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Review

Animal models of human psychopathology based on individual differences in novelty-seeking and anxiety

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ABSTRACT

The role of individual factors in behavioural neuroscience is an important, but still neglected area of research. The present review aims to give, first, an outline of the most elaborated theory on animal behaviour, and second, an overview of systematic approaches of historic and present animal models of human psychopathology based on individual differences. This overview will be focused on animal models of unselected subjects (i.e. natural variance of a specific behaviour within a given population) and selected breeding for a specific behaviour. Accordingly, an outline of the personality model from Gray and McNaughton of individual behaviour in animals is given first. Then, a comprehensive overview of past and current animal models in novelty-seeking (i.e. psychomotor activation and exploration behaviour) based on systematic individual differences and its relationship to addiction is presented. Third, this will be followed by a comprehensive overview of individual differences in previous and present animal models for anxiety. Finally, critical aspects of such approaches in animal research are discussed, and suggestions are given where to go from here.

Contents

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Abbreviations: BrdU, 5-bromo-2′-deoxyuridine; 5-HIAA, 5-hydroxyindole acetic acid; 5-HT, 5-hydroxytryptamine, serotonin; 8-OH-DPAT, 8-hydroxy-2-di-*N*-propylamino-notetralin; ACTH, adrenocorticotropic hormone; AHA, Australian high avoidance; ALA, Australian low avoidance; APO-SUS, apomorphine-susceptible; APO-UNSUS, apomorphine-unsusceptible; BAS, Behavioural Activating System; BIS, Behavioural Inhibition System; BNST, bed nucleus of the stria terminalis; CRH, corticotropin-releasing hormone; DA, dopamine; DNA, deoxy-ribonucleic acid; DOPAC, 3,4-dihydroxyphenylacetic acid; DSP-4, *N*-(2-chloroethyl)-*N*-ethyl-2-bromobenzylamine; EAE, experimental autoimmune encephalomyelitis; FFFS, Fight/Freezing/Flight System; Floripa H, Floripa high; Floripa L, Floripa low; GABA, γ-aminobutyric acid; GR, glucocorticoid receptor; HAB, high anxiety-related behaviour; HDS, high DPAT sensitive; HOA, high open arm; HPA, hypothalamus–pituitary–adrenal; HR, high responder; HRA, high rearing activity; IFN, interferon; Ig, immunoglobulin; IL, interleukin; LAB, low anxiety-related behaviour; LDS, low DPAT sensitive; LOA, low open arm; LR, low responder; LRA, low rearing activity; MDMA, 3,4-methylenedioxymethamphetamine (“ecstasy”); mRNA, messenger ribonucleic acid; NA, noradrenaline; NMDA, *N*-methyl-D-aspartate; PAG, periaquaeductal gray; p-ERK1/2, phosphorylation of extracellular signal-regulated kinase1/2; PVN, nucleus paraventricularis; QTL, quantitative trait loci; RHA, Roman high avoidance; RHA/Verh, Roman high avoidance (Switzerland); RLA, Roman low avoidance; RLA/Verh, Roman low avoidance (Switzerland); SHA/Bru, Syracuse high avoidance; SLA/Bru, Syracuse low avoidance; SSRI, selective serotonin reuptake inhibitor; THA, Tokai high avoider.

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1. Introduction

Quantitative individual behavioural differences were not systematically addressed until the late 18th century when interest was directed to the 'personal equations' used by astronomers for measuring stellar transits. Then, scientists discovered not only differences between individuals, but also that the individual's 'personal equation' also varied over time, suggesting that the rather large individual differences were not invariant. These differences involved visual as well as auditory reaction times, and attention and vigilance also played a role (Anastasi 1958, cited from Brush, 1991). Today, one of the major challenges of personality research is to understand the causes of individual differences and their consequences in terms of fitness, adaptive capacity, and individual vulnerability to diseases. Animal research has also been used to investigate individuality. Thus, there is a range of methods that can be applied in different species (for review see Gosling, 2001). In this literature, individuality is defined as a collection of behavioural or physiological traits, both innate and acquired, that distinguish one individual from near relatives, which as far as possible share the same genetic and environmental background.

The role of individual difference factors in behavioural neuroscience is an important, but still neglected area of research. One problem is the need for higher numbers of participants or subjects than the commonly used approach. Accordingly, research issues requiring many subjects (e.g., dose–response effects) are often neglected in favour of less demanding inquiries. In the last years, however, the necessity of an individual approach for research on biology/behaviour relationships has become more and more important. Despite the progress in examining biopsychological processes in humans, behavioural neuroscience in animals remains indispensable. For example, do animals show substantial differences in behaviour, physiology, or pharmacological reactivity? What are the relationships between these parameters and how consistent are they? What are the key domains of individual behavioural differences that have physiological relevance? More importantly, can these domains predict *a priori* the outcome of experimental manipulations? To what extent do certain stable characteristics of the organism shape physiological outcomes, before and after experimental manipulations? These questions are important to answer if animal models of diseases are to be developed in order to investigate in depth individual susceptibility to diseases or psychiatric disorders.

The present review aims, first, to give an outline of some of the most important theories of individual behaviours in animals and humans, and second, an overview of all systematic approaches of historic and present animal models of human psychopathology based on individual differences in novelty-seeking and anxiety, to the best knowledge of the authors. It was our intention to include all systematic animal models relating to anxiety and novelty-seeking within one review for the first time. Finally, critical aspects of studying individual behaviour in animals are discussed, and suggestions are given where to go from here.

2. Theories of individual behaviour

It is out of the scope of this work to provide a comprehensive overview of the most relevant biopsychological theories of individual behaviour in animals (e.g., Depue and Lenzenweger, 2005; Gray and McNaughton, 2000; McNaughton and Corr, 2004; White and Depue, 1999), and human personality (Cloninger, 2003; Zuckerman, 1984; for overviews see Amelang et al., 2006; Hennig and Netter, 2005; McAdams, 2001; Pervin and John, 2001). But one of the most influential theories on the neurobehavioural system of approach and avoidance behaviour by Gray and subsequent developments by him and others shall be briefly described. A selection of the most critical parts of this personality theory shall be roughly outlined to which the following findings on approach, avoidance, and their respective biological correlates can be related to. The theory by Gray (1982), Gray and McNaughton (2000), and the modifications from McNaughton and Corr (2004) has been depicted because it appears as the most elaborated animal theory of anxiety/fear and novelty-seeking behaviour.

2.1. The personality model from Gray and McNaughton

In accordance to his teacher Hans-Jürgen Eysenck, Jeffrey Alan Gray stated that personality differences are based on distinct brain systems. However, Gray (1981) postulated that these different systems are also characterised by distinct sensitivities for cues of reward and punishment, thus proposing the "reinforcement