Figure S1. Cell type proportions at different time points. Comparison of the size of each cellular cluster between WT and PD conditions (a) at day 30 (D30) and (b) at day 60 (D60) of organoid culture expressed as a proportion of the total amount of cells belonging to the respective cluster in the single cell RNAseq object.

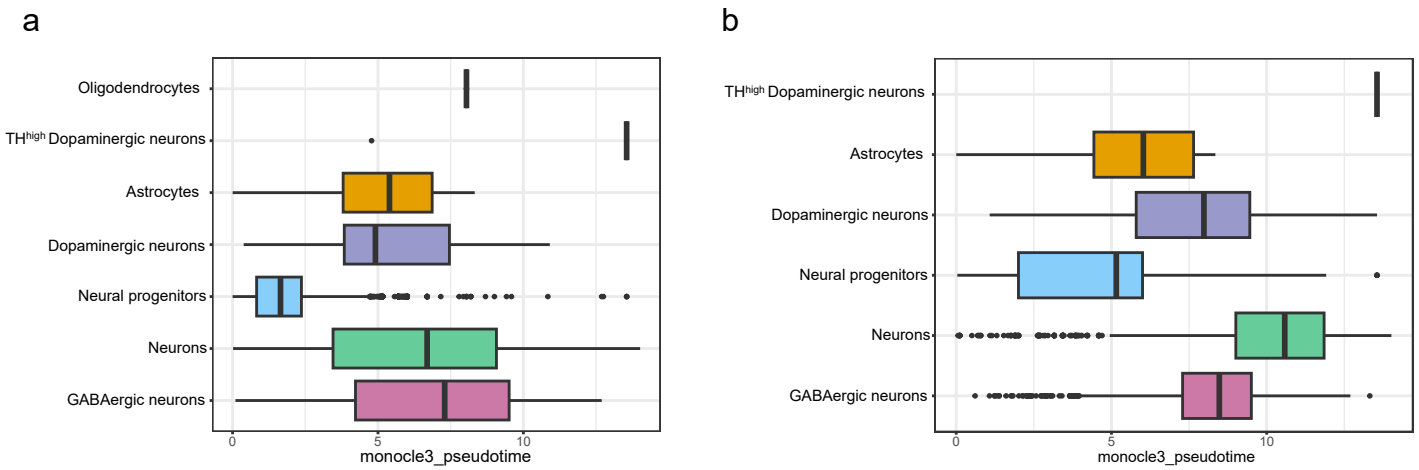

Figure S2. MIRO1 mutant organoids show loss of vulnerable dopaminergic neurons and altered developmental path of cellular populations. (a) Estimated pseudotime for all cell types in WT midbrain organoids (combined day 30 and day 60). (b) Estimated pseudotime for all cell types in PD midbrain organoids (combined day 30 and day 60).

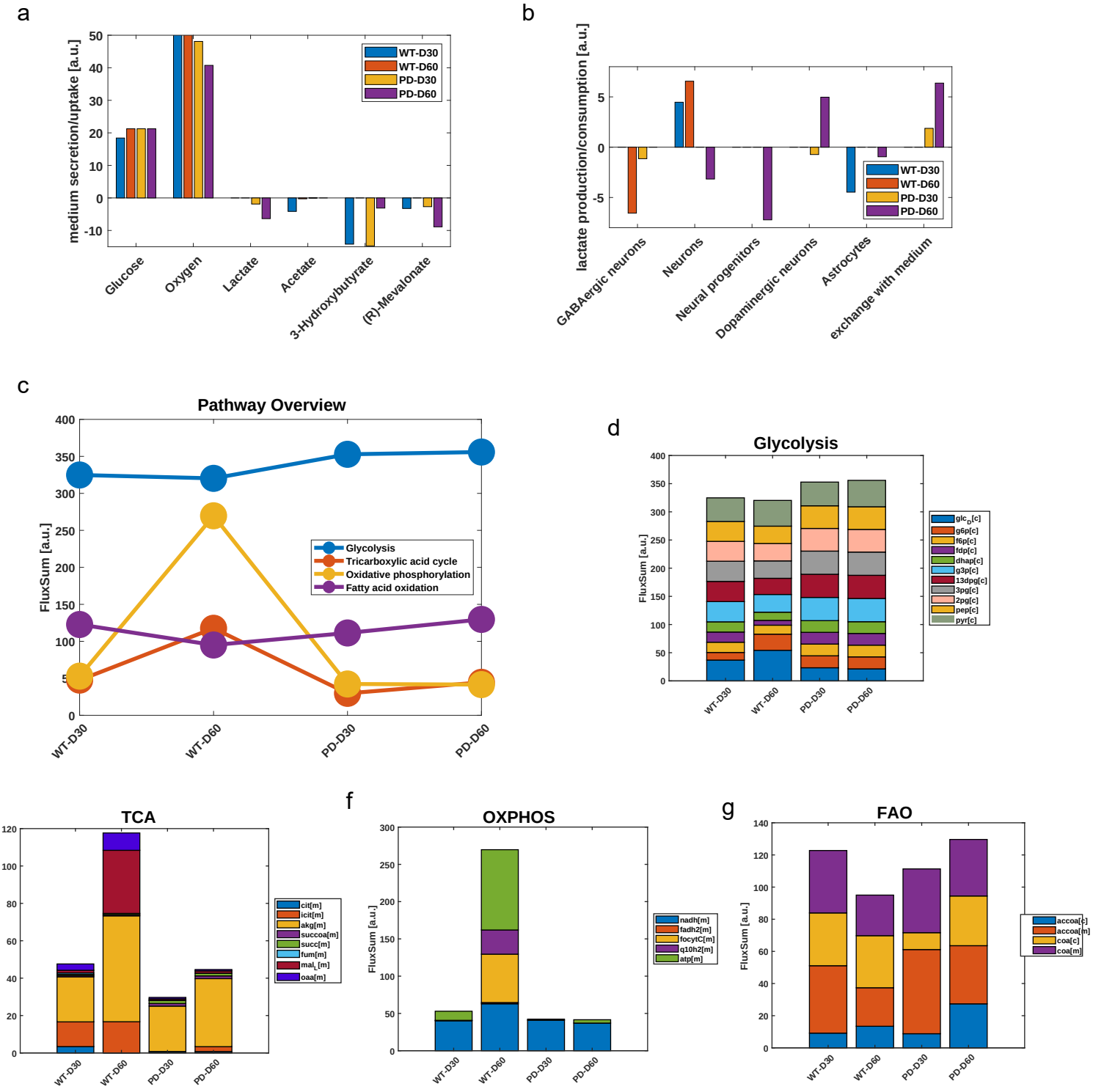

Figure S3. Multi-cell population metabolic modelling predictions are insensitive to maximal oxygen increase. (a) Predicted medium uptake and secretion rates of midbrain organoids for key metabolites. Positive values [a.u.] indicate uptake of the respective metabolite and negative values [a.u.] indicate secretion. (b) Predicted lactate inter-cellular exchange between different cell types. Negative values [a.u.] indicate production of the respective metabolite and positive values [a.u.] indicate uptake (or secretion to the medium). (c) Fluxsum estimates show the metabolic dependence of the midbrain organoid conditions in each energy pathway. Estimates are done by the sum of relevant metabolites (see Table S5) within the respective pathway. (d-g) Metabolic activities are estimated by calculating the FluxSum (in [a.u.]) per metabolite across all cells of the organoid (sum of incoming metabolic fluxes in FBA solution) and are shown as bar plots of key metabolites per metabolic pathway (complete metabolite names corresponding to abbreviations are summarized at Table S5).

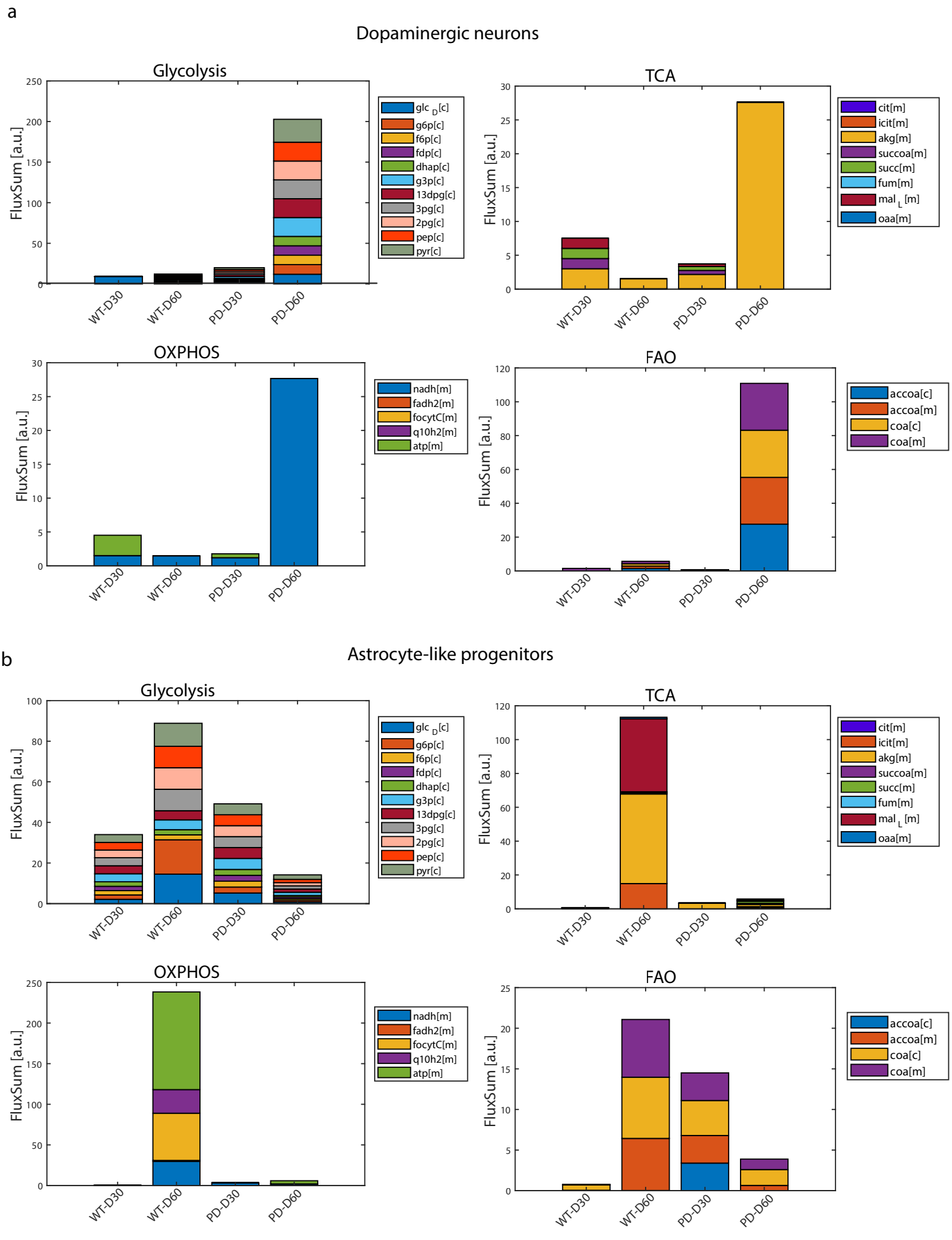

Figure S4. Multi-cell population modelling predicts differential activities of core metabolic pathways in WT vs PD conditions. Estimated FluxSum (in [a.u.]) per metabolite (sum of incoming metabolic fluxes in FBA solution) in (a) dopaminergic neurons and (b) astrocytes and are shown as bar plots of key metabolites per metabolic pathway.

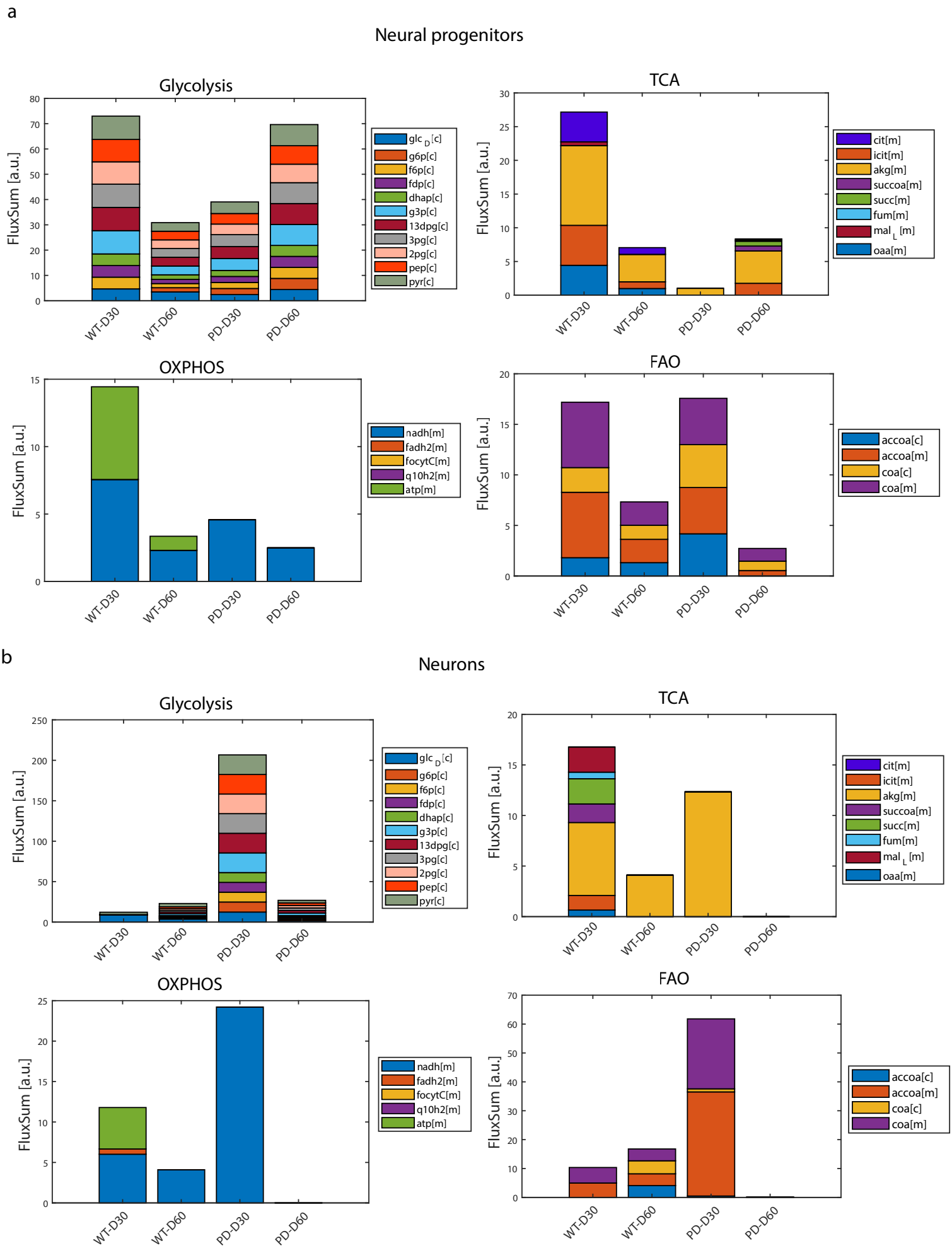

Figure S5. Multi-cell population modelling predicts differential activities of core metabolic pathways in WT vs PD conditions. Estimated FluxSum (in [a.u.]) per metabolite (sum of incoming metabolic fluxes in FBA solution) in (a) neurons and (b) neural progenitor cells and are shown as bar plots of key metabolites per metabolic pathway.

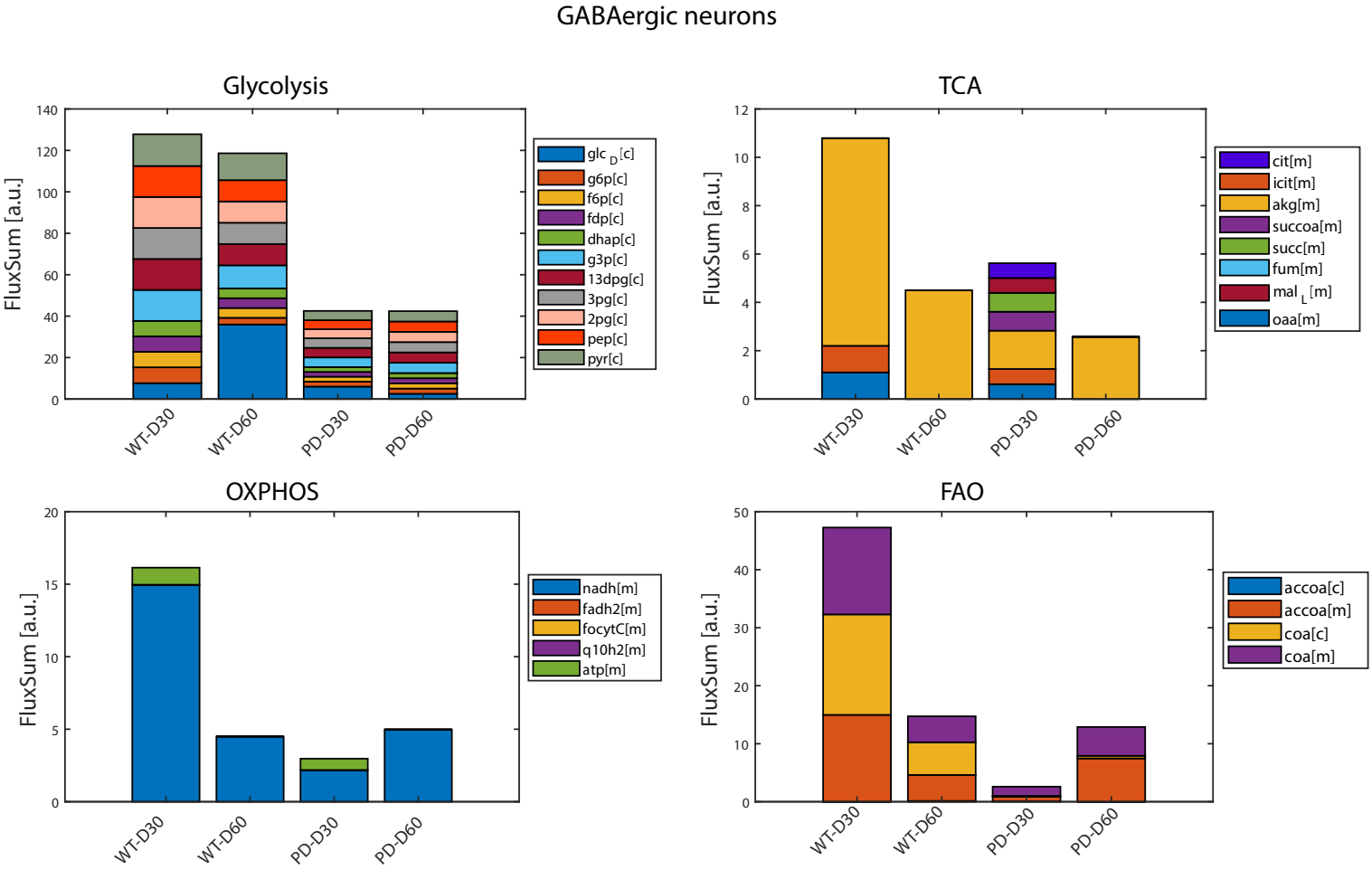

Figure S6. Multi-cell population modelling predicts differential activities of core metabolic pathways in WT vs PD conditions. Estimated FluxSum (in [a.u.]) per metabolite (sum of incoming metabolic fluxes in FBA solution) in GABAergic neurons and are shown as bar plots of key metabolites per metabolic pathway.