The identification of the mutated familial hemiplegic migraine (FHM) genes stimulated interest in the link between genotype and phenotype using both molecular studies and animal models. The functional consequences of the FHM mutations in humans are unknown. Genotyped FHM patients offer us the chance to study the interplay between genotype and phenotype and may be regarded as a valuable genetic migraine model. We therefore examined the relationship between FHM mutations and the known migraine-inducing substances glycercyl trinitrate (GTN) and calcitonin gene related peptide (CGRP). Provocation experiments showed that both GTN and CGRP failed to induce more migraine-like attacks in FHM-patients with pure FHM phenotype than in healthy controls. These data indicate that the FHM genotype does not confer hypersensitivity to migraine triggers such as GTN and CGRP and raise the question whether FHM is a useful genetic model for common migraines.