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EDITORIAL

Neural parasitology: how parasites manipulate host behaviour

The ability of parasites to alter the behaviour of their hosts fascinates both scientists and non-scientists alike. One reason that this topic resonates with so many is that it touches on core philosophical issues such as the existence of free will. If the mind is merely a machine, then it can be controlled by any entity that understands the code and has access to the machinery.

This special issue of *The Journal of Experimental Biology* highlights some of the best-understood examples of parasite-induced changes in host brain and behaviour, encompassing both invertebrate and vertebrate hosts and micro- and macro-parasites. The observation that parasitic infection can modify specific host behaviours is an old one (see Moore, 2002). The general consensus has been that these parasites have evolved the ability to manipulate host behaviour in order to advance their own reproductive success (Moore, 2002). Unfortunately, there has been a lack of information on two key points of this hypothesis. Firstly, it has proved difficult to unequivocally demonstrate that changes in host behaviour benefit the parasite (i.e. enhance parasitic fitness). Secondly, the mechanisms that parasites use to change host behaviour were completely unknown for many years, particularly in the case of vertebrate host systems.

Undoubtedly, the design and interpretation of investigations in this field is hampered by our inadequate understanding of the physiological basis of 'normal' host behaviour, even when uninfected, making the identification of possible parasitic mechanisms difficult. Furthermore, distinguishing between parasitic and host effects on host behaviour is not straightforward. For example, infected animals, including humans, can exhibit a range of so-called general 'sickness' behaviours (Dantzer, 2001). These may reflect key adaptive responses of the host immune infection in an effort to combat or at least minimize the impact of infections. Under certain conditions, the same behavioural alterations observed may, however, be directly mediated or manipulated by the parasite itself to enhance transmission (Adamo, 2012). Furthermore, parasites may utilize the same or similar mechanistic routes to achieve their effect, thereby exacerbating the difficulties of distinguishing between the two. Finally, many cases of parasitic manipulation occur in host–parasite systems in which the host is not a typical model for behavioural neuroscience research. Work in these systems is therefore hindered by a lack of background information and species-specific neuroethological techniques and measurements. In other systems, even where information about the host is available, the experimental host may be exposed to unnaturally high parasite doses and/or unnatural laboratory-constrained research conditions. Such studies are thus often unrepresentative for monitoring the types of traits that may be under selection in the wild. Dealing with these methodological issues is a major focus of this special issue.

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There has, nevertheless, been a leap in our understanding of parasitic manipulation over the past few years. Part of the advance has been due to recent developments in neuroscience and molecular technologies, and this special issue highlights these successes. However, it also demonstrates the need for a multi-disciplinary integration of studies concerning the molecular, biochemical and physiological aspects of infection with studies on the evolutionary, ecological and behavioural functions of host behavioural change.

How parasites manipulate their hosts is not an arcane topic, fascinating merely because it inspires the macabre (e.g. Schlozman, 2011). There are practical reasons for understanding how they exert their effects. Parasites are ubiquitous – and many have a predilection for the 'immunologically privileged' site of the central nervous system because it shelters them from the full fury of the host's immune system (Galea et al., 2007). However, this location also provides a parasite with direct 'access to the machinery' to alter host behaviour. Classic examples include the protozoan *Toxoplasma gondii*, where parasite-induced changes in the behaviour of its rodent intermediate host appear to enhance transmission to the feline definitive host (Webster, 2007). What *T. gondii* does to manipulate its rodent host is highly germane, as it appears to be doing the same thing in human brains. Papers in this issue present evidence that *T. gondii* also alters human behaviour and may be involved in the etiology of serious mental disorders such as schizophrenia. The latter also highlights the utility of studying natural host–parasite manipulations as potential avenues for further research into animal models of specific human affective disorder symptoms. Unfortunately, however, the public health significance of such parasitic infections on the pathogenesis, prognosis, treatment and outcome of human disease, especially perhaps those of the brain and 'mind', is still underappreciated.

Parasites also provide a unique window into the functioning of the uninfected brain. Neurobiologists tend to manipulate a subject's behaviour using approaches that target specific neural areas and/or specific neurotransmitter systems. Parasites use other, often multiple, mechanisms, far 'sloppier' in their neuroanatomical targets but still capable of precise behavioural control. Such multiple routes likely reflect that we are dealing with selection and evolution rather than 'intelligent design'. Nevertheless, the multifaceted approach of parasites illustrates novel methods for altering brain and behaviour. Exploring these mechanisms will uncover previously unknown principles of neural control.

Thus, the research discussed in this special issue opens new opportunities for further research. One successful outcome of *The Journal of Experimental Biology* symposium (hosted by The Company of Biologists) that generated this special issue is the determination of many of the participants to carry out research that synthesizes information and approaches from multiple levels of analysis. We hope that this issue will help stimulate and foster further multi-disciplinary research and collaboration.

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Guest Editors

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