A BIOBEHAVIORAL PROFILE OF AN ULCER SUSCEPTIBLE RAT STRAIN

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Selye not only formalized the stress concept, but made stress the legitimate subject of scientific inquiry. Since his seminal publications, we recognize that stress is a ubiquitous phenomenon that is related to the development of many diseases, including mood disorders. Everyone is exposed to stress in one form or another, but not all individuals succumb to the effects of stress. It is also intriguing that, in some cases, a seemingly innocuous stressor can cause profound disturbances in some subjects, but have little effect on others. This problem of subject variability is countered by examining the effects of stress in an individual that is either hyperreactive to stress, or is either predisposed to the illness under study. Therefore stress hyperreactive animal strains are valuable tools in studying the connections between disease states and stress. We have observed that the Wistar Kyoto (WKY) rat strain is vulnerable to stress effects.

The WKY rat strain was developed as the normotensive control strain to the spontaneously hypertensive rat (SHR). While the WKY rat may be an appropriate control strain for hypertension studies, the strain manifests certain behavioral idiosyncrasies and cannot be considered a normal control strain for behavioral studies. Our investigations have indicated that WKY rats manifest distinct behavioral and physiological responses to stress. These responses suggest the presence of a biobehavioral profile in WKY rats with stress ulcer susceptibility and behavioral depression as major manifestations of this profile.

BEHAVIORAL STUDIES

When WKY rats are observed in the open field test of emotionality, they exhibit little exploratory behavior. WKY rats rapidly adopt an immobile posture in the Porsolt forced swim test. In addition, WKY rats readily acquire a learned helplessness response. The forced swim test and the learned helplessness procedure are putative models of depression. WKY rats score highly in both procedures. Therefore, we have suggested that WKY rats are prone to depressive behavior.

While WKY rats typically obtain high score on behavioral tests of depressive behavior, the question remains whether other tests of emotional behavior will also
discriminate between WKY rats and rats from other strains. To address this question, WKY, Wistar and Fischer-344 (F-344) rats were exposed to one of three behavioral test of anxiety\textsuperscript{11}. Thus, rats from all three strains were exposed to either the defensive-withdrawal test\textsuperscript{12}, the elevated plus maze\textsuperscript{13}, or the defensive burying test\textsuperscript{14}. Anxiolytic agents typically influence behaviors in these three tests. Following behavioral testing, all rats were then exposed to the ulcerogenic water-restraint procedure\textsuperscript{15}. None of these tests were consistently effective in discriminating WKY rats from the other two strains, except the defensive burying test. The response, however, of WKY rats in the defensive burying test was unorthodox. The "anxiety" response in defensive burying involves burying, with bedding material, a shocking prod that protrudes from one of the test enclosure walls. Rats from the other strains invariably showed this burying response after being shocked by the prod, but WKY rats consistently withdrew to the opposite corner of the cage and remained immobile throughout the testing period. We believe that this immobility response is just another manifestation of depressive behavior in WKY rats. In addition, WKY rats in this study had more ulcer when subsequently exposed to restraint stress\textsuperscript{11}.

WKY rats also perform consistently on different tests of depressive behavior. WKY and Wistar rats were exposed, in a semi-random fashion, to the open field test, the defensive burying test, the Porsolt forced swim test, and the learned helplessness paradigm. The forced swim test was positively correlated with the learned helplessness procedure and, to a lesser degree with defensive burying, but these relationships were observed only in WKY rats, not Wistar rats. We concluded that WKY rats represented a more sensitive strain for detecting possible relationships between putative animal models of depression. Following the conclusion of the behavioral testing, all rats were exposed to water-restraint stress. WKY rats also had more ulcers than Wistar rats\textsuperscript{16}.

If the predominant coping strategy for WKY rats is freezing and immobility, then WKY rats should be superior in adopting a passive avoidance response, wherein the learned response involves the inhibition of a prepotent active response. We observed this to be the case when WKY, Wistar and F-344 rats were tested in two passive avoidance procedures - a platform step-down procedure and a light chamber - dark chamber one-way avoidance procedure. Rats were assigned to either one of the two procedures and then exposed to water-restraint stress. WKY rats not only adopted these passive avoidance responses faster that Wistar and F-344 rats, but demonstrated a fascinating behavior in the one-way avoidance task. While rats from the other strains would re-enter, during extinction trials, the dark compartment in which shock had been previously experienced, WKY rats would straddle the threshold between the two chambers for the duration of the testing period. We have labelled this behavior, "ambivalence behavior," and propose that it reflects the decision-making paralysis that characterizes depressed patients. WKY rats also had more ulcer following water-restraint stress\textsuperscript{17}.

The propensity to recall unpleasant memories contributes to the symptomatology of depression\textsuperscript{18}. This phenomenon was observed in WKY rats. WKY and Wistar rats were trained on a one-way avoidance task (i.e., the unpleasant event) but were also exposed to grid shock, either prior to (i.e., the proactive treatment) or after (i.e., the retroactive treatment) passive avoidance training. Subsequent test trials revealed that the retention of the unpleasant event was more pronounced for the proactive treatment, and this effect was dramatically greater in WKY rats as compared to Wistar rats.