



Swansea University  
Prifysgol Abertawe



## Cronfa - Swansea University Open Access Repository

---

This is an author produced version of a paper published in :  
*Journal of Insect Physiology*

Cronfa URL for this paper:  
<http://cronfa.swan.ac.uk/Record/cronfa31200>

---

### Paper:

Azambuja, P., Garcia, E., Waniek, P., Vieira, C., Figueiredo, M., Gonzalez, M., Mello, C., Castro, D. & Ratcliffe, N. (2016). *Rhodnius prolixus*: from physiology by Wiggleworth to recent studies of immune system modulation by *Trypanosoma cruzi* and *Trypanosoma rangeli*.. *Journal of Insect Physiology*  
<http://dx.doi.org/10.1016/j.jinsphys.2016.11.006>

---

This article is brought to you by Swansea University. Any person downloading material is agreeing to abide by the terms of the repository licence. Authors are personally responsible for adhering to publisher restrictions or conditions. When uploading content they are required to comply with their publisher agreement and the SHERPA RoMEO database to judge whether or not it is copyright safe to add this version of the paper to this repository.  
<http://www.swansea.ac.uk/iss/researchsupport/cronfa-support/>

## Accepted Manuscript

Title: Translational Neuroscience and Mental Disorders—bridging the gap between animal models and the human condition

Author: John Rodgers



PII: S0149-7634(16)30605-4  
DOI: <http://dx.doi.org/doi:10.1016/j.neubiorev.2016.10.001>  
Reference: NBR 2619

To appear in:

Author: Caroline Blanchard

PII: S0149-7634(16)30605-4  
DOI: <http://dx.doi.org/doi:10.1016/j.neubiorev.2016.10.001>  
Reference: NBR 2619

To appear in:

Author: Stefano Parmigiani

PII: S0149-7634(16)30605-4  
DOI: <http://dx.doi.org/doi:10.1016/j.neubiorev.2016.10.001>  
Reference: NBR 2619

To appear in:

Author: Paul Brain

PII: S0149-7634(16)30605-4  
DOI: <http://dx.doi.org/doi:10.1016/j.neubiorev.2016.10.001>  
Reference: NBR 2619

To appear in:

Received date: 3-10-2016

Please cite this article as: Brain, Paul, Translational Neuroscience and Mental Disorders—bridging the gap between animal models and the human condition. *Neuroscience and Biobehavioral Reviews*

<http://dx.doi.org/10.1016/j.neubiorev.2016.10.001>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

ACCEPTED MANUSCRIPT

# 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

ACCEPTED MANUSCRIPT

**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 Scientific 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**  
*University of Parma, Italy*  
and  
**Paul Brain**  
*University of Swansea, U.K.*

*CONTENTS*

**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

**GUEST EDITORIAL**

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

RODGERS, R.J., D.C. BLANCHARD, S. PARMIGIANI and P.F. BRAIN

**PREFACE**

**Bob Blanchard: a neurobiological legacy and appreciation**

BRAIN, P.F.

**REVIEWS**

**Aligning physiology with psychology: translational neuroscience in neuropsychiatric drug discovery**

McARTHUR, R.A.

**Translating dynamic defense patterns from rodents to people**

BLANCHARD, D.C.

**Defensive immobility reactions in humans: a contribution for dimensional trans-diagnostic approach to PTSD**

VOLCHAN, E., ROCHA-REGO, V., BASTOS, A.F., OLIVEIRA, J.M., FRANKLIN, C., GLEISER, S., BERGER, W., SOUZA, G.G.L., OLIVEIRA, L., DAVID, I.A., ERTHAL, F.S., PEREIRA, M.G. and I. FIGUEIRA

**The periaqueductal gray and primal emotional processing critical to influence complex defensive responses, fear learning and reward seeking**

MOTTA, S.C., A.P. CAROBREZ and N.S. CANTERAS

**Translational approach to the pathophysiology of panic disorder: focus on serotonin and endogenous opioids**

GRAEFF, F.G.

**The endocannabinoid system as a target for novel anxiolytic drugs**

PATEL, S., M.N. HILL, J.F. CHEER, C.T. WOTJAK and A. HOLMES

**Obsessive Compulsive Disorder (OCD): from animal models to human patients**

EILAM, D.

**Studies into abnormal aggression in humans and rodents: methodological and translational aspects**

HALLER, J.

**Oxytocin and vasopressin systems modulate distributed neural networks and contribute to diversity in social behaviors from evolutionary and translational perspectives**

JOHNSON, Z.V. and L.J. YOUNG

**The BTBR mouse model of idiopathic autism – current view on mechanisms**

MEYZA, K. and D.C. BLANCHARD

**A proposal for new rehabilitative intervention on Moebius Syndrome patients after ‘smile surgery’. Proof of concept based on mirror neuron system properties and hand-mouth synergistic activity**

FERRARI, P.F., A. BARBOT, B. BIANCHI, G.GAROFALO, N. BRUNO, G. COUDE, C. BERTOLINI, M. ARDIZZI and E. De STEFANI

**What makes us tic? Translational approaches to study the role of stress in Tourette Syndrome**

GODAR, S.C. and M. BORTOLATO

**How does sex matter? Behaviour, stress and neurobehavioural disorders**

PALANZA, P. and S. PARMIGIANI

**Rodent models of depression-cardiovascular comorbidity: bridging the known to the new**

CARNEVALI, L., R. STATELLO and A. SGOIFO

**Stress, overeating and obesity: insights from human studies and preclinical models**

RAZZOLI, M., C. PEARSON, S. CROW and A. BARTOLOMUCCI

**Bench to bedside in appetite research: lost in translation?**

RODGERS, R.J.

**Internet addiction in adolescence: neurobiological, psychosocial and clinical issues.**

CERNIGLIA, L., ZORATTO, F., CIMINO, S., LAVIOLA, G., AMMANITI, M. and W. ADRIANI

**Inter-generational influences of ancestral environments on the biology of descendent generations**

DIAS, B.G.

**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



## ACCEPTED MANUSCRIPT

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, deplors 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

ACCEPTED MANUSCRIPT

**Preface**

Bob Blanchard: A Neurobiological Legacy and Appreciation

Paul, F. Brain,  
College of Science,  
Swansea University,  
Swansea, SA2 8PP,  
United Kingdom

Email: [p.f.brain@swansea.ac.uk](mailto:p.f.brain@swansea.ac.uk)

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 20<sup>th</sup> 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 difficulty 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.

## REFERENCES

Blanchard, R.J., Blanchard, D.C., 1984. Eds Advances in the Study of Aggression Volume 1, Academic Press, New York.

Blanchard, R.J., Brain, P.F., Blanchard, D.C., Parmigiani, S. 1989. Eds Ethoexperimental Approaches to the Study of Behavior, Kluwer Academic Publishers, Dordrecht.

Brain, P.F., 1992. Understanding the behaviours of feral species may facilitate design of optimal living conditions for common laboratory rodents. *Animal Technology* 43, 99-105.

Brain, P.F., Benton, D., 1981. Eds The Biology of Aggression, Sijthoff- Noordhoff, Alphen aan den Rijn, The Netherlands.

Brain, P.F., Mainardi, D., Parmigiani, S., 1989a. Eds House Mouse Aggression: A Model for Understanding the Evolution of Social Behaviour, Harwood Academic Publishers gmbh, Chur, Switzerland.

Brain, P.F., Parmigiani, S., Blanchard, R.J., Mainardi, M., 1989b. Eds Fear and Defence, Harwood Academic Publishers gmbh, Chur, Switzerland.

Haug, M., Benton, D., Brain, P.F., Olivier, B., Mos, J., 1991. Eds. The Aggressive Female, CIP-Gegevens Koninklijke Bibliotheek, Den Haag.

Rodgers, R.J., Cooper, S.J., 1987. Eds Endorphins, Opiates and Behavioural Processes, John Wiley and Sons Ltd., London.

vom Saal, F.S., Parmigiani, S., 1994. Eds Infanticide and Parental Care, Harwood Academic Publishers gmbh, Chur, Switzerland.