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Effects of Diet on Sensitivity to Social Defeat Stress in Mice*



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There is a well-established link between stress exposure and risk for psychiatric disorders. However, only a small subset of stress-exposed subjects develops symptoms of psychiatric disorders. These individuals are termed stress-sensitive. The majority of stress-exposed subjects prove resilient. Both environmental and genetic factors likely contribute to stress-sensitivity or stress-resiliency. One potential environmental factor is diet. The purpose of this experiment is to identify whether a diet high in fat or sucrose will influence sensitivity to social defeat stress (SDS) in mice as measured by anxiety- and depression-like behavior.

Using a 2x3 design, C57BL6/N mice (C57) were assigned to either SDS or non-stress (NS) and sub-divided by a high sucrose diet (HSD), a high fat diet (HFD) or a standard chow (Chow) diet. During the SDS exposure, C57s were placed in the home cage of an older, larger, aggressive mouse (CD-1) for five minutes, during which the CD-1 attacked the C57. For the remaining 24 hours, the mice were housed together with sensory but not physical contact possible through a Plexiglas divider. This procedure was repeated for 10 days with a novel CD-1 resident each day. Experimental diets were administered only during these 10 days of SDS. To assess sensitivity or resiliency to the SDS, behavior was measured in the social interaction test (SI), open field test (OF), elevated zero maze (EZM), and tail suspension test (TST). The SI test measures social avoidance as the ratio of time spent in an interaction zone with the social target present vs. a social target absent. In this test, a ratio <1 is interpreted as social avoidance. OF measures anxiety-like behavior and locomotion; decreased percent time in the center is interpreted as anxiety-like behavior. EZM measures approach / avoidance; decreased percent time in open areas is interpreted as anxiety-like behavior and decreased rearing is interpreted as non-exploratory behavior. TST measures behavioral despair; increased percent time immobile is interpreted as depressive-like behavior.

Compared to control subjects, all stress-exposed mice, regardless of diet, exhibited decreased social interaction in the SI test. SDS mice also exhibited increased anxiety-

like behavior in the OF as measured by decreased percent time in the center and increased anxiety-like behavior in the EZM as measured by decreased percent time in the open areas. Interestingly, there was also a main effect of diet in the EZM; HFD mice from either stress group had a trend for increased rearing, or exploratory behavior, compared to the HSD mice (Post-hoc Tukey test, $p = 0.064$). There was also a main effect of diet in the OF test; NS mice on the Chow diet exhibited the least anxiety-like behavior as measured by increased percent time in the center compared to the NS mice on HFD and HSD, which had a decreased percent time in the center, similar to the SDS mice ($p = 0.022$).

Our results suggest that consuming an unhealthy diet high in fat or sucrose can increase anxiety, even in the absence of stress. Future directions include analysis of hormones in blood plasma and expression of hypothalamic genes relevant to interactions between stress, diet, and behavior.

*This scholar and faculty mentor have requested that only an abstract be published.