Recent Advances Regarding the Role of Corticosteroids in the Elasmobranch Stress Response

Los Recientes Avances en Cuanto al Papel de los Corticosteroides en la Respuesta al Estrés de Elasmobranquios

Les Progrès Récents Concernant le Rôle des Corticostéroïdes dans la Réponse au Stress Élasmobranches

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EXTENDED ABSTRACT

In most vertebrates, corticosteroids facilitate survival of stressors by mobilizing energy reserves and directing energy away from other systems including reproduction and immunity. Therefore long-term activation of the endocrine stress axis is deleterious, and may affect survival and/or reproductive fitness. Due to the adverse effects of chronic stress, understanding the physiology of the stress response is vital to informing population management and conservation decisions.

The elasmobranch stress response is poorly understood, particularly with regard to activation of the endocrine stress axis and the production and downstream actions of corticosteroid hormones. The primary circulating corticosteroid hormone in elasmobranchs is 1a-hydroxycorticosterone, or 1a-B (Idler and Truscott 1966). This hormone is unique to elasmobranchs and is thought to function both as a glucocorticoid (GC) hormone during stress, and as a mineralocorticoid (MC) hormone during osmoregulation (see Anderson 2012 for review). However, the novel molecular structure of 1a-B poses an impediment to its measurement and laboratory synthesis; therefore, detailed information regarding the physiological effects of 1a-B is lacking. Furthermore, efforts to examine the downstream GC vs. MC actions are confounded by a lack of sequence and functional knowledge regarding the corticosteroid receptors of elasmobranch fishes.

In an effort to characterize the role of 1a-B in the elasmobranch stress response, we captured Atlantic stingrays (*Dasyatis sabina*) and exposed them to simulated hook and line stress. *D. sabina* were serially sampled over the course of the stressor to obtain individual time series, and released at the conclusion of the experiment. To examine activation of the endocrine stress axis, we used a direct assay to measure the concentration of plasma corticosteroids; additionally, to examine the physiological effects of acute stress, as well as to investigate the GC vs. MC actions of 1a-B, we measured additional plasma components including glucose, chloride, urea, and total osmolality. The results of this experiment demonstrate that capture stress in *D. sabina* is characterized by significant increases in plasma corticosteroids, glucose, and osmolality. This is the first study to use serial sampling to demonstrate increases in corticosteroid secretion by individual elasmobranchs in response to acute stress, and the associated elevations in corticosteroids, glucose, and osmolality suggest that corticosteroids play a central role in mediating the elasmobranch stress response similar to that observed in other vertebrate taxa. Additionally, increases in glucose and osmolality corresponding to elevated concentrations of plasma corticosteroids provide *in vivo* evidence for the hypothesized dual GC and MC role of the dominant elasmobranch corticosteroid, 1a-B.

To further advance our understanding of the dual physiological role of 1a-B, we isolated sequences encoding *D. sabina* corticosteroid receptors. In most vertebrates, GC and MC actions are mediated through two receptors, the glucocorticoid receptor (GR) and the mineralocorticoid receptor (MR). However, little is known regarding the activity of these receptors in elasmobranchs as no full mRNA sequences are available. In this study, we used degenerate PCR coupled with rapid amplification of cDNA ends (RACE) to isolate mRNAs encoding both the GR and MR in *D. sabina*, and then compared the *D. sabina* sequences to those from other vertebrate taxa to examine similarities in protein structure that might lend insight into the functioning of these receptors in elasmobranchs. Alignment of the *D. sabina* MR protein sequence with that of other vertebrate taxa revealed a high level of conservation in both the DNA binding domain of the receptor and in amino acid residues involved in binding the steroid ligand (1a-B). A similar analysis in the GR also revealed conservation of key amino acid residues involved in steroid binding. These results suggest that the elasmobranch MR and GR function in a fashion similar to other vertebrate corticosteroid receptors.

This study advances our understanding of the elasmobranch stress response by characterizing the secretion of corticosteroids during acute stress, providing *in vivo* evidence for the dual GC and MC actions of 1a-B, as well as critical molecular tools for elucidating the function of receptors involved in mediating 1a-B's dual roles. Future studies should build on these results and seek to answer several important questions, including whether or not the novel structure of 1a-B elicits physiological responses that differ from those of corticosteroids in other taxa, and how the dual GC and MC functions of 1a -B are differentially regulated. Such studies will contribute to our understanding of elasmobranch stress physiology, directly addressing a critical gap in elasmobranch research.

LITERATURE CITED

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