Neuroscience and Biobehavioral Reviews 37 (2013) 1254–1296

Contents lists available at SciVerse ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review

Systematic review, structural analysis, and new theoretical perspectives on the role of serotonin and associated genes in the etiology of psychopathy and sociopathy

Bariş O. Yildirim*, Jan J.L. Derksen[1]

Radboud University, Department of Clinical Psychology, Nijmegen, the Netherlands

ARTICLE INFO

Article history:
Received 4 December 2012
Received in revised form 9 April 2013
Accepted 17 April 2013

Keywords:
Behavioral neurophysiology
Behavioral genetics
Neurogenetics
Temperament
Psychopathy
Cluster B personality disorders
Sociopathy
Homeostasis
Allostasis
Serotonin
TPH
5HTT
5HT1A
5HT2C
5HT3
GABA-A
Testosterone
Gene–gene interactions
Gene–environment interactions

ABSTRACT

Since its theoretical inception, psychopathy has been considered by philosophers, clinicians, theorists, and empirical researchers to be substantially and critically explained by genetic factors. In this systematic review and structural analysis, new hypotheses will be introduced regarding gene–gene and gene–environment interactions in the etiology of psychopathy and sociopathy. Theory and research from neurobiological and behavioral sciences will be integrated in order to place this work in a broader conceptual framework and promote synergy across fields. First, a between groups comparison between psychopathy and sociopathy is made based on their specific dysfunctions in emotional processing, behavioral profiles, etiological pathways, HPA-axis functioning, and serotonergic profiles. Next, it is examined how various polymorphisms in serotonergic genes (e.g., TPH, 5HTT, HTR1A, HTR2A, HTR2C, and HTR3) might contribute either individually or interactively to the development of these disorders and through which specific biological and behavioral endophenotypes this effect could be mediated. A short introduction is made into mediating variables such as GABAergic functioning and testosterone which could potentially alter the decisive effect of serotonergic genotypes on behavior and physiology. Finally, critical commentary is presented on how to interpret the hypotheses put forward in this review.

Contents

* Corresponding author at: Department of Clinical Psychology, Radboud University Nijmegen, De Kluyskamp 1002, 6545 JD Nijmegen, The Netherlands. Tel.: +31 646118681.
E-mail addresses: onur.yildirim@live.nl (B.O. Yildirim), j.derksen@psych.ru.nl (J.J.L. Derksen).
[1] Department of Clinical Psychology, Room: A.07.04B, Radboud University Nijmegen, Montessorilaan 3, 6525 HR Nijmegen, The Netherlands. Tel.: +31 (0)24 36 12666.

0149-7634/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.neubiorev.2013.04.009

1. Introduction

Contemporary theories argue that the etiology of psychopathic traits is partially rooted in a constitutionally based emotional hyporesponsivity resulting in fearlessness and dampened emotional empathy (i.e., callous/unemotional traits) thereby impeding the development of an internalized moral conscience and significantly increasing the risk for antisocial behavior (Blair, 1995, 2006a; Blair et al., 2005; Fowles and Dindo, 2006; Fowles and Kochanska, 2000; Frick and Morris, 2004; Hare, 1993; Kochanska, 1991, 1993, 1995, 1997; Kochanska et al., 1994, 2002; Lykken, 1995; Skeem et al., 2003, 2007). Empirical studies report that psychopathic traits show strong genetic correlations in childhood ($h^2g \approx 0.70$) and adulthood ($h^2g \approx 0.60$) (Blonigen et al., 2003; Vernon et al., 2008; Viding et al., 2005, 2008), high stability throughout life (Frick et al., 2005; Blonigen et al., 2006), and are strongly predictive of antisocial behavior in children (Viding et al., 2005, 2008), adolescents (Frick et al., 2005), and adults (Blonigen et al., 2006). Interestingly, a larger variance of antisocial behaviors is explained by genetic factors when psychopathic traits are present ($h^2g = 0.80$ versus $h^2g = 0.30$) indicating that antisocial behavior in psychopathic individuals is somehow more strongly rooted in constitution (Viding et al., 2005). In light of the emerging support for strong heritable contributions to psychopathy, the next step is identifying possible determinants on the level of specific polymorphisms and alleles. Gunter et al. (2010) review the neurogenetic correlations of different antisocial spectrum disorders (suicide, substance abuse, aggression, antisocial personality disorder, and psychopathy) but do not provide in depth theoretical analyses on the differentiation between these conditions in terms of their characteristic endophenotypic pathways and the specific genotypical profiles associated with these pathways. Glenn (2011a) systematically reviews the potential genetic basis for endophenotypes uniquely observed in psychopathy (i.e., emotional hyporesponsivity) but focuses solely on the serotonin transporter gene (i.e., 5HTTLPR).

Before identifying monoaminergic foundations of complex psychological disorders, a solid theoretical framework is needed that provides an explanation into how (neuro)physiology could contribute to socio-emotional development and behavioral expressions (Miller, 2010). An especially accurate theoretical model can be achieved through the framework of homeostasis and allostasis because physiological processes naturally follow these universal laws to maintain the internal environment and promote adaptation and well-being (Schulkin, 2003). Since monoaminergic processes influence the "physiology of the brain", it is theorized that the monoaminergic *contribution* to psychological disorders could be understood in the context of a *dysfunctional homeostatic or allostatic regulation of specific neurophysiological processes*, ultimately sensitizing or desensitizing the readiness for specific behavioral expression. The gap between monoaminergic genes and behavior could thus possibly be explained through intermediary neuro- and psychophysiological processes.

First introduced by Cannon (1929), the term "homeostasis" refers to the processes by which a relative constancy of physiological function is automatically maintained around an internal and biologically relevant operating range or set-point that promotes health and well-being (Berntson and Cacioppo, 2007; Schulkin, 2003). When this homeostatic state is disrupted by salient events and physiological demands, feed-back systems reflexively trigger dynamic equilibrium adjustments that serve to autoregulate towards the biologically relevant operating range, or establish new homeostatic equilibria, such that growth promoting processes can be re-initiated (Azmitia, 2007; Berntson and Cacioppo, 2007; Schulkin, 2003). However, temporary disruptions in these baseline operating ranges are highly adaptive and serve partly to alarm the organism of an affectively salient event in order to promote re-evaluations and modifications of ongoing behavior or motivational tendencies (Schulkin, 2003). One plausible hypothesis is that homeostatic regulation of monoaminergic processes mediates stability (stronger regulation) versus flexibility (weaker regulation) in the natural resonation of endocrinological and physiological processes to stressful and emotional events with non-optimally high stability/low flexibility leading to an uncoupling of internal states to salient events (e.g., socio-emotional detachment) and non-optimally low stability/high flexibility leading to dysregulation of internal states (e.g., emotion and motivation) in response to salient events (e.g., threat and reward).

In contrast to homeostasis which signifies autoregulation towards an internal set-point, allostatic regulations shifts these operating ranges when the organism encounters, or when there is a possibility of encountering new challenges, rewards, and/or threats that require an active and mobilizing coping response (Beauchaine et al., 2011; Berntson and Cacioppo, 2007; Schulkin, 2003). Thus at the heart of allostasis is the depiction of change through sympathetic, catecholaminergic, and hypothalamic-pituitary-adrenal axis (HPA-axis) activation in order to maintain or achieve a preparatory state that is adaptive to salient circumstances (real or perceived and predicted or unpredicted) (Schulkin, 2003). Allostasis is therefore highly important for shifting physiological operating ranges thereby mobilizing energy and attentional resources towards a specific goal (i.e., the fuel) whereas homeostatic autoregulation provides the necessary equilibrium adjustments to maintain system-integrity throughout different ranges of physiological functioning (i.e., the oil). Both ultimately serve to promote stability in homeostasis but allostasis achieves this goal by mobilizing energy in response to potentially or immediately salient events and initiating adaptive coping behaviors which ultimately ensure that the homeostatic state can be maintained in the long-term. Furthermore, allostasis can be reactive or predictive in nature (Schulkin, 2003). Reactive allostasis refers to the potentiation of physiological processes (e.g., phasic catecholamine/HPA-axis reactivity) in response to unexpected and immediately salient events such as the fight-or-flight response to imminent threat, arousal response to unexpected rewards, and the mobilization of energy resources in response to immediate challenges, and serves to mount an ad-hoc