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Sommario/riassunto	Down syndrome (DS), caused by the triplication of chromosome 21, is the most common genetic cause of intellectual disability (ID). Individuals with DS commonly exhibit unique neuropsychological profiles that emerge during specific developmental stages across the lifespan, often characterized by early developmental delay, cognitive strengths and weaknesses, behavior and mental health issues, and age-related cognitive decline, frequently resulting in early-onset Alzheimer's disease. These profiles are unique compared to other individuals with ID and reflect the genetic mechanisms and neuroanatomic features underlying the distinct neuropsychological phenotype associated with DS. This Special Issue aims to highlight the recent advancements in understanding the neuropsychological phenotype associated with DS across the lifespan. The lifespan perspective will cover four developmental stages: (1) early childhood; (2) school age; (3) young adulthood, and (4) older adulthood. Authors contributed cutting-edge original research studies and comprehensive reviews that address a broad range of topics related to DS, including early developmental trajectories, cognitive functioning, language, adaptive skills, behavior and mental health, assessment and diagnosis, age-related cognitive decline, and medical issues related to the neuropsychological phenotype and neuroimaging.