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### **Layers response to a suboptimal diet through phenotype and transcriptome changes in four tissues**

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Poultry meat and eggs are major sources of nutrients in the human diet. The long production career of laying hens expose them to biotic or abiotic stressors, lowering their production. Understanding the mechanisms of adaptation to stress is crucial for selecting robust animals and meeting the needs of a growing human population. In this study, financed by the French ChickStress and the European Feed-a-Gene (grant agreement no. 633531) programs, we compared the effects of a 15%-energy-reduced diet (feed stress, FS) vs a commercial diet (control, CT) on phenotypic traits and adipose, blood, hypothalamus and liver transcriptomes in two feed-efficiency-diverging lines. Phenotypic traits showed differences between lines or diets, but no line × diet interaction. In the FS group, feed intake (FI) increased and hens had lower body- and abdominal adipose weight, compared to CT group. We found no differences in egg production or quality. At the transcriptomic level, 16,461 genes were expressed in one or more tissues, 41% of which were shared among tissues. We found differentially expressed genes between lines or diet in all tissues, and almost no line × diet interactions. Focusing on diet, adipose and liver transcriptomes were unaffected. In blood, pathways linked to amino acids, monosaccharides, and steroid metabolism were affected, while in the hypothalamus, changes were observed in fatty acid metabolism and endocannabinoid signalling. Given the similarities in egg production, the FS animals seem to have adapted to the stress by increasing FI and by mobilizing adipose reserves. Increase in FI did not appear to affect liver metabolism, and the mobilization of adipose reserves was apparently not driven at the transcriptomic level. In blood, the pathways linked to metabolic processes suggest a metabolic role for this tissue in chicken, whose erythrocytes are nucleated and contain mitochondria. FI increase might be linked to the hypothalamic pathway of endocannabinoid signalling, which are lipid-based neurotransmitters, notably involved in the regulation of appetite.