Our study found that patients clustered together regardless of mutation, but that they had some overlap with controls when all metabolites were taken into account. Multivariate feature selection identified 18 influential metabolites for RTT patients and 17 for hypo-glutamatergic disorders, while univariate hypothesis testing found 17 significantly altered metabolites in RTT and 7 in hypo-glutamatergic disorders. There were 10 metabolites in RTT and 7 in hypo-glutamatergic disorders that were selected by both methods. Of these, only 4 metabolites (3-hydroxyanthranilic acid, trigonelline, galactose, and indole-3-propionic acid) had increased concentrations in RTT and 2 (trigonelline and indole-3-propionic acid) in hypo-glutamatergic disorders. Pathway analysis showed that these metabolites were mostly involved in amino acid and energetic metabolism, especially in tryptophan and galactose metabolism. The two groups of patients showed highly similar metabolic profiles, though 11 metabolites (3-hydroxyanthranilic acid, leucine, glycerol, d-xylitol, 4-hydroxyphenyllactic acid, d-fructose, galactose, d-gluconic acid, saccharic acid, myo-inositol, sedoheptulose) were identified as altered on RTT but not on hypo-glutamatergic disorders. This could be due to the smaller number of hypo-glutamatergic patients that were available for the study, and it may be worthwhile for further studies to replicate this analysis on a larger cohort of these specific disorders.