The laboratory mouse (strain MF1) was used as a model animal to study the hypothalamic mechanisms underlying food intake in lactating animals. Sixty female mice exposed to 21°C were fed high fat (HF), medium fat (MF) and low fat (LF) diets ad libitum between days 4 and 18 of lactation. Also fifteen (15) non-reproductive females exposed to 21°C but used as controls were fed ad libitum on the same diets (HF, MF; and LF) for 14 days. Fifteen (15) lactating/reproductive females each from HF, MF and LF-fed groups and 5 non-reproductive controls each from HF, MF and LF-fed groups were weighed and killed by CO2 inhalation on day 18 of lactation. Brains from both the reproductive and non-reproductive females were processed for studies on hypothalamic neuropeptides. Results indicated that lactation decreased pro-opiomelanocortin (POMC) and increased neuropeptide Y (NPY) and agouti-related peptide (AgRP) gene expression determined by in situ hybridisation in the hypothalamic arcuate nucleus (ARC). There was no significant change in suppressor of cytokine signalling-3 (SOCS-3) expression (P>0.05) in the ARC during lactation. Activated NPY and AgRP or exigenic pathways and attenuated anorexigenic POMC pathways in the hypothalamus probably promoted the hyperphagia of lactation in the MF1 mice. Since NPY and AgRP increased (P0.05) but SOCS-3 was unchanged probably indicate that the MF1 mice were sensitive to the action of leptin. Keywords: neuropeptide y (NPY), agouti-related peptide (AgRP), pro-opiomelanocortin (POMC), suppressor of cytokine signalling-3 (SOCS-3), leptin.