A119 · One Age, Many Clocks: System-Specific Metabolomic Aging and Its Links to Diet, Cognition, and Mortality

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Aging is a heterogeneous process that unfolds at different rates across multiple biological systems. Conventional single-tissue biological clocks collapse this multidimensional complexity into a single estimate, obscuring the system-level variability that is most relevant for understanding healthy aging. To address this limitation, we developed a set of system-specific aging clocks trained on metabolomics data, representing a methodological advance from single-tissue to multi-system biological age estimation. Each clock independently captures biological age acceleration within a distinct metabolic system, enabling decomposition of an individual's aging trajectory into a profile of system-level estimates and uncovering patterns a single clock would mask. Applying these clocks revealed striking inter-individual heterogeneity: some participants showed consistent age acceleration across all systems, others exhibited system-wide deceleration, and many demonstrated discordant profiles. We clustered participants into subgroups based on their multi-system aging profiles and examined their associations with (1) intake profiles across 19 nutrient groups; (2) cognitive performance assessed using neuropsychological tests, including the Trail Making Test and Digit Symbol Substitution Test; and (3) mortality risk. Subgroups characterized by concordant healthy aging profiles showed significantly better dietary behaviors, including good balance of macronutrients, alongside more favorable cognitive outcomes and reduced mortality risk. Subgroups with discordant or accelerated profiles showed poorer outcomes across all three domains. Notably, subgroup membership predicted mortality and cognitive outcomes better than any individual clock alone, underscoring the value of the multi-clock framework. These findings demonstrate that aging is system-specific and highlight the potential of system-specific metabolomic clocks to disentangle this complexity and enable precision interventions that target metabolic systems to extend health span.

One Age, Many Clocks: System-Specific Metabolomic Aging and Its Links to Diet, Cognition, and Mortality

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