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Review

GILZ: Glitzing up our understanding of the glucocorticoid receptor in psychopathology

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ABSTRACT

Dysfunction of the hypothalamic–pituitary–adrenal axis, particularly the glucocorticoid receptor, is a commonly implicated link between stress and psychopathology. GR abnormalities are frequently reported in depression, and these anomalies must be resolved before depressive symptoms remit. This biological finding is rendered clinically relevant by the knowledge that only select antidepressants alter GR function. The relationship between GR dysfunction and other diseases associated with psychiatric stress, such as post-traumatic stress disorder (PTSD) and fibromyalgia, is also documented. However, as laboratory constraints limit the utility of GR testing, other measures of GR activity, such as levels of GR-induced genes, may have greater clinical value. In this review, glucocorticoid-induced leucine zipper (GILZ), a product of GR-initiated gene transcription, will be discussed in the context of GR dysfunction in psychopathology.

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1. Introduction

Selye (1950) linked the experience of psychological stress to the function of the hypothalamic–pituitary–adrenal (HPA) axis. Depression, a significant disease that is projected to become the leading cause of burden of disease by 2030, is associated with stress, so much data has emerged since 1950 to connect depression to the HPA axis (Pariante, 2003; World Health Organisation, 2008). However, the precise nature of the relationship between the HPA axis and depression varies widely across studies, as both HPA axis hyperactivity and hypoactivity are reported in depression, as illustrated in Fig. 1 (Carroll et al., 2012; Cassano and Fava, 2002; Gold and Chrousos, 2002; Heuser et al., 1998; Raadsheer et al., 1994; Sigalas et al., 2012; Starkman, 2013; van Rossum et al., 2006; Webster et al., 2002).

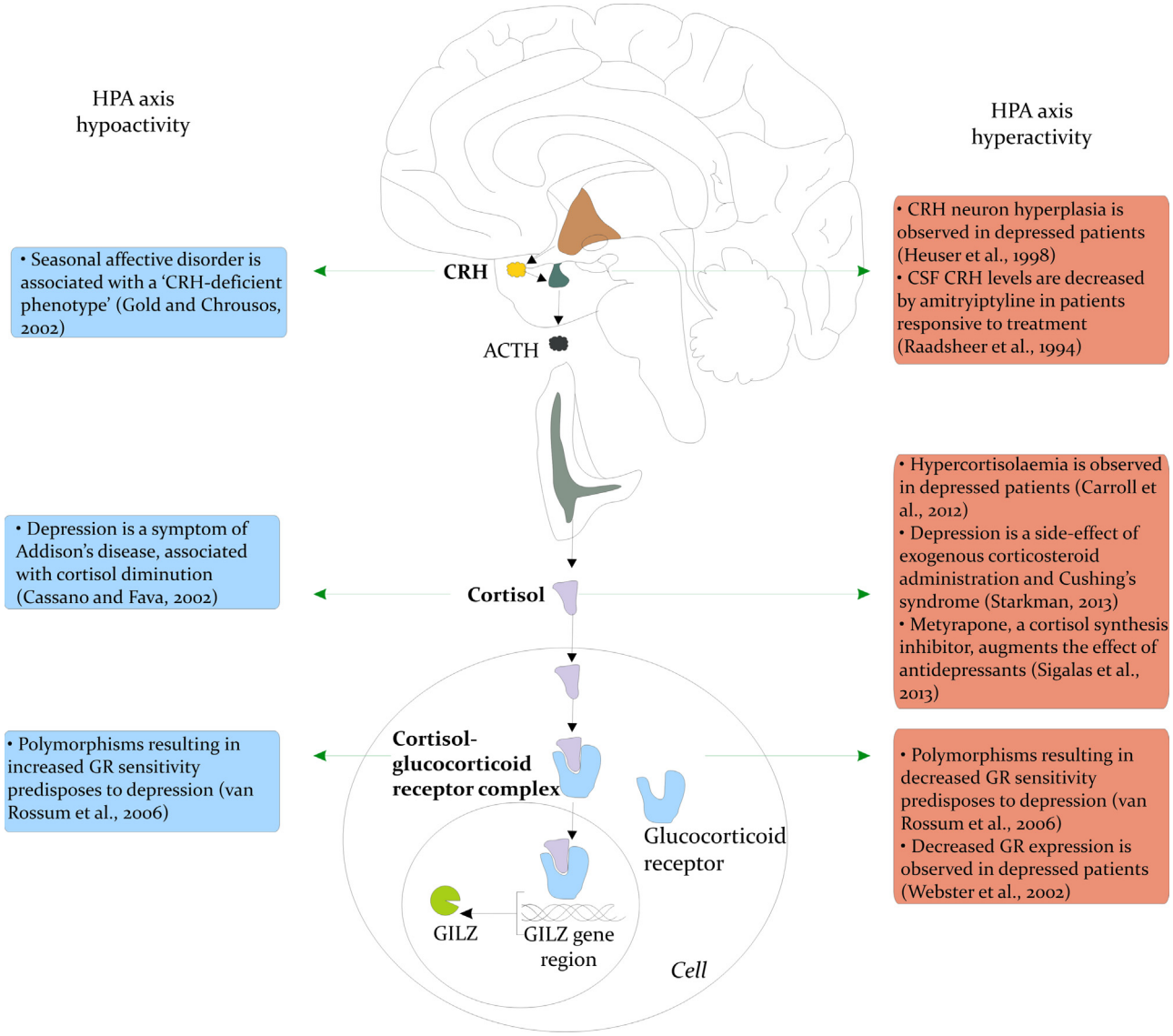

Fig. 1 – Many biological substrates in the hypothalamic–pituitary–adrenal axis are dysfunctional in depression. This dysfunction may reflect HPA axis hypoactivity (blue) or HPA axis hyperactivity (red). CRH: corticotrophin releasing hormone. ACTH: adrenocorticotrophic hormone. CSF: cerebrospinal fluid. GR: glucocorticoid receptor. GILZ: glucocorticoid-induced leucine zipper.