Summary Report on *Evolutionary Approaches to Disease and Health*

The fifth of six seminars in the ESRC Seminar Series
Darwin's Medicine: Evolutionary Psychology and its Applications

19th March 2010, Darwin Room, Brunel University

Report prepared by Gillian Pepper, Brunel University

'Evolutionary Approaches to Disease and Health' is the only seminar of the series to focus on evolutionary medicine. Though the title of the series, "Darwin's Medicine", is similar to the term "Darwinian Medicine", it was intended as a metaphor for the possible applications of Darwinian theory for the benefit of society. This particular seminar however, was focused specifically on how Darwinian thinking can enhance medical knowledge (Darwinian Medicine).

The seminar brought together a group of international experts on evolutionary medicine to share their ideas about how Darwinian theory can help to improve medical theory, practice and education. It enabled communication between academics, medical professionals, policy makers and others with an interest in evolutionary approaches to health and disease. Talks covered a broad range of medical topics, from infectious disease to depression and schizophrenia.

Opening remarks were given by Dr Michael Price, Co-Director of the Centre for Culture and Evolutionary Psychology at Brunel University, who led the organisation of the seminar. He set the scene by highlighting the applied value of the presentations for the day. Dr Price also emphasised the diversity of the audience, which he hoped would bring about innovative interdisciplinary collaborations.

1st Speaker – Professor Martin Brüne

This talk focused on how an evolutionary perspective can enhance understanding of schizophrenia and the benefits of using a symptom-based approach. Prof. Brüne outlined the "evolutionary paradox" of the existence of schizophrenia – that patients are at a reproductive disadvantage versus the general population. He highlighted that schizophrenia is ubiquitous, occurring across cultures at a rate of about 1%.

Prof. Brüne outlined hypotheses regarding possible compensatory advantages for people who are heterozygous for genes that otherwise cause vulnerability to schizophrenia. Advantages proposed by researchers include superior creative abilities, charisma and leadership capabilities and reduced susceptibility to cancer.

Prof. Brüne went on to summarise the genetic approaches to investigating schizophrenia and highlighted the fact that the search for genes with major effect sizes has, so far, been unsuccessful. He suggested that this may be due to the diversity of schizophrenia phenotypes, which are currently poorly defined. He highlighted the danger of the "1% dogma" and suggested that there is more subtle variation in schizophrenia phenotypes than is currently acknowledged. He argued that instead of viewing this complex phenotype as a single disease, examining individual symptoms or symptom constellations is more useful, and that evolutionary thinking can be useful in guiding the generation of testable hypotheses.

Prof. Brüne suggested an approach that draws on the "social brain" hypothesis - that humans have evolved mechanisms that process social stimuli in a way which maximised individual inclusive fitness in the evolutionary past – e.g. Theory of Mind. From this perspective, Prof. Brüne described Schizophrenia symptoms as a "set of complex and contextually inappropriate defence mechanisms" - extreme versions of traits that increased inclusive fitness in the ancestral context, but become maladaptive if expressed outside normal variation. He gave examples including persecutory delusions and impaired perspective-taking. He also went on to describe how the density of von economo neurons in the human brain relates to the development of social cognition, how this differs in schizophrenia patients, and the possible diagnostic applications of these findings.

Discussion topics following the talk included;

- the continuum between childhood development and adult schizophrenia, and the need for further investigation in this area;
- the possible cross-cultural variation in reporting of schizophrenia due to differences in the tolerance of symptoms by different cultures.

Online information:

http://www.ruhr-uni-bochum.de/igsn/research/details/bruene.html

Key reference:

M. Abdel-Hamid, C. Lehmkämper, C. Sonntag, G. Juckel, I. Daum, M. Brüne (2009)
Theory of mind in schizophrenia: The role of clinical symptomatology and neurocognition in understanding other people's thoughts and intentions
Psychiatry Research, Volume 165, Issue 1, Pages 19-26

2nd speaker -Professor Rick Maizels

This talk focused on host-parasite co-evolution, with a particular focus on helminth parasites and the human immune response. Prof. Maizels gave an introduction to the vertebrate immune system and how it has co-evolved in close and constant association with infectious organisms. He described how helminth parasites occupy a predominantly extracellular niche in the gut and vasculature tissues of their hosts. Helminths can infect people for many years, without untoward effects, and are present in a large proportion of the world's population. This prevalence is possible due to the helminths' ability to suppress immune reactivity – an effect that has already been harnessed by companies which offer live helminths to treat autoimmune disease and allergy (though Prof. Maizels was keen to highlight the risks of using helminths as a treatment).

Though in the ancestral past, most individuals would have carried helminth parasites for most of their lives, improved sanitation and housing over the last century has seen the effective elimination of these infections from many developed countries. The socio-economic changes that have led to the elimination of these parasites are mirrored by an increase in autoimmune diseases and allergies. Prof. Maizels explained that our immune system, tuned to optimal fitness in the presence of parasites, may overcompensate in their absence. This idea is the basis of the "Hygiene Hypothesis."

Prof. Maizels presented evidence from developing countries where helminths remain prevalent, and from animal models. This evidence supports the idea that helminths minimise their host's immune response by promoting immune regulation. Prof. Maizels concluded however, that different helminth species, and varying intensities of infection, exert very different pressures on the host immune system. As a result there is no optimal gene type in defence against parasites. Helminth infections may therefore have promoted immune polymorphism, rather than genetic fixation, resulting in alleles which produce susceptibility to autoimmunity and allergy. This, he argued, could be the downside to an otherwise beneficial host-parasite co-evolutionary process.

Discussion topics included;

- the risks of treating autoimmune conditions with live parasites and the risks of reactivity;
- the possible implications for cancer prevention;

- the potential effect of intentional helminth infection on the ability to resist bacterial pathogens;
- and the impact of helminth infection on the efficacy of vaccinations.
- The conclusion was that more investigation is needed in all of these areas.

Online information:

http://maizelsgroup.biology.ed.ac.uk/

Key reference:

Hewitson, J.P., Grainger, J.R. and Maizels, R.M. (2009) Helminth immunoregulation – the role of parasite secreted proteins in modulating host immunity. *Molecular and Biochemical Parasitology* **167** : 1-11

3rd speaker – Professor Gillian Bentley

This talk gave an evolutionary perspective on reproductive pathologies. Prof. Bentley explained the idea that certain pathologies occur as a result of a "mismatch" between our current and evolutionary environments, and that this principle can be extended to the study of developmental environments. In other words, mismatches can occur between the environment experienced during growth and that encountered later in life. She outlined the concepts of 'foetal programming' and the 'thrifty phenotype' in the context of Life History Theory. She explained how different developmental environments can contribute to phenotypic variability. She outlined that environmental mismatches may be the cause of metabolic disorders such as obesity, type 2 diabetes and a range of reproductive disorders.

Prof. Bentley presented the results of a study on immigrant Bangladeshi women in the UK and the impact of their developmental environment on their reproductive profiles. The study found that Bangladeshi women who were raised in Bangladesh had lower salivary progesterone levels as adults than those who moved to the UK before 8 years of age. Ovulation rates were also lower in Bangladeshi women raised in Bangladesh than in those raised in the UK. Prof. Bentley proposed that this could be a result of differences in the pathogenic environments (since the women migrating to the UK from Bangladesh were mostly from affluent families, the findings are unlikely to be due to differences in nutritional status).

Prof. Bentley summarised the clinical implications of her work, including those for breast cancer risk and ovarian reserve. She also emphasised how public health messages and health education could be shaped by her findings.

Discussion topics included;

- the fact that low birth weight seems to be preserved in second generation Bangladeshi women in the UK - the possible link in genetics and epigenetics;

- what the implications of the cross-cultural variation of hormone profiles might be for the suitability of some oral contraceptives;
- the possible impacts that nutritional status might have on menstruation;
- how these findings are being adopted clinically and what knowledge transfer lessons can be learned and applied for evolutionary biology as a whole

Online information:

http://www.dur.ac.uk/anthropology/research/projects/project_details/?mode=project&id=339

Key reference:

Nunez-de la Mora, Alejandra. & Bentley, Gillian R. 2008. Early life effects on reproductive function. In *New Perspectives on Evolutionary Medicine*. Trevathan, W., Smith, E.O. & McKenna, J.J. Oxford.: Oxford University Press. 149-168.

4th Speaker - Dr William Hanage

This talk focused on the evolution of infectious disease.

Dr Hanage highlighted the changing causes of mortality in the 20th Century and the importance of co-evolutionary arms races between parasites and their hosts. He focused on the ability of bacteria and viruses to 'import evolutionary innovation' (e.g. drug resistance) in the form of genes from distantly related organisms via horizontal gene transfer. He highlighted the implications of this process for antibiotic resistance.

Dr Hanage then went on to outline an evolutionary perspective on the relationship between set-point viral load in HIV-1 and infectiousness. He proposed that the virus has adapted to ensure maximum potential for transmission during an asymptomatic period. He stressed the importance of understanding how selection pressures for increased virulence or transmission could unwittingly be created and highlighted the need for more research into such issues.

Discussion topics included;

- whether HIV infection results in behaviour changes that increase the likelihood of transmission;
- the need to gather data on co-infection;
- homogeneity effects
- the necessity for increased research focus on the evolution of infectious disease – particularly to guide public health policies that might otherwise unwittingly create selection pressures for enhanced transmission or evolution toward virulence

Online information:

http://www1.imperial.ac.uk/medicine/people/w.hanage/publications/

Key reference:

Fraser C; Hollingsworth D; Chapman D; de Wolf F; Hanage WP. (2007). Variation in HIV-1 set-point viral load: Epidemiological analysis and an evolutionary hypothesis. *Proc Natl Acad Sci USA*

5th Speaker - Professor Paul Gilbert

This talk introduced an evolutionary approach to depression, focussing on the role of social rank and compassion.

Prof. Gilbert introduced questions about the adaptive value of depression. He described it as 'increased threat detection coupled with a lowering of affect,' which he proposed might have functioned to minimise risk of harm and conserve resources in ancestral threat situations. He outlined a 'defeat model', the principle of 'attachment loss' and the links between shame and depression. He linked low rank (social defeat) to depression and submissiveness.

Prof. Gilbert recognised that depression-like behaviours are seen throughout the animal kingdom, but postulated that humans are more susceptible to depression because they have a capacity for self-awareness and reflection, which can lead to self-criticism (he likened this to people 'stimulating their own threat systems.') Prof. Gilbert then demonstrated that by teaching people to recognise their self-criticising behaviour, therapies can be directed towards activating 'anti-depressant mechanisms' linked to experiences of social affiliation and compassion. That is, people can learn to reflect inwardly with self-compassion rather than self-criticism.

Discussion topics included;

- whether depression could be categorised as an extreme or 'malignant' sadness;
- whether 'Skinnerian medicine' could contribute something to the picture and if there should be a focus on why/how affiliation has become so important;
- sex differences in depression and the importance of kin networks in defending against post-natal depression;
- potential investigation into the link with Theory of Mind and whether autistic and Aspergers syndrome sufferers are less susceptible to depression;
- the implications of the evolutionary approach for bipolar disorder

Online information:

http://www.derby.ac.uk/mhru/publications

Key reference:

Gilbert, P. (in press) Evolved minds and compassion focused imagery in depression. In: L. Stropa (eds). Imagery and the Threatened Self: Perspectives on Mental Imagery in Cognitive Therapy. London: Routledge

6th Speaker – Professor Mervyn Singer

This talk covered evolved responses to survive critical illness and 'the maladaptive forces of modern medicine.'

Prof. Singer introduced the concept of the mismatch between recovery from trauma in ancestral environments, and that in the modern developed world. He emphasised the degree to which the natural recovery process can be disrupted by use of sedatives, artificial feeding, antibiotics and anti-inflammatory drugs.

Prof Singer emphasised that advances in technology, medicine and nutrition mean we may maintain an artificial and unnatural existence for patients during periods of critical illness that may last weeks, if not months. Though this saves some lives, he proposed that attempts to modify physiological and biochemical variables to 'normal' values may, in fact, be deleterious. He also proposed that many therapies are probably counter-adaptive. He gave the example of catecholamines, which are used to increase blood pressure in shock states. He claims that catecholamines act as an additional external stressor to an already intrinsically stressed body, and are possibly harmful or counterproductive. If this is true, it may be that patients survive in spite of, rather than because of, some medical interventions.

Prof. Singer concluded by emphasising the need to reappraise approaches to treating critical illness and the need for greater awareness of how to intervene in line with natural adaptive processes.

Discussion topics included;

- the possibility of investigating whether outcomes are better in 'nicer' intensive care units (i.e. those with fewer external stressors);
- weaknesses of medical models that do not incorporate biopyschosocial ones;
- what knowledge there is about trauma survival without medical interventions;
- the medico-legal implications of the potential harmful nature of interventions;
- the medico-legal implications of not intervening;
- the potential of the 'permissive approach';
- the ethical question as to whether intensive care units should be in the business of 'prolonging death';

Online information:

http://www.ucl.ac.uk/slms/people/show.php?personid=12289

Key reference:

Singer et al (2004) Multiorgan failure is an adaptive, endocrine-mediated, metabolic response to overwhelming systemic inflammation. The Lancet, Volume 364, Issue 9433, Pages 545 – 548

Keynote speaker - Professor Randolph Nesse M.D.

This talk gave a broad perspective on the contributions that evolutionary biology can make to medicine.

Prof. Nesse argued that 'medicine without evolution is like engineering without physics.' Though he admitted that millions of doctors practice medicine every day without understanding evolutionary biology, he stressed that learning evolutionary biology would make physicians more effective, and more satisfied with their work. He made the distinction between proximate and ultimate explanations of disease, noting that the latter is much neglected by medicine.

Prof. Nesse demonstrated the value of understanding that natural selection shapes vulnerability to disease, not disease itself. He outlined six key points:

Selection is slow;

1. There are mismatches created by evolutionary lag
2. We are in competitions with organisms that are evolving more rapidly

Selection is constrained;

3. Trade-offs…
4. …and historical constraints mean organisms are flawed and vulnerable

Misunderstanding;

5. Organisms are selected for reproductive success – not for health and happiness
6. Defences and pain signals are selected for - not health and happiness

Prof. Nesse went on to outline other cases where an evolutionary biological approach can inform medicine, including the understanding generated by evidence from host-pathogen coevolution (see speakers 2 and 4).

Prof. Nesse's key message was that while evolution offers some direct applications in medicine, its power lies in explaining why things are as they are (as physics does for engineering). He proposed that investing in evolutionary education for physicians pay off in three ways:

1. Researchers who already use some evolution find greater power as they have opportunities to learn the details; infectious disease and genetics offer good examples.
2. New answers come from asking new evolutionary questions about why the body is the way it is; studies of gout, bilirubin, sex differences in mortality and depression are good examples.
3. It is more accurate to replace the outmoded metaphor of the body as a machine with a more biological model of the body as a bundle of tradeoffs shaped by natural selection to maximize Darwinian fitness.

Discussion topics included;

- whether researchers can learn more by examining healthy people and what makes them healthy, than by fixating on sick people and what makes them sick (the salutogenic model);
- the implications of the mismatch hypothesis – is it more important to focus on the interaction between genes and environment than to search for genes 'for' a disease? Will defining syndromes more tightly reveal genetic associations?
- genetic susceptibility to addiction and whether it is a by-product of something adaptive

Online information:

http://www-personal.umich.edu/~nesse/

Key reference:

Nesse et al. (2009) Making evolutionary biology a basic science for medicine. PNAS 107: 1800-1807

Panel Discussion

The panel discussion focused on ways to 'strengthen the bridge' between medicine and evolutionary biology.

There were suggestions that rather than push evolutionary biology as a subject into undergraduate medical curricula, it should be possible to integrate evolutionary perspectives into existing courses where they have something specific to offer. For example, it is important to have a good understanding of the evolution of antibiotic resistance, to prevent the introduction of well-meaning, but ineffective attempts to prevent its build-up. Case studies about this (and other key applications) could be

inserted into existing curricula to demonstrate the importance of evolutionary theory and generate deeper understanding.

Delegates thought that rather than attempt to influence a culture change in the medical field, evolutionary biologists could simply encourage medics to ask different questions about the evolution of infectious agents and of susceptibility to disease. It was noted that medics are often interested in evolutionary biology, but are hampered by an incomplete understanding of fundamental principles – leading to confusion. It was acknowledged that evolutionary biologists need to support medics by correcting misunderstandings and offering useful guidance.

Discussants suggested scientists working for pharmaceutical companies might act as part of the 'bridge' between medicine and evolutionary biology, since they are likely to have had training which includes evolutionary biology. It was suggested that further work is needed to engage with this audience.

The hurdle of political ideals and 'bad PR' for the evolutionary sciences was discussed. It was acknowledged that popular press about evolutionary biology – and in particular evolutionary psychology, often focused on the 'darker side' of human nature. People from outside the evolutionary field also tend to commit a naturalistic fallacy (to assume that what is natural is good/desirable) when interpreting evolutionary science's findings. This can lead to negative 'gut' reactions about the science itself (including assumptions that the science is politicised in some way). Political objections to evolutionary sciences then hamper attempts to communicate its important findings in a neutral and objective way. It was proposed that a greater effort might be made to emphasise evolutionary psychological findings about the positive and prosocial side of human nature. However, it was cautioned that to do this could be to risk the neutrality of the science and that a simpler solution would be to take steps to ensure that interpretations do not fall foul of the naturalistic fallacy.

Key reference:

Stearns et al. (2010) Evolutionary perspectives in health and medicine. *PNAS* 107; Suppl 1: 1691-1695