity of twinning in humans in general.

3.5. Variation caused by post-natal environmental conditions

Resources are one of the most important environmental factors affecting survival, growth and reproduction of individual organisms (Roff 2002). However, we do not fully understand how variation in resources within populations can affect the strength of natural selection. I discovered clear evidence in work V that the environmental conditions, and in particular wealth available to individuals, have considerable effects on life-history traits, trade-offs between the traits, as well as on the strength of natural selection on the traits. I found that mothers of wealthier classes had better survival throughout their lifespan, they had their first child earlier, had more children whose survival was better, and they had more grandchildren in the end compared to poorer mothers. In poor women, natural selection was stronger on earlier age at first reproduction than for age at last reproduction, whereas in wealthier women age at last reproduction was the more important. This is in accordance with life-history theory that predicts that in iteroparous organisms an increase in extrinsic mortality selects for optimal life history that shifts towards earlier reproduction and higher reproductive effort (Cichoń 2001). Divergent evolution of wealth classes was not possible, since only 60% of daughters had the same wealth class as their mothers, and gene flow between wealth classes was high. Nevertheless, this work demonstrates that resource availability can potentially cause variation in the strength of natural selection, and thus can potentially affect the maintenance of variation in life-history traits.

3.6. Phenotypic and genetic correlations between life-history traits

Since many life-history traits are correlated, relationships between traits are important for understanding total selection on a trait of interest (Lande & Arnold 1983). In work V, I constructed hierarchical path models to analyse interactions between studied life-history traits. I found, for example, that late age at first reproduction has a negative effect on fecundity, while late age at last reproduction has a positive effect on fecundity. Because these two traits are positively correlated, selection on one trait will also affect the other trait. In other words, selection on one trait can be neutralized by selection on the other trait. So far we know this only at the phenotypic level. To understand genetic constraints, analysis of genetic correlations is necessary. In work I, I found a positive genetic correlation between age at first reproduction and lifespan and between mean inter-birth interval and lifespan, which suggests antagonistic pleiotropy between early reproduction and longevity, since women who started reproduction earlier had shorter lifespan. However, age at first reproduction did not have a significant amount of additive genetic variation, which might affect the importance of a negative correlation between age at first reproduction and lifespan. However, this result and the genetic correlation between birth-intervals and adult lifespan suggests possible genetic constraints between reproduction and longevity, which is in accordance with antagonistic pleiotropy theory that suggests that reproduction is negatively correlated with longevity. Furthermore, we might not even expect negative genetic correlations between life-history traits; because of the standing genetic variance in condition, caused by high mutational input, we might actually expect positive genetic correlations between traits (Houle 1991). Even though my results might give some indication of genetic correlations between human life-history traits, more studies from different populations and larger datasets are needed to make any strong conclusions about genetic correlations between human life-history traits.

4. CONCLUSIONS AND FUTURE PROSPECTS

Finnish church-book records have proven to be a useful source of human life-history data (e.g. Käär et al. 1996; Helle et al. 2005, Lahdenperä et al. 2004; Lummaa 2007). One of the main advantages of these data is that we can measure lifetime reproductive success, which is a close measure of long term fitness (see methods). In most studies in the field of human evolutionary biology, and especially in evolutionary psychology, the connection between the trait of interest and fitness is unclear. For example, the key word "evolutionary psychology" gives 820 hits in Web of Science, and the most popular area within the field is human mate choice. Yet, practically none of these studies has been able to investigate whether and how the studied preferences (e.g. for smaller waist-to-hip size, more symmetrical or masculine/feminine face, or certain body odour) actually translates into the increased reproductive success, even if these traits are assumed to be signs of good genes or body condition. Moreover, most fitness-related traits are involved in complex networks with possible negative and positive underlying correlations between the traits, and selection on the traits may also operate indirectly, as illustrated by work V of the thesis. Finally, such networks may be further complicated by negative and positive genetic correlations between the traits (I) and varying levels of heritability expressed in the traits according to sex (I) and age (II), making simple conclusions on character evolution based on single traits of limited value.

In this thesis, one of my primary aims was to investigate the heritability of key human life-history traits. This has been very important, since many studies have shown phenotypic selection on human life-history traits (e.g. Käär et al. 1996, Helle et al 2005, Lahdenperä et al. 2004), but they have had very little information on the heritable basis of these traits. In this thesis, I have shown that life-history traits, especially expressed in females, have heritable genetic variation (I), and that the amount of variation that is heritable can vary during an individual's lifespan (II). These results suggest that human life-history traits have the potential to evolve in the face of selection during recent centuries. This thesis provides more information on the potential of human life history traits to evolve, and represents an important step in uniting phenotypic selection and genetic response to selection when investigating human life-history evolution. However, to connect selection and heritable variation in order to estimate the potential for microevolution, we should also take into account how environmental variation can affect natural selection. Environmental variation can affect both the selection pressure and the amount of heritable variation in a given trait. For example, Wilson et al. (2006) discovered that while harsh environmental conditions were associated with strong selection for increased birth weight in wild sheep, harsh environmental conditions were also associated with low genetic variance. In contrast, good environments were associated with relaxed selection and higher genetic variance. This kind of mismatch between the strength of selection and heritable genetic variation can possibly explain why traits do not necessary express expected responses to selection (Wilson et al. 2006). For example, in these historical populations, wealth affects the strength of selection (V), but it is possible that the amount of heritable variation can also vary between the wealth classes. Estimating selection in different wealth classes is possible, but estimating genetic variation requires large datasets, and is one of the questions to be studied more in the future. Moreover, not only current, but also the early, developmental environmental conditions can create variation between individuals, as shown in work IV where I demonstrated that female twins, who had a male as co-twin have reduced reproductive success, most likely due to exposure to testosterone *in utero*. This can have effects on optimal maternal sex-ratios, as mothers who produced opposite-sex twins had significantly fewer grandchildren than mothers who produced same-sex twins.

While phenotypic interactions between traits can be studied, more information of the underlying genetic correlations is needed. Unfortunately, estimating genetic correlations between traits needs very large data sets, which are hard to obtain (Falconer & Mackay 1996). However, results from work (I) suggests that a negative genetic correlation between reproduction and longevity might exists in women.

In modern human populations, industrialisation and the resulting demographic transition offers an interesting turning point for evolution of human life-history traits. In humans, a rapid change in direction/strength of selection on life-history traits might have happened recently. Natural selection might have favoured certain personality types over others, since psychological factors, such as willingness to mother/father a child might be more important in terms of reproductive success today than before industrialisation, because of effective family planning. Furthermore, research on how economic uncertainty relates to reproductive decision making can be related to evolution of life-history traits in variable environmental conditions. Research on human life-history evolution can help to understand variation in human survival, reproduction and longevity in historical as well as contemporary populations.

5. ACKNOWLEDGEMENTS

First of all, I want to thank my supervisors: Dr. Virpi “täti” Lummaa, who has been the perfect supervisor for a PhD student; giving support and advice when needed while providing the freedom to develop personal ideas. I’m grateful for my other supervisor Professor Jukka Jokela for his wide knowledge on evolution and for all the help he has offered during these (long) years. I also want to thank Dr. Samuli Helle, who I persuaded to be my supervisor in the middle of writing this thesis, since he was present in Turku and shared an office with me; he was the one who had to answer my countless questions about statistics and evolution.

I want to acknowledge co-authors for all their help with manuscripts: Dr. Andrew Russell who has helped with the English language in the introduction and in the manuscripts of this thesis, and for his endless supply for ideas, Dr. Loeske Kruuk for offering a Marie Curie Training site in Edinburgh and teaching me quantitative genetics, and Dr. Anne Charmantier for teaching me to use the ASReml-program in Oxford. I want to thank Dr. Alistair Wilson for random regression analyses.

I have been privileged to be part of such an enthusiastic and brilliant research group. Mirkka Lahdenperä has shared the lonely PhD- student status in the University of Turku, and she has helped to collect the Sursill data, and helped me with our discussions countless times. I also owe thanks to Charlotte Faurie, Ian Richard and Duncan Gillespie for contributing help with language and developing ideas with our discussions. Our meetings have always been fruitful scientifically, but they have always been also great fun.

I want to thank all the people working in the Section of Ecology, especially Professors Erkki Korpimäki and Kai Norrdahl, Niina Kukko and Matti Ketola for all the help with practical arrangements. All the PhD-students have contributed in the scientific atmosphere in the section. Special thanks also go to Tapio van Ooik, Johanna Toivonen, Harri Vehviläinen, and Susanna Saari for being opponents in practise defences and giving valuable comments on the manuscripts. I would not have survived without my friends in the university during writing this thesis; Mirkka, Päivi, Outi, Riitta, Nanne, Liisa, Tapio, Roosa and others were irreplacable company at lunch- and coffee-time, as well as outside the campus. Thank you all!

I want to acknowledge Iikko B. Voipio for providing the Sursill genealogical database for scientific use, and genealogists Aino Siitonen, Kimmo Pokkinen and Timo Verho for collecting the Finnish demographic data, and Niina Anttila for spending many days on tracking the occupations of people from the database. Also, I want to thank Professor

Erik Svensson and Doctor Eesa Koskela for reviewing this thesis, their comments helped me to make last improvements to the introduction. The Academy of Finland, Finnish Cultural Foundation, Marie Curie Fellowship and Suomalainen Konkordia-liitto have given financial support to conduct this thesis.

I’m grateful to my parents for supporting my choice to study biology. My warmest gratitude goes to Esko, who has offered continuous support, help, and love, and Ossi and Anna for existing.

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