DEVELOPMENT OF AN EXTERNALLY VALID MOUSE MODEL OF DEPRESSION THROUGH L-TRYPTOPHAN DIETARY DEPLETION AND NEONATAL CORTICOSTERONE ADMINISTRATION

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Depression, a pathology characterised by mood and neuro-vegetative disturbances, depends on a multi-factorial contribution of individual predisposition (e.g. diminished serotonergic transmission) and environmental factors (e.g. neonatal abuse or neglect). Despite these evidences, most animal models of depression only address one or the other factor thereby resulting of poor face validity. Here we describe a novel animal model of depression aimed at holding construct, face and predictive validity. In order to mimic the aforementioned factors in the development of depressive-like alterations, mouse pups have been reared by dams exposed to corticosterone (the "stress hormone") in the drinking water, and/or to an L-tryptophan (serotonin precursor) deficient diet. Four groups of CD1 mouse dams (N=12-13 per group) were exposed to Animal Facility Rearing conditions (AFR group), given access to the L-tryptophan restricted diet between postnatal day (P)0-8 (T group), to corticosterone between P1-8 (C group) or both (TC group). Maternal behaviour was observed between P0-10 (3 daily, 75-min sessions); daily water intake and pups’ body weight were also measured. Active maternal care steadily declined in all groups throughout lactation and was significantly higher in AFR dams compared to C, T and TC dams. Thus, AFR dams displayed significantly more active nursing (arched back nursing and licking) than all treated dams. Time-budget wise, while T dams showed more activity out of the nest, C and TC dams showed increased resting time. Additionally, C dams showed increased water intake compared to T, AFR and TC; T dams had the lowest water intake. Pups' body weight increased steadily in all groups between P 11-23. However, C and TC pups were significantly lighter than both T and AFR. Additionally, data on anxiety- and depressive-like behaviour in adolescent and adult offspring will be presented. Although preliminary, these data support the hypothesis that a combination of natural predispositions and environmental stress, be the latter in the form of corticosterone administration, reduced maternal care or both, contribute to induce disturbances isomorphic to human depression. The route of administration and the possibility to control the independent variables predisposing to depressive-like symptoms disclose novel avenues towards the development of valid animal models.