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NEUROSCIENCE & BIOBEHAVIORAL REVIEWS

Special Issue
Translational Neuroscience & Mental Disorders
Bridging the gap between animal models and the human condition

Guest Editors
John Rodgers
Caroline Blanchard
Stefano Parmigiani
and
Paul Brain

Editor-in-Chief
Giovanni Laviola

Special Issue

Dedicated to the memory of Bob Blanchard (1937-2013)

Translational Neuroscience & Mental Disorders

Bridging the gap between animal models and the human condition

A Joint Workshop of the International School of Ethology (Director: Stefano Parmigiani) and International School of Neuroscience (Director: Pier Ferrari)

Ettore Majorana Foundation & Centre for Scientifc Culture
(Director: Antonio Zichichi)

Erice, Sicily
November 4-9 2016

Guest Edited by

John Rodgers
University of Leeds, U.K.
Caroline Blanchard
University of Hawaii, U.S.A.
Stefano Parmigiani
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GUEST EDITORIAL

Neuroscience and Biobehavioral Reviews: Special issue on Translational Neuroscience & Mental Disorders – bridging the gap between animal models and the human condition

The world of behavioural neuroscience was deeply saddened by the loss in November 2013 of one of its main players, Bob Blanchard. In response, a number of formal events were planned to commemorate Bob's contributions to our understanding of brain and behaviour. One of these was a plenary symposium (organised by Brandon Pearson and Cliff Summers) at the 2015 Annual Meeting of the International Behavioral Neuroscience Society (IBNS) in Victoria BC while another was a dedicated issue of the journal Physiology & Behavior (Volume 146, 2015) guest-edited by Jaap Koolhaas and Sitse de Boer. A third event, longer in the planning, was initiated by Stefano Parmigiani (University of Parma) who, early in 2014, contacted Caroline Blanchard (University of Hawaii), John Rodgers (University of Leeds) and Paul Brain (Swansea University) with the idea of honouring Bob's contributions to behavioural neuroscience by arranging an international workshop on translational neuroscience and mental disorder. It was further proposed that the workshop be held under the joint auspices of the International Schools of Ethology and Neuroscience at the Ettore Majorana Foundation and Centre for Scientific Culture (EMFCSC) in Erice, Sicily. The four of us worked together closely in developing a programme that would not only reflect Bob's strongly held beliefs in the bidirectional relationship between preclinical and clinical research but also significant recent progress across a range of neuropsychiatric disorders. We are deeply indebted to Antonio Zichichi (President, EMFCSC) for including the workshop as part of the 2016 programme of activities. The meeting eventually took place November 4-9 2016, and attracted a capacity number of registrations that included a high proportion of young scientists.

This special issue of Neuroscience and Biobehavioral Reviews comprises contributions from all main speakers at the Erice workshop. The collection commences with a personal appreciation by Paul Brain who worked closely with Bob on the organisation of several major conferences and publication of their proceedings. For ease of reference, reviews on closely related themes have been grouped together. Bob McArthur's broad-ranging and insightful analysis of issues surrounding translational neuroscience in neuropsychiatric drug development nicely sets the scene for what is to come. And, given Bob Blanchard's main research interests, it is no coincidence that the first group of reviews relate to advances in our understanding of defense, aggression and their clinical significance (Blanchard, Volchan, Motta et al, Patel et al, Eilam, and Haller). Another sub-discipline that has received considerable research attention in recent times is social neuroscience. Here, Johnson and Young consider the role/s of oxytocin and vasopressin systems in diverse social behaviours while Meyza and Blanchard

present a current view on the BTBR mouse model of idiopathic autism. Ferrari and colleagues then outline their proposal for a novel rehabilitative intervention based on the mirror neuron system in Moebius Syndrome patients after 'smile surgery', following which a series of reviews consider the role of stress in: Tourette Syndrome (Godar & Bortolato), sex differences in neurobehavioral disorders (Palanza & Parmigiani), depression-cardiovascular comorbidity (Carnevali et al), and overeating and obesity (Razzoli et al). Mechanisms of appetite regulation are also the focus of the contribution from Rodgers who, in reviewing polypharmacy for weight control, deplores the continuing lack of attention to behavioural analysis in preclinical drug development. The penultimate review by Cerniglia et al addresses internet addiction in adolescence from neurobiological, psychosocial and clinical perspectives, while the final intriguing analysis by Brian Dias examines recent research suggesting that acquired risk factors for psychopathology can be transmitted through non-genomic, epigenetic mechanisms to subsequent generations.

We are convinced that readers will be just as excited by the contents of this special issue as were delegates with the corresponding presentations at the Erice Workshop. Such excitement will hopefully translate into the motivation to take further forward many of the new research ideas and findings documented in the following pages. Finally, as the Special Issue would not have existed without them, sincere thanks go to all our contributors, and to a host of hard-working independent referees, as well as the Editor-in-Chief of the journal (Gianni Laviola) and support staff at Elsevier (Saranya, Maha and Clement).

John Rodgers
Caroline Blanchard
Stefano Parmigiani
Paul Brain
November 2016

Preface

Bob Blanchard: A Neurobiological Legacy and Appreciation

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We are all fully aware of whose life we are celebrating at this memorial conference in Sicily. I will not dwell too much on Bob's early academic career in Boston and at the University of Iowa (it is well-documented elsewhere) but will 'cut to the chase' to detail his importance to the people gathered here.

Bob Blanchard (along with his wife and research side-kick, Caroline) was an innovative and enthusiastic researcher, working across the behavioural sciences, neurobiology and psychopharmacology. The thing about Bob was that he could always find something meaningful to do even under the most unpromising of circumstances. Much of his research was directed to the wild rat (*Rattus norvegicus)* a beast that shows a much more impressive range of agonistic behaviour than domesticated strains, but he did study attack and defence in other animal species, including the odd bear.

Bob arrived at the University of Hawaii in 1964 where he and Caroline set up laboratories that generated impressive numbers of diverse publications over the decades, often utilising cutting edge technologies. Possibly as a result of their relative geographical isolation, Bob and Caroline developed a habit of roaming the globe in search of ideas and people with similar obsessions. The result of one such trip, in 1972, led to the setting up of the International Society for Research on Aggression (ISRA) in a room of the Prince hotel in Tokyo by a small group of scholars at the 20th International Congress of Psychology meeting. The idea was to gather scientists, from Anthropology to Zoology, who had an interest in the factors (biological, social and situation) that influenced conflict-related activities. This proved to be an excellent vehicle for cross-disciplinary studies on aggression as well as the exchange of ideas (it seems to have clarified some of the issues surrounding this important concept). Bob was active as an early secretary of ISRA and was President of the organisation from 1992-1994. ISRA's adoption of *Aggressive Behavior* as its 'house publication' also helped to establish that journal as a viable outlet for high quality research.

I and the other guys of the editorial panel for this volume, started to get to know Bob and Caroline at a NATO conference on 'The Biology of Aggression' (Brain and Benton, 1981). We subsequently all (at various times) visited the Blanchards in Hawaii before creating an Americano (Bob and Caroline) - Anglo (me and John Rodgers) - Italo (Stefano Parmigiani) axis, sharing research ideas, expertise and contributing to each other's book publications (e.g. Blanchard and Blanchard, 1984; Brain et al 1989a;b; Haug et al, 1991; Rodgers and Cooper, 1987; vom Saal and Parmigiani, 1994).

The axis (Bob being a powerful advocate) recognised the specific strengths and weaknesses of the two currently existing broad approaches (Psychology and Ethology) to behavioural sciences. They viewed this as particularly important if people were to attempt to use animal 'models' to evaluate potential treatments for human neuroses and psychoses. They needed to find behavioural expressions in laboratory animals that were clearly comparable to phenomena in our own species. Experimental

animal psychology is characterised by (if carried out properly) having good experimental control of variables but is weaker when one attempts to determine the utility of the responses to the animal (the ultimate utility question). Animals are generally placed in situations (e.g. mazes, Skinner boxes etc) where the animal has very limited options (sometimes not reflecting the organism's sensory capacities or its normal *modus operandi*). Conversely. Ethology (traditionally conducted in the 'field') generally has poor experimental control of variables (we often know little about the animal being studied including its earlier experiences- although this is changing with some sophisticated use of attached monitoring devices) but the survival value of behaviours (if they reliably occur in most members of a species) is intrinsic (otherwise, the activities would have been eliminated by natural selection).

Bob was a strong advocate of putting Animal Psychology and Ethology together to maximise the strengths and minimise the weaknesses. He suggested that an 'ethoexperimental' approach could be created by:-

a) Providing more 'naturalistic' situations for animals in the laboratory (such as his Visible Burrow System for wild and domesticated rats). To some extent, this even anticipated a fashion for providing 'environmental enrichment' for captive animals in zoos to improve their ranges of expressed behaviour as well as providing pointers for more humane housing of laboratory animals (Brain, 1992).

b) Moving some psychological paradigms (e.g. Skinner box equivalents) into the field where one could 'ask animals questions' under more realistic circumstances.

Bob's advocacy led to some members of the informal axis organising a NATO-funded conference in Italy that generated the volume, published in 1989 'Ethoexperimental Approaches to the Study of Behavior' edited by Bob, myself, Caroline Blanchard and Stefano Parmigiani. The approach proved truly innovative and produced (in some quarters) major changes in how the activities of laboratory animals are viewed and their relevance as 'models' of human conditions.

It is, perhaps worth commenting that prior to developing this focus, the humble laboratory rat had often been housed in conditions where it could not burrow (the wild rat is an inveterate digger of tunnel systems) as was often posed questions reliant on its sense of vision (being a largely nocturnal animal, it is much more dependent on its olfactory and touch senses). Add to that the fact that laboratory rats had been selected over decades for their ease of handling by humans, and one had difficult to interpret situations. The new focus in both rats and mice was much more on situations comparable to their normal existence and items we could clearly identify as threats to their existence.

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