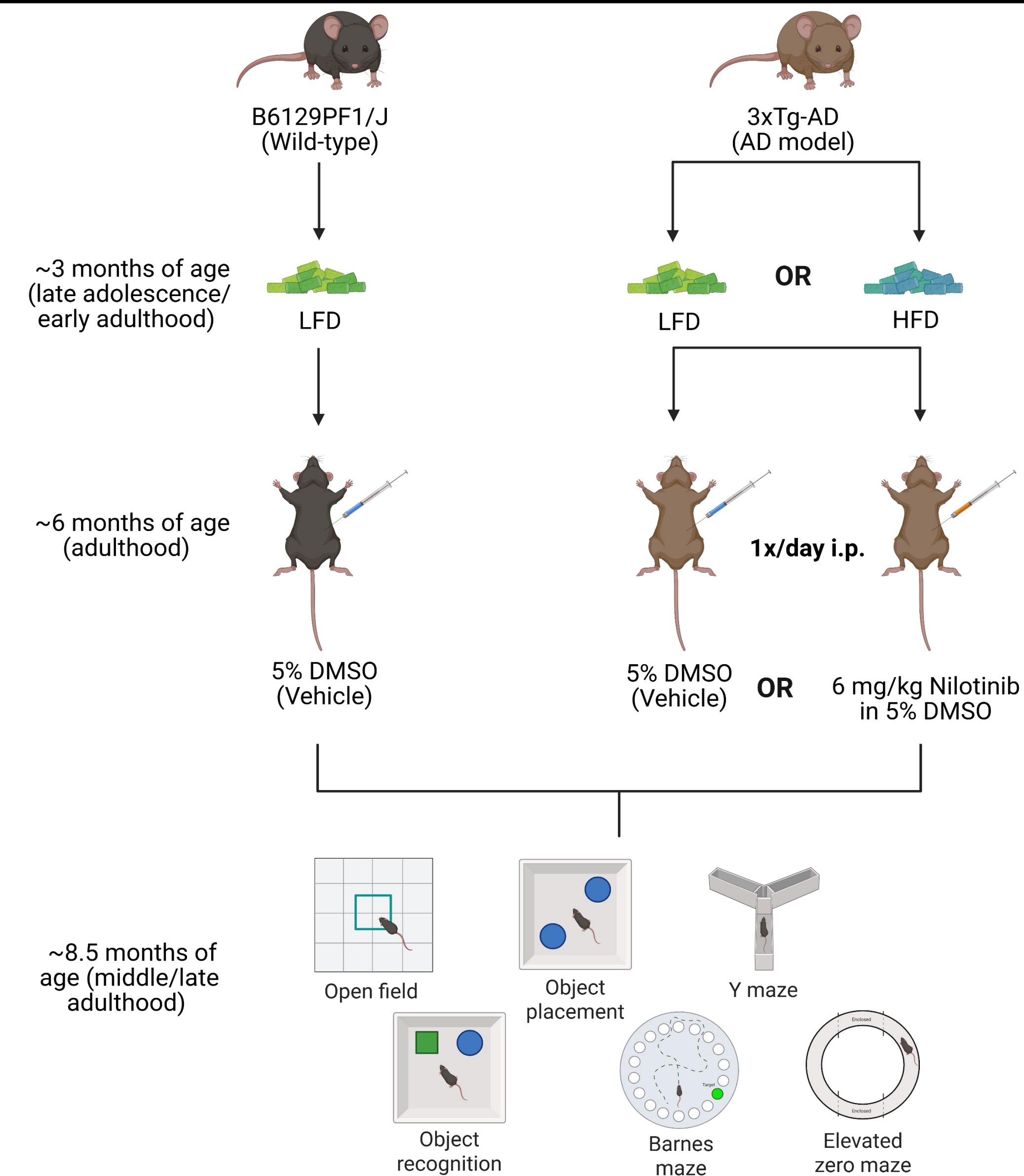


HFD induced significant metabolic impairments in 3xTg-AD mice, including increased weight, adiposity, and impaired glucose tolerance, with effects more pronounced in females than in males. In the open field, 3xTg-AD mice showed reduced locomotor activity and exploratory behavior compared to control mice, regardless of diet. Nilotinib treatment partially improved exploratory behavior and reduced anxiety-like behavior in male 3xTg-AD kept on LFD. This group also showed trends toward improved performance in spatial recognition memory (Object Placement Test) and long-term spatial memory (Barnes Maze).

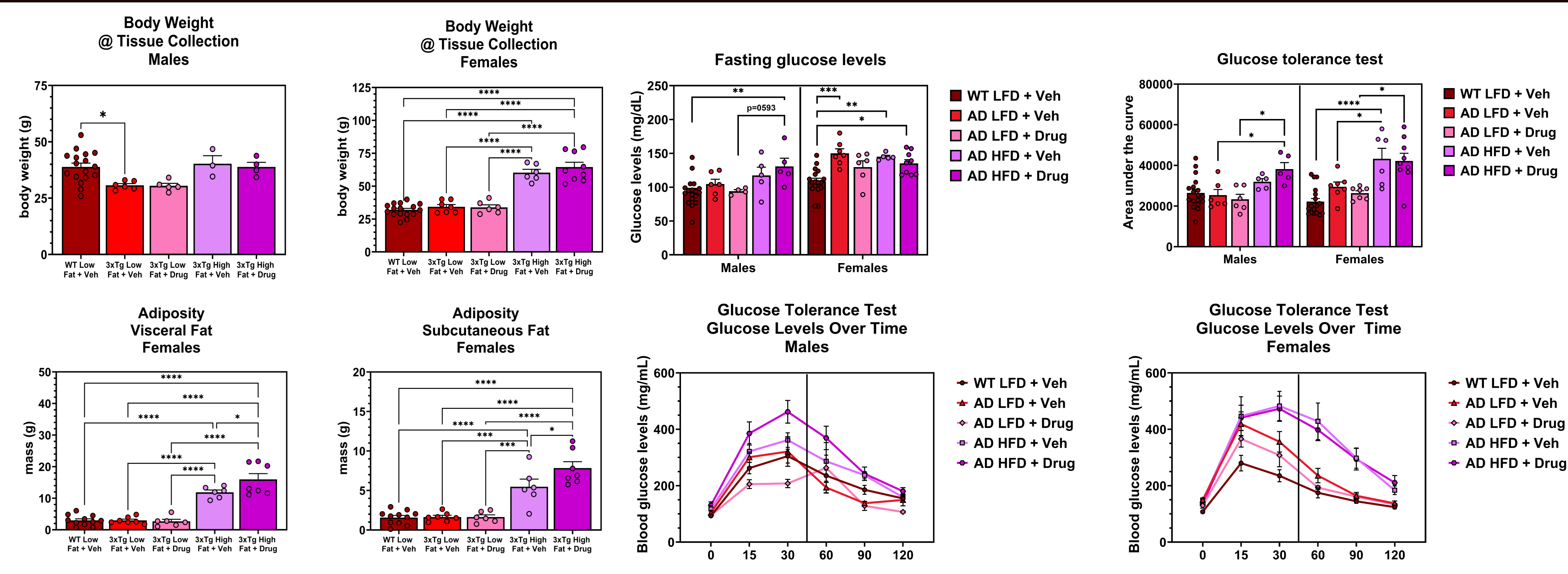
BACKGROUND

--**Alzheimer’s disease (AD)** is neurodegenerative disorder characterized by extracellular amyloid-β plaque deposition, intracellular aggregates of hyperphosphorylated tau, synaptic dysfunction, and neuroinflammation, all of which contribute to progressive cognitive decline [PMID: 26921134]
--Increasing evidence links **metabolic disorders**, such as obesity and type 2 diabetes, to a higher risk of AD, potentially through mechanisms involving insulin resistance, mitochondrial dysfunction, chronic inflammation, and cerebrovascular/BBB dysfunction [PMID: 30022099; PMID 32993686]. These processes may impair neuronal bioenergetics and disrupt protein-clearance pathways, contributing to the accumulation of neurotoxic proteins.
--Therapeutic strategies that enhance autophagic clearance, such as the FDA-approved tyrosine kinase inhibitor **nilotinib**, have therefore emerged as potential approaches to mitigate AD pathology. [PMID: 39459541]
--This study examined whether **high-fat diet–induced metabolic dysfunction** alters cognitive, mitochondrial, and neuropathological outcomes in 3xTg-AD mice, and whether nilotinib treatment can mitigate AD pathology and associated cognitive-behavioral deficits.

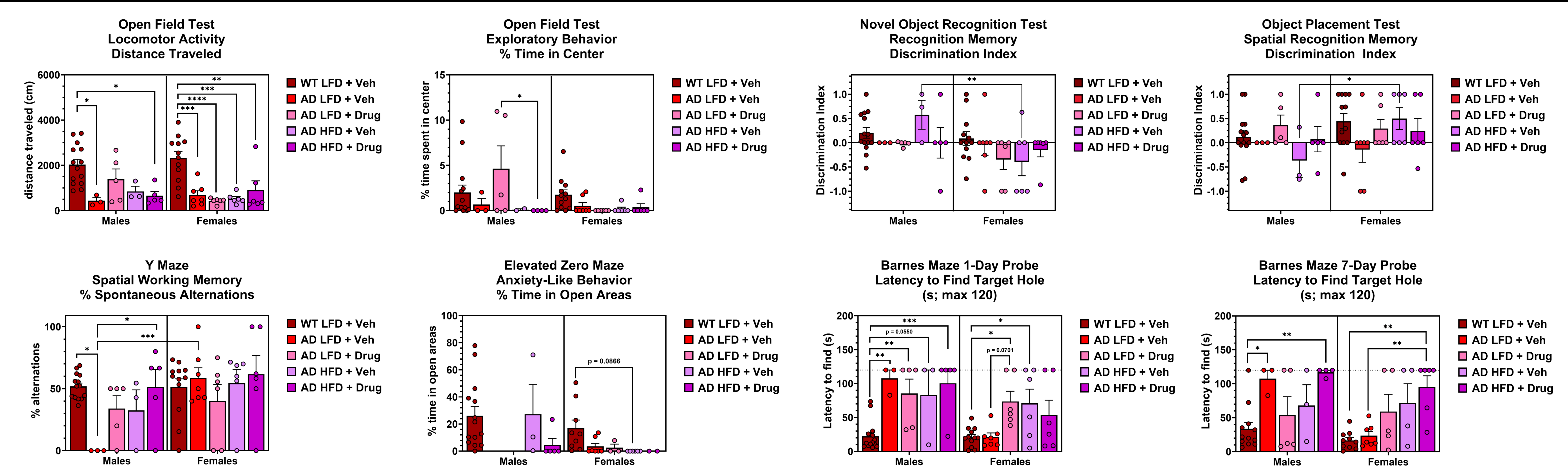
METHODOLOGY



METABOLIC RESULTS



BEHAVIORAL RESULTS



ACKNOWLEDGMENTS

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