BERA VIOURAL AND HORMONAL INDICES OF ANXIOLYTIC AND ANXIOGENIC DRUG ACTION IN THE SHOCK PROD DEFENSIVE BURYING/AVOIDANCE PARADIGM

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INTRODUCTION

The bodily response of mammals to stressful situations is characterized by a complex pattern of behavioural, endocrine and autonomic changes (Fig. 1). A variety of these so-called "stress" indices are nowadays routinely employed as the dependent variable in animal models designed for studying the neuropharmacological mechanisms of stress/anxiety and, in particular, for evaluating the potential anti-stress or anxiolytic actions of new compounds. These include: suppressed operant behaviour (Geller & Seifert, 1960; Vogel et al., 1971), startle potentiation (Davis, 1979), decreased exploratory activity (Crawley, 1981; Meert & Colpaert, 1984; Yamamoto & Ueki, 1987), decreased social interaction (File, 1980), increased burying behaviour (Treit et al., 1981), and elevated plasma corticosteroid concentrations (Lahti & Baruhn, 1974; Le Fur et al., 1979; Gram & Christensen, 1986). It is generally assumed that compounds with anti-stress or anxiolytic activity are characterized by their potency to inhibit or block these changes, while the ability to induce or enhance them is a reflection of anxiogenic or pro-stress properties. The usefulness and shortcomings of different animal models of stress/anxiety have been extensively reviewed by Treit (1985), and will not be discussed further in this chapter.

However, in contrast to the multimodality (Figure 1), complexity and heterogeneity of the stress response (Bohus et al., 1987, De Boer, 1990), the above listed animal
models make use of only one single (mostly unidirectional) behavioural or hormonal index of stress, fear and/or anxiety. As a result, the interpretation of anxiolytic drug action is complicated and may lead to "false negatives" and/or "false positives". Therefore it seems attractive to study anxiolytic drug effects in a test-situation that allows several different behavioural and autonomic/endocrine manifestations of stress/anxiety to be measured simultaneously.

Profile of responses to stress/anxiety

![Diagram showing various responses to stress/anxiety](image)

**Behavioral** | **Endocrine** | **Autonomic**
--- | --- | ---
Locomotor activity | Pituitary hormones | Sympathetic activity +
novel environ. - | B-END + | bloodpressure +
familiar environ. + | ACTH + | temperature +
Withdrawal + | PRL + | heart rate +
Immobility + | VP + | plasma NA +
Grooming + | GH - | plasma FFA +
burying + | TSH - | plasma renin +
Startle + | LH/FSH - | plasma glucose +
Ingestion - | Adrenal hormones | Parasympathetic activity -
Exploration - | corticosteroids + | gastric acid secretion -
Sexual activity - | Adrenaline + | gastric emptying -
Social interaction - | Pancreatic hormones | gastric ulceration +
Operant responding - | glucagon + | fecal excretion +
 | insulin +/- | Immune functions -

Fig. 1 A schematic overview of the various neurochemical, electrophysiological, behavioural, endocrine and autonomic parameters which are affected when an organism is exposed to stressful or anxiety-provoking stimuli. "+" indicates an increase in the measure. "-" a decrease.