**THE NON-HUMAN PERSPECTIVE ON THE NEUROBIOLOGY OF TEMPERAMENT, PERSONALITY, AND PSYCHOPATHOLOGY: WHAT’S NEXT?**

Neil McNaughton

Department of Psychology and Brain Health Research Centre

University of Otago, Dunedin, New Zealand

Philip J. Corr

Department of Psychology

City, University of London, UK

**ORCID ID:** NMcN = 0000-0003-4348-8221  
In *Neurobiology of temperament, personality and psychopathology: What's next?*

(ed) Irina Trofimov and Alan Pickering

Special Issue of *Current Opinion in Behavioral Sciences*

Words: 3,271 [excluding abstract and references; including figure legends]

References: 67 [5 annotated] Figures: 2 [4 max]

Correspondence to:

Professor Neil McNaughton

Department of Psychology

University of Otago

PO Box 56

Dunedin 9054

New Zealand

Phone: 64 3 479 7634

Fax: 64 3 479 8335

E-mail: neil.mcnaughton@ otago.ac.nz

# Abstract

Fundamental neurobiological processes are usually evolutionarily conserved. Even with the availability of modern imaging techniques, neurobiological fundamentals of mental constructs are most easily studied in animals and less obscured by cognitive elaboration and social complexity. There is a move to seeing psychopathology as an extreme position in a multidimensional trait spectrum. Even zebrafish provide useful models of psychopathology, so it is a small step to seeing animals in general, and laboratory rodents in particular, as useful models of non-pathological trait processes. Animal breeding, pharmacology, and neural models of states provide a basis for understanding traits in all animals, including humans – particularly if we view traits as *relatively* unchanging sensitivities of neural systems that generate myriad momentary states, matching density state-trait distributions in human personality psychology. Gaps in past animal work on states do need to be filled in the future; but, crucially, all work with homologies needs both neural and behavioural translational checks. We see a major development in “What’s next?” as the recent combination of virtual world models (most obviously so far with virtual predators) with fMRI and scalp EEG brain recordings in humans. Albeit virtual, coarse, and superficial, this combination (especially with the addition of drugs) can provide strong tests of neurobiological models of states and traits originally derived from animal work. Once fully translated, such human work can, in turn, raise questions that require further animal work to answer. We see the future as needing both more animal work and more, synergistic, translational human work if we are to uncover the neurobiology of personality, its role in psychopathology, and its evolution. [264 words]

Keywords:

Highlights

* Non-human work linking personality and psychopathology is sparse
* Cross-species comparison can clarify the neural basis of states, traits, and symptoms
* Non-humans can also model autism, schizotypy, attention deficit, and stress-resilience
* Selective breeding has separated multiple defensive traits with hormone variation
* Human fMRI with virtual predators confirms homology of non-human neuropsychology

# Introduction

Our main goal in discussing “What’s Next?” for a non-human (and particularly rodent) perspective on personality is to convince the scientific community that there is a need for one. Given acceptance of this perspective, in principle, its importance for neurobiology (both mechanistic and, by definition, phylogenetic) and psychopathology follows. Currently non-human work on personality structure, often in primates, tends to borrow from, more than inform, systems such as the Big Five [1-3]. Conversely, trait-linked psychopathology-oriented work, often in rats, occurs in silos that have little impact on general personality research and little connection with each other [but see 4,5 for recent primate exceptions]. We believe this separation is a grave failing.

People are often reluctant to see their mirror in other animals. They share the supposed Victorian response to a lecture on Darwin, “Descended from the apes! My dear, we will hope it is not true. But if it is, let us pray that it may not become generally known.” [[1]](#footnote-1) We will not repeat here our arguments for phylogenetic continuity of the biology of cognition and emotion [6]. Our key conclusion was that analysing non-human behaviour is preferable to human behaviour and, particularly, to human verbal behaviour. We, thus, agree with Darwin that non-human behaviour is “less likely to deceive us” [7]. That said, care must always be taken when attempting translation between species; especially from some single highly standardized model [8] in a healthy mouse to a clinical trial in disordered humans [9].

Many would accept that non-human neurobiology is useful for understanding cognitive and emotional processes. But even they may not accept non-linguistic animals as useful for understanding traits reflected in scales derived from essentially lexical analysis. Two points should be noted here.

First, use of a questionnaire scale does not entail that what is measured is merely lexical. Veridical verbal report can be an immediate, cheap, and easy record of long-term consistencies in patterns of behaviour (and so of the processes that gave rise to the patterns and their consistency). Observer reports of behaviour in non-humans show that “The latent trait model of personality that was developed by differential psychologists is a good model for describing primate personality” [10, p. 4]. Thus, primate and other “animal personality research does not break from trait theories of personality. Instead, it enriches trait theories by conceiving of traits as not belonging to a species, but as expressed, with some modifications, across species” [1, p. 12]. Consistent *patterns* define the trait of interest (which may underlie scores on a range of different scales), which will arise from “causal processes in the functioning of personality and treatment of psychopathology” [11, Figure 3, p 132].

Second, the *consistency* of personality, [i.e., patterns of Affect, Behaviour, Cognition, and Desire: ABCD; 12], will often vary among individuals depending on the settings of simply modulatory systems that are phylogenetically old, highly conserved, and fundamental to psychopathology [13]. Analysis of simpler animals should make the causal [13] and adaptive [2,14] nature of traits clearer; with the human case often reflecting superficial phylogenetically-late rostral additions to a common fundamental caudal control system. That is, phylogeny generally adds more selective sensory filters and more extensive goal-subgoal scaffolding to trait systems with structures that have highly conserved adaptive functions.

We provide below brief examples of ways animal work can impact on our understanding of personality traits in general, their neurobiology, and the links of both to psychopathology. We assume (see also Figure 2) a hierarchy of traits and a partially matching trait-like hierarchy for psychopathology [11,15-17] where assessment of disorder can often be viewed as assessing traits [18].

We believe non-human work across a range of species can provide a clear picture of: 1) the neural organisation of state systems that express both trait characters and psychopathological symptoms; 2) the pharmacological nature of conserved neuromodulatory and hormonal systems that exert trait-like control of behaviour; and, 3) of the evolution of traits as exemplified by breeding and genetic modification and as assessed by comparative observation [2,14].

Finally, since all species differ in how they express conserved systems, we look at novel translational work, focussed on human defensive traits, that uses virtual predators and imaging to test models based on non-human neuropsychology. Such comparative work determines phylogenetic homologies, and so indicates functions, while nonetheless directly testing their applicability to the human species normally tested by personality psychologists. In this regard, non-human work allows a complete personality neuroscience to rival any of the other applications of neuroscience within psychology.

Our overview focuses on traits linked to defensive behaviour. There is a substantial body of work on defensive systems, their phylogeny, effects of breeding, and human homology. Defence provides clear parallels between non-humans and humans; and between normal variation and psychopathology at its extremes. The intersection of personality and psychopathology (particularly with fear and anxiety) may seem to limit us to only more primitive aspects of states and traits, and exclude more "human" ones. But our approach can be extended to all aspects of human states and traits, if we make similar allowances for variation in surface elaboration as we must among other species.

There is a range of other less-developed areas where the same approach can be taken in principle. For example [for review see 19], maternal immune activation not only results in autism and schizophrenia in humans but (particularly in interaction with genetic risk factors) can be used to generate animal models of these disorders and so, potentially, of human traits such as schizotypy [20]. As with trait measures in humans, challenge tests can be used to separate animals into high and low scoring groups[[2]](#footnote-2); showing, for example, that with stress-resilient versus stress-susceptible females and males susceptibility and gender interact in determining both baseline and stress-related brain rhythm changes across different structures [21]. Likewise, fish can provide useful models not only of anxiety and fear but also of autism spectrum, attention deficit, and serotonin-related stress disorders [22-24].



Figure 1. Repulsion, inhibition, and attraction systems in the brain [from 13, based on 25]. Hierarchical organisation results in moment-to-moment state changes that depend on “motivational distance” (resulting from the interaction of specific outcome value with general trait sensitivity. Panic proneness as a facet could depend on the sensitivity of the PAG to its specific inputs, trait anxiety could depend on endogenous benzodiazepine control of the inhibition system, and metatrait stability could depend on control of all three systems by serotonin [26] with other monoamines or hormones providing sources of additional traits. Abbreviations: OFC = orbital frontal cortex; PAG = periaqueductal grey.

# Main text of review

## Understanding State Control

Traits are consistencies in *patterns* of ABCD through time. Events, memories, and imagination elicit moment-to-moment state changes. The resultant ABCD will vary depending both on the current input to the relevant neural systems and the long-term sensitivities of the systems to that input. Understanding state control will, therefore, be important whether we view traits as density distributions of states [27,28] or more mechanistically as long-term settings of modulatory control systems that account for state distributions [13]. So, the neurobiology of traits rests on a foundation of the neural control of states – about which non-human work provides considerable information. This is particularly clear for the conserved “survival circuits” [29] that provide the basis for the most basic motivation-related traits, which are particularly important for psychopathology.

The Reinforcement Sensitivity Theory (RST) of Personality [see 30], in particular, has an explicit origin in the integration of a mass of non-human with human data [31]. Recent developments of the neuropsychology of RST [25,32] include a detailed symmetrical neurology (Figure 1). Importantly, this picture of normal behavioural control and so normal trait variation, even with the most phylogenetically old elements, also accounts for key details of psychopathology [33].

## Understanding trait control

Traits, having high or low values across individuals, simplify ABCD variation within a population. They involve systems where both high and low reactivity will have adaptive benefits and costs and so there will be “balancing selection (where selection itself maintains genetic variation)” [34, p. 554].

But how is this variation controlled? Selection of animals for particular behavioural characters shows how personality traits can evolve; and also provides an interesting guide as to the way superficially unrelated characters may be combined during such selection.

While laboratory rats may not be good models for the entire range of human behavior, the hormonal basis of emotional behavior has many homologies [and use of] experimental subjects with contrasting differences in endocrine function and behavior is a powerful experimental tool.

[35, p. 370]

Let us look at some examples. The classic silver fox experiment, selecting only for a single tameness (prosocial-toward-humans) score, found decreased stress hormones and increased serotonin; but it also obtained dog-like features such as floppy ears, curly tails, and juvenile body forms [for review, see 36] – and even a decrease in tooth size [37]. Likewise, the Maudsley Reactive/Non-Reactive rat strains were obtained by selection on a single simple character (defecation in response to open field stress) but differ on such a wide range of related responses that they have been taken as a model of emotionality or neuroticism. Unlike the foxes, they differ in their prolactin, but not pituitary-adrenal (e.g. corticosterone), responses to stressors and so are not a complete model of general stress reactivity [35]. A third pattern is seen in “rats bred for low [locomotor] response to novelty [who] exhibit high levels of inhibition, anxiety-related behaviors, passive stress coping, and anhedonia compared to high novelty responding rats that vigorously explore novel environments, exhibit greater impulsivity, aggression, and risk-taking” [38, p. 2]. The high responders have *higher* stress-induced corticosterone but *reduced* hippocampal glucocorticoid receptor expression and a higher tendency to self-administer corticosterone. Interestingly, they also show reduced epigenetic effects of stressful manipulations on their offspring.

The common story, here, is that some very simple, situation-specific, character may be used as the basis for selection but the strains then separate on deeper underlying (often hormonal) control factors. Hormonal (corticosterone), neurohormonal (benzodiazepine), and neuromodulatory (serotonin) factors have widespread action across the brain and so changes in their response affects systems as a whole (as well as physical morphology in the fox case), not just individual behaviours. Critically for translation to humans, these hormones and their fundamental effects will be highly conserved even if detailed superficial expression varies across species [13,24,35].

The potential for linkage of this approach with state theory is shown by a recent attempt to generate a model of a form of trait anxiety linked to generalized anxiety disorder (GAD). So-called ‘contextual’ fear conditioning (in contrast with conditioning to a simple stimulus) produces freezing behaviour that is sensitive to anxiolytic drugs. This contextual conditioning has been used as a basis for *bi-directional* selection of the Carioca high (CHF) and low (CLF) freezing strains of rat, with differences appearing after only 3 generations. Importantly, the differences generalise to “several behavioral tests, including the elevated plus maze (EPM), the social interaction test and defensive responses that are induced by electrical stimulation of the dorsal periaqueductal gray” [39, p. 2].

Critically for its GAD equivalence, CHF/CLF show normal cued fear conditioning [40] and normal depression in the forced swim test [41]. Also [42], conditioning itself was not the key aspect of selection: the CHF showed high and the CLF showed low anxiety-related responses, relative to unselected control (CTL), in an ethological test; where CLF but not CHF rats, also showed a reduced benzodiazepine anxiolytic response compared to CTL. CHF also react more strongly to chronic unpredictable mild stress [43].

Interestingly, CHF rats consume more alcohol (with females even more than males) and less saccharine than CLF and CTL – results that “support the hypothesis that there is a positive relationship between anxiety and alcohol intake, and provide further evidence for the use of CHF rats as a model of GAD” [44, p. 1]. The use of bidirectional selection is interesting at the neural level (see Figure 1) since CHF brain activation by contextual cues was high in the locus coeruleus, periventricular nucleus of the hypothalamus (PVN), and lateral portion of the septal area and low … in the medial portion of the septal area, dentate gyrus, and prelimbic cortex (PL) compared to CTL animals. [Whereas,] CLF rats exhibited a decrease … in the PVN, PL, and basolateral nucleus of the amygdala and increase in the cingulate and perirhinal cortices compared to CTL animals. [So, CHF and CLF had] opposing influences on the PVN, the main structure involved in regulating the hypothalamic–pituitary–adrenal neuroendocrine responses observed in anxiety disorders.

[45, p. 1].

These activity patterns could have resulted from differences in 5-HT2A expression [39] but could have been bidirectionally distinct. Bidirectional selection for high and low anxiety-related-behaviour in the elevated + maze, for example, produces increased periaqueductal grey and decreased superior colliculus activity, respectively, relative to normal mice; and distinct maladaptive changes in defence reactions [46].

The choice of a simple, well-understood, task (and control tests) is important with such learning-based breeding experiments, if simple understandable traits are to be studied. The Roman high- (RHA) and low- (RLA) avoidance rats were subjected to bidirectional selection for speed of acquisition of a 2-way avoidance task. While anxiolytic drugs produce a superficially paradoxical improvement in 2-way avoidance learning (due to a selective effect on passive but not active avoidance), behaviour in the task will also clearly depend on a range of other factors (including the capacity for 1-way avoidance). Unsurprisingly, therefore, RHA differ from RLA on many traits: proactive coping; sensation/novelty seeking; innate preference for natural and drug rewards; and high impulsivity.

High levels of impulsivity are associated with several neuropsychiatric conditions including attention-deficit hyperactivity disorder, obsessive compulsive disorder, schizophrenia, and drug addiction. [So,] RHA rats [may] represent a valid genetic model, with face, construct, and predictive validity, to investigate the neural underpinnings of behavioral disinhibition, novelty seeking, impulsivity, vulnerability to drug addiction as well as deficits in attentional processes, cognitive impairments and other schizophrenia-relevant traits.

[47, p.1]

The Roman rat model shows clear and interesting trait results of breeding for a simple learning score but, unlike the simpler Carioca rat model, poses the question as to what is the nature and number of the traits that have been selected for. They are clearly not specific to 2-way avoidance (and anxiolytic action) as such and extend beyond defensive behaviour to changes in responses to positive reinforcers.

## Explicit non-human to human translation

When comparing species, ensuring homology is important [see, e.g., 48]. In commenting on two papers that appeared in the same issue of Nature Human Behaviour, we asked

How can we test whether humans are like rodents when responding to threats? The clearest view of the nature of, and distinctions between, fear and anxiety in both rats and mice comes from ‘ethoexperimental’ exposure to predators, the effects of which we can subject to challenge with anxiolytic and panicolytic drugs and translate to people.

How do we expose people to a real predator in an experiment? Doing so, especially while asking them to remain still in [an fMRI] scanner, sounds tricky. This problem has been solved using virtual worlds that contain [virtual] ‘predators’ that deliver real-world pain.

[49, p. 1]

BJ Fung, et al. [50, p.702] used such a paradigm [see also 51] to show that trait anxiety (as measured by the Spielberger State Trait Anxiety Inventory) was unrelated to escape under urgency but “individuals with higher trait anxiety escaped earlier during slow threats” and, consistent with Figure 1, “trait anxiety positively correlated with activity in the vHPC, mPFC, amygdala and insula”. vHPC (ventral hippocampal) activity has also been shown to be more related to avoidance in approach-avoidance conflicts than to threat per se [52], while hippocampal lesions affect approach to threat and amygdala escape from it, but not vice versa [53] - as in the non-human literature.

Also consistent with Figure 1, CW Korn and DR Bach [54, p. 733] used behaviour modelling coupled with fMRI to “provide a decision-theoretic outlook on the role of the human hippocampus, amygdala and prefrontal cortex in resolving approach–avoidance conflicts relevant for anxiety and integral for survival”. Such tasks also show human hippocampal and amygdala activity in the theta band that can be directly compared to rodent results [55]. Conversely, the simple behavioural measures of risky foraging in such tasks can be linked to gender, IQ, self-reported cognitive complexity, and self-reported daringness [56].

# Conclusions

Experimental work on animal traits, even in the well-studied defensive systems that we have reviewed, has so far focussed on links between behavioural and morphological traits [36] or models of psychopathology [e.g., 24,35,39] as has human translation [e.g., 32,50]. While informing personality, these studies do not directly target it as a primary topic. Conversely, the animal literature on personality structure has followed the main human literature [10] in using self/other report with limited connections to mechanisms and psychopathology.

Future experimental animal work should move beyond a blinkered single-disorder-model approach to not only the nature of the underlying general population traits involved but also questions of the relation these psychopathology-linked traits to more general work on animal personality structure [1,2]. While in human work personality and psychopathology are seen as related hierarchies [15,57-60] there is as yet no simple or direct translation between them as systems (nor between them and the non-hierarchical RDoC approach [61,62]); although there are points of contact where constructs can be tentatively treated as the similar, if not identical (Figure 2). Indeed, it is possible that a single psychopathological dimension will best be explained as the result of interaction between two or more normal personality traits rather than being an extreme of a single such trait [63]. Animal work, particularly cross-breeding or drug-strain interaction tests [42], would be particularly useful under these circumstances. Starting with low level syndromes/aspects (e.g., panic, fear, anxiety, obsession) anchored in a detailed neuropsychology of conserved survival circuits (e.g., Figure 1) should provide a common anchor for all of these classifications.



Figure 2. Comparison (based on [64,65]) of RDoC and HiTOP with addition of a tentative comparison of HiTOP with the Big 5. Note that HiTOP “fear’ has been renamed “threat” and fear and anxiety included as separate syndromes (matching both RDoC and Figure 1). Red arrows represent positive correlations, blue represent negative ones. The mappings of even simple elements are not one-to-one and the systems’ structures are different: RDoC has no official hierarchical structure; HiTOP has a single highest order factor (termed a super-spectrum and constituting the general factor of psychopathology or *p-factor*) with 3 embedded super-spectra, each reflecting covariance of a pair of spectra; Big 5 has only two separate highest order factors (metatraits). The same conserved neural systems must control the individual trait patterns of affects, behaviors, cognitions and desires [12] that are meant to be encapsulated by each of these classifications. It should follow that both with animal personality and human classifications their common underlying neuroscience should ultimately provide a foundation for translation between them.

A final crucial step, which we are beginning to take, is to match detailed animal work on neural systems to necessarily more coarse-grained human translation while ensuring the homology of the tests involved both behaviourally [51] and pharmacologically [32,66,67] to generate biomarkers of human disorder [68]. In the ideal case, here, non-human and human experiments would be planned in parallel or be directly linked one to the other and both would aim to understand (mechanistically and phylogenetically) both the underlying specific traits and the higher order structure within which those traits are embedded.

# Acknowledgements

None

# Disclosures

The authors declare no conflict of interest.

# References

1. Weiss A: **Personality Traits: A View From the Animal Kingdom**. *Journal of Personality* 2018, **86**:12-22.

2. Masilkova M, Weiss A, Slipogor V, Konecna M: **Comparative assessment of behaviorally derived personality structures in golden-handed tamarins (Saguinus midas), cotton-top tamarins (Saguinus oedipus), and common marmosets (Callithrix jacchus)**. *Journal of Comparative Psychology* 2020, **134**:453-466.

3. Delgado MM, Sulloway FJ: **Attributes of conscientiousness throughout the animal kingdom: An empirical and evolutionary overview**. *Psychol Bull* 2017, **143**:823-867.

4. Latzman RD, Freeman HD, Schapiro SJ, Hopkins WD: **The contribution of genetics and early rearing experiences to hierarchical personality dimensions in chimpanzees (Pan troglodytes)**. *Journal of Personality and Social Psychology* 2015, **109**:889-900.

5. Weiss A, Wilson VAD, Hopkins WD: **Early social rearing, the V1A arginine vasopressin receptor genotype, and autistic traits in chimpanzees**. *Autism Research* 2021, **14**:1843-1853.

6. McNaughton N, Corr PJ: **Animal cognition and human personality**. In *The Reinforcement Theory of Personality*. Edited by Corr PJ: Cambridge University Press; 2008:95-119.

7. Darwin C: *The expression of the emotions in man and animals*. Chicago, Illinois: University of Chicago Press; 1965/1872.

8. Richter SH, Garner JP, Würbel H: **Environmental standardization: cure or cause of poor reproducibility in animal experiments?** *Nature Methods* 2009, **6**:257-261.

9. Garner JP: **The significance of meaning: Why do over 90% of behavioral neuroscience results fail to translate to humans, and what can we do to fix it?** *ILAR Journal* 2014, **55**:438-456.

10. Weiss A: **A human model for primate personality**. *Proceedings of the Royal Society B: Biological Sciences* 2017, **284**:20171129.

11. DeYoung CG, Krueger RF: **A cybernetic theory of psychopathology**. *Psychological Inquiry* 2018, **29**:117-138.

12. Revelle W: **Experimental Approaches to the Study of Personality**. In *Handbook of Research Methods in Personality Psychology*. Edited by Robins B, Fraley RC, Krueger RF: Guilford Press; 2007:37-61.

\*\*\*13. McNaughton N: **Personality neuroscience and psychopathology: should we start with biology and look for neural-level factors?** *Personality Neuroscience* 2020, **3**:e4.

\*\* Detailed justification of a phylogenetic approach to personality, existing biology-based theories, and conservation of modulatory control factors in hierarchical systems over the course of evolution.

14. Adams MJ, Majolo B, Ostner J, Schulke O, De Marco A, Thierry B, Engelhardt A, Widdig A, Gerald MS, Weiss A: **Personality structure and social style in macaques**. *J Pers Soc Psychol* 2015, **109**:338-353.

15. Kotov R, Krueger RF, Watson D: **A paradigm shift in psychiatric classification: the Hierarchical Taxonomy Of Psychopathology (HiTOP)**. *World Psychiatry* 2018, **17 (February)**:24-25.

16. Sellbom M, Carragher N, Sunderland M, Calear AL, Batterham PJ: **The role of maladaptive personality domains across multiple levels of the HiTOP structure**. *Personality and Mental Health* 2020, **14**:30-50.

\*\*17. Latzman RD, DeYoung CG, The Hitop Neurobiological Foundations Workgroup: **Using empirically-derived dimensional phenotypes to accelerate clinical neuroscience: the Hierarchical Taxonomy of Psychopathology (HiTOP) framework**. *Neuropsychopharmacology* 2020, **45**:1083-1085.

\*\* Recent perspective on the HiTOP approach to psychopathology and emphasising that poor progress in mental disorder biomarker development is due “largely to the shortcomings of current categorical diagnostic systems, rather than intrinsic limitations of biological approaches” (p 1083).

18. DeYoung CG, Chmielewski M, Clark LA, Condon DM, Kotov R, Krueger RF, Lynam DR, Markon KE, Miller JD, Mullins-Sweatt SN, et al.: **The distinction between symptoms and traits in the Hierarchical Taxonomy of Psychopathology (HiTOP)**. *Journal of Personality* 2020, **n/a**.

\*19. Bergdolt L, Dunaevsky A: **Brain changes in a maternal immune activation model of neurodevelopmental brain disorders**. *Progress in Neurobiology* 2019, **175**:1-19.

\* Broad review of MIA and its interaction with genetic risk factors as a means of generating animal models of autism and schizophrenia.

20. Lenzenweger MF: **Schizotypy, schizotypic psychopathology and schizophrenia**. *World Psychiatry* 2018, **17**:25-26.

21. Theriault K, Manduca J, Perreault M: **Sex differences in innate and adaptive neural oscillatory patterns link resilience and susceptibility to chronic stress in rats**. *Journal of psychiatry & neuroscience: JPN* 2021, **46**:e200117.

22. de Abreu MS, Genario R, Giacomini ACVV, Demin KA, Lakstygal AM, Amstislavskaya TG, Fontana BD, Parker MO, Kalueff AV: **Zebrafish as a model of neurodevelopmental disorders**. *Neuroscience* 2020, **445**:3-11.

\*23. Fontana BD, Franscescon F, Rosemberg DB, Norton WHJ, Kalueff AV, Parker MO: **Zebrafish models for attention deficit hyperactivity disorder (ADHD)**. *Neuroscience & Biobehavioral Reviews* 2019, **100**:9-18.

\* Focussed review of zebrafish as a model of ADHD (see also reference 22 for a brief review of neurodevelopmental disorders in general).

24. Soares MC, Gerlai R, Maximino C: **The integration of sociality, monoamines and stress neuroendocrinology in fish models: applications in the neurosciences**. *Journal of Fish Biology* 2018, **93**:170-191.

25. Silva C, McNaughton N: **Are periaqueductal gray and dorsal raphe the foundation of appetitive and aversive control? A comprehensive review**. *Progress in Neurobiology* 2019, **177**:33-72.

26. DeYoung CG: **Cybernetic Big Five Theory**. *Journal of Research in Personality* 2015, **56**:33-58.

27. Fleeson W: **Toward a structure- and process-integrated view of personality: Traits as density distributions of states**. *Journal of Personality and Social Psychology* 2001, **80**:1011-1027.

28. Rauthmann JF, Schmitt M: **Personality traits as state density distributions: Revisiting Fleeson**. In *Personality and individual differences: Revisiting the classic studies* Edited by Corr PJ: Sage; 2019:225-244.

29. Mobbs D, LeDoux JE: **Editorial overview: Survival behaviors and circuits**. *Current Opinion in Behavioral Sciences* 2018, **24**:168-171.

30. Corr PJ (Ed): *The Reinforcement Sensitivity Theory of Personality* Cambridge: Cambridge University Press; 2008.

31. Gray JA, McNaughton N: *The Neuropsychology of Anxiety: An enquiry into the functions of the septo-hippocampal system* (2 ed.). Oxford: Oxford University Press; 2000.

32. McNaughton N: **What do you mean “anxiety”? Developing the first anxiety syndrome biomarker**. *Journal of the Royal Society of New Zealand* 2018, **48**:177-190.

33. Graeff FG, Del-Ben CM: **Neurobiology of panic disorder: From animal models to brain neuroimaging**. *Neuroscience & Biobehavioral Reviews* 2008, **32**:1326-1335.

34. Penke L, Denissen JJA, Miller GF: **The evolutionary genetics of personality**. *European Journal of Personality* 2007, **21**:549-587.

35. Blizard DA, Eldridge JC, Jones BC: **The defecation index as a measure of emotionality: Questions raised by HPA axis and prolactin response to stress in the maudsley model**. *Behavior Genetics* 2015, **45**:368-373.

36. Dugatkin LA: **The silver fox domestication experiment**. *Evolution: Education and Outreach* 2018, **11**:e16.

37. Wood EK: **Dental size reduction in the domesticated silver fox: implications for the domestication syndrome model**. Edited by. University of Iowa: University of Iowa; 2020. vol PhD.]

38. Clinton SM, Unroe KA, Shupe EA, McCoy CR, Glover ME: **Resilience to stress: Lessons from rodents about nature versus nurture**. *The Neuroscientist* 2021:1073858421989357.

39. León LA, Castro-Gomes V, Zárate-Guerrero S, Corredor K, Mello Cruz AP, Brandão ML, Cardenas FP, Landeira-Fernandez J: **Behavioral Effects of Systemic, Infralimbic and Prelimbic Injections of a Serotonin 5-HT2A Antagonist in Carioca High- and Low-Conditioned Freezing Rats**. *Frontiers in Behavioral Neuroscience* 2017, **11**:A117.

40. Macedo-Souza C, Maisonnette SS, Filgueiras CC, Landeira-Fernandez J, Krahe TE: **Cued Fear Conditioning in Carioca High- and Low-Conditioned Freezing Rats**. *Frontiers in Behavioral Neuroscience* 2019, **13**:285.

41. Dias GP, Bevilaqua MCdN, Silveira ACD, Landeira-Fernandez J, Gardino PF: **Behavioral profile and dorsal hippocampal cells in carioca high-conditioned freezing rats**. *Behavioural Brain Research* 2009, **205**:342-348.

42. Cavaliere DR, Maisonnette S, Krahe TE, Landeira-Fernandez J, Cruz APM: **High- and Low-conditioned behavioral effects of midazolam in Carioca high- and low-conditioned freezing rats in an ethologically based test**. *Neurosci Lett* 2020, **715**:134632.

43. Lages YV, Maisonnette SS, Marinho B, Rosseti FP, Krahe TE, Landeira-Fernandez J: **Behavioral effects of chronic stress in Carioca High- and Low-Conditioned Freezing rats**. *Stress* 2021, **24**:602-611.

44. Bezerra-Karounis MA, Krahe TE, Maisonnette S, Landeira-Fernandez J: **Alcohol intake in Carioca High- and Low-conditioned Freezing rats**. *Pharmacol Biochem Behav* 2020, **197**:173019.

45. León LA, Brandão ML, Cardenas FP, Parra D, Krahe TE, Cruz APM, Landeira-Fernandez J: **Distinct patterns of brain Fos expression in Carioca High- and Low-conditioned Freezing Rats**. *PLoS One* 2020, **15**:e0236039.

46. Genewsky A, Albrecht N, Bura SA, Kaplick PM, Heinz DE, Nußbaumer M, Engel M, Grünecker B, Kaltwasser SF, Riebe CJ, et al.: **How much fear is in anxiety?** *BioRxiv* 2018, **385823**:draft.

47. Giorgi O, Corda MG, Fernandez-Teruel A: **A genetic model of impulsivity, vulnerability to drug abuse and schizophrenia-relevant symptoms with translational potential: The roman high- vs. Low-avoidance rats**. *Frontiers in Behavioral Neuroscience* 2019, **13**:A145.

48. Ojala KE, Bach DR: **Measuring learning in human classical threat conditioning: Translational, cognitive and methodological considerations**. *Neuroscience & Biobehavioral Reviews* 2020, **114**:96-112.

\*49. McNaughton N: **Brain maps of fear and anxiety**. *Nature Human Behaviour* 2019, **3**:662-663.

\* News & Views commentary on references 50 and 53. See also references 51 and 52

50. Fung BJ, Qi S, Hassabis D, Daw N, Mobbs D: **Slow escape decisions are swayed by trait anxiety**. *Nature Human Behaviour* 2019, **3**:702-708.

51. Qi S, Hassabis D, Sun J, Guo F, Daw N, Mobbs D: **How cognitive and reactive fear circuits optimize escape decisions in humans**. *Proceedings of the National Academy of Sciences* 2018, **115**:3186-3191.

52. Abivardi A, Khemka S, Bach DR: **Hippocampal representation of threat features and behavior in a human approach–avoidance conflict anxiety task**. *The Journal of Neuroscience* 2020, **40**:6748-6758.

53. Bach DR, Hoffmann M, Finke C, Hurlemann R, Ploner CJ: **Disentangling Hippocampal and Amygdala Contribution to Human Anxiety-Like Behavior**. *The Journal of Neuroscience* 2019, **39**:8517-8526.

54. Korn CW, Bach DR: **Minimizing threat via heuristic and optimal policies recruits hippocampus and medial prefrontal cortex**. *Nature Human Behaviour* 2019, **3**:733-745.

55. Tzovara A, Meyer SS, Bonaiuto JJ, Abivardi A, Dolan RJ, Barnes GR, Bach DR: **High‐precision magnetoencephalography for reconstructing amygdalar and hippocampal oscillations during prediction of safety and threat**. *Human Brain Mapping* 2019, **40**:4114-4129.

56. Bach DR, Moutoussis M, Bowler A, Neuroscience in Psychiatry Network c, Dolan RJ: **Predictors of risky foraging behaviour in healthy young people**. *Nature Human Behaviour* 2020:in press.

57. Widiger TA, Sellbom M, Chmielewski M, Clark LA, DeYoung CG, Kotov R, Krueger RF, Lynam DR, Miller JD, Mullins-Sweatt S, et al.: **Personality in a hierarchical model of psychopathology**. *Clinical Psychological Science* 2018, **7**:77-92.

58. Allen TA, Carey BE, McBride C, Bagby RM, DeYoung CG, Quilty LC: **Big Five Aspects of Personality Interact to Predict Depression**. *Journal of Personality* 2018, **86**:714-725.

59. Ludeke SG, Bainbridge TF, Liu J, Zhao K, Smillie LD, Zettler I: **Using the Big Five Aspect Scales to translate between the HEXACO and Big Five personality models**. *Journal of Personality* 2019, **87**:1025-1038.

60. Mann FD, DeYoung CG, Tiberius V, Krueger RF: **Stability and well-being: Associations among the Big Five domains, metatraits, and three kinds of well-being in a large sample**. *Journal of Personality* 2021:online.

61. Insel T, Cuthbert B, Garvey MG, Heinssen R, Pine DS, Quinn K, Sanislow C, Wang P: **Research Domain Criteria (RDoC): toward a new classiﬁcation framework for research on mental disorders**. *American Journal of Psychiatry* 2010, **167**:748-751.

62. Carcone D, Ruocco AC: **Six Years of Research on the National Institute of Mental Health’s Research Domain Criteria (RDoC) Initiative: A Systematic Review**. *Frontiers in Cellular Neuroscience* 2017, **11**:A046.

63. McNaughton N, Glue P: **Ketamine and neuroticism: a double-hit hypothesis of internalizing disorders**. *Personality Neuroscience* 2020, **3**:e2.

64. Michelini G, Palumbo IM, DeYoung CG, Latzman RD, Kotov R: **Linking RDoC and HiTOP: A new interface for advancing psychiatric nosology and neuroscience**. *Clin Psychol Rev* 2021, **86**:102025.

65. Kotov R, Krueger RF, Watson D, Cicero DC, Conway CC, DeYoung CG, Eaton NR, Forbes MK, Hallquist MN, Latzman RD, et al.: **The Hierarchical Taxonomy of Psychopathology (HiTOP): A quantitative nosology based on consensus of evidence**. *Annual Review of Clinical Psychology* 2021, **17**:83-108.

66. Shadli SM, Glue P, McIntosh J, McNaughton N: **An improved human anxiety process biomarker: characterization of frequency band, personality and pharmacology**. *Translational Psychiatry* 2015, 5:e699.

\*\*67. Shadli SM, High O, Byers B, Gibbs P, Steller R, Glue P, McNaughton N: **Human anxiety-specific "theta" occurs with selective stopping and localizes to right inferior frontal gyrus**. *Behavioral Neuroscience* 2020, **134**:547-555.

\*\*Recent detailed example of neural basis, drug sensitivity, and general signal homology of the first specific human trait biomarker directly derived from an animal model and detailed neuropsychological theory.

\*\*68. Shadli SM, Ando LC, McIntosh J, Lodhia V, Russell BR, Kirk IJ, Glue P, McNaughton N: **Right frontal anxiolytic-sensitive EEG ‘theta’ rhythm in the stop-signal task is a theory-based anxiety disorder biomarker**. *Scientific Reports* 2021, **11**:19746.

\*\*First report of a human trait-linked, theoretically-based, biomarker for a human psychiatric disorder

1. Traceable back in various forms to the 1890s; see comments on https://scienceblogs.com/laelaps/2009/08/11/i-have-developed-something-of. [↑](#footnote-ref-1)
2. This approach makes assessment of interactions more powerful and simpler than if the continuous variable is used in a correlational approach. [↑](#footnote-ref-2)