
Supplementary materials: System dynamics model equations

Below the coupled system of algebraic-differential equations is provided for the auxiliaries and stocks. In these equations, θ_i represents the parameter that describes the relationship between the variable on the left-hand side of the equation as a function of the variable immediately to its right. The stocks and auxiliaries change over time whereas constants do not and thus have a “(t)” next to them to indicate a specific point in time.

Note that, in the auxiliary equations, only interactions between stocks and constants were included. This is due to the relatively large amount of missing values in the features that operationalize the auxiliary variables (see table 1 of the paper). Moreover, as discussed in the paper, all stock and auxiliary equations were adjusted for age, and all auxiliary equations were additionally adjusted for male sex (a constant) to correct for possible confounding effects. Finally, only those interaction terms that were preselected are shown for the stocks. That is, these terms had a relatively high total Sobol index, indicating they would be important to estimate (see Appendix D of the paper).

All parameters $\theta_1 \dots \theta_{250}$ were estimated in the model selection procedure. Several of these parameters were set to zero as part of the model selection procedure. The values of the estimated parameters are provided in the supplementary materials table.

AUXILIARIES

Healthy dietary patterns

$$\begin{aligned} \text{Mediterranean diet score} = & \theta_1 + \\ & \theta_2 \cdot \text{GDS}(t) + \\ & \theta_3 \cdot \text{Currently married} + \\ & \theta_4 \cdot \text{Received education} + \\ & \theta_5 \cdot \text{Age}(t) + \\ & \theta_6 \cdot \text{Male sex} + \\ & \theta_7 \cdot \text{GDS}(t) \cdot \text{Currently married} + \\ & \theta_8 \cdot \text{GDS}(t) \cdot \text{Received education} + \\ & \theta_9 \cdot \text{Currently married} \cdot \text{Received education} \end{aligned}$$

Physical activity

$$\begin{aligned} \text{METs hours per week} = & \theta_{10} + \\ & \theta_{11} \cdot \text{ADAS-cog-13}(t) + \\ & \theta_{12} \cdot \text{GDS}(t) + \\ & \theta_{13} \cdot \text{Currently married} + \\ & \theta_{14} \cdot \text{Received education} + \\ & \theta_{15} \cdot \text{Motor strength impairment} + \\ & \theta_{16} \cdot \text{Age}(t) + \\ & \theta_{17} \cdot \text{Male sex} + \\ & \theta_{18} \cdot \text{ADAS-cog-13}(t) \cdot \text{GDS}(t) + \\ & \theta_{19} \cdot \text{ADAS-cog-13}(t) \cdot \text{Currently married} + \\ & \theta_{20} \cdot \text{ADAS-cog-13}(t) \cdot \text{Received education} + \\ & \theta_{21} \cdot \text{ADAS-cog-13}(t) \cdot \text{Motor strength impairment} + \\ & \theta_{22} \cdot \text{GDS}(t) \cdot \text{Currently married} + \\ & \theta_{23} \cdot \text{GDS}(t) \cdot \text{Received education} + \\ & \theta_{24} \cdot \text{GDS}(t) \cdot \text{Motor strength impairment} + \\ & \theta_{25} \cdot \text{Currently married} \cdot \text{Received education} + \\ & \theta_{26} \cdot \text{Currently married} \cdot \text{Motor strength impairment} + \\ & \theta_{27} \cdot \text{Received education} \cdot \text{Motor strength impairment} \end{aligned}$$

Sleep quality

$$\begin{aligned} \text{PSQI} = & \theta_{28} + \\ & \theta_{29} \cdot \text{METs hours per week}(t) + \\ & \theta_{30} \cdot \text{FDG-PET}(t) + \\ & \theta_{31} \cdot \text{GDS}(t) + \\ & \theta_{32} \cdot \text{Currently married} + \\ & \theta_{33} \cdot \text{Age}(t) + \\ & \theta_{34} \cdot \text{Male sex} + \\ & \theta_{35} \cdot \text{FDG-PET}(t) \cdot \text{GDS}(t) + \\ & \theta_{36} \cdot \text{FDG-PET}(t) \cdot \text{Currently married} + \\ & \theta_{37} \cdot \text{GDS}(t) \cdot \text{Currently married} \end{aligned}$$

Experienced stress

$$\begin{aligned} \text{Cortisol plasma} = & \theta_{38} + \\ & \theta_{39} \cdot \text{PSQI}(t) + \\ & \theta_{40} \cdot \text{GDS}(t) + \\ & \theta_{41} \cdot \text{Currently married} + \\ & \theta_{42} \cdot \text{Age}(t) + \\ & \theta_{43} \cdot \text{Male sex} + \\ & \theta_{44} \cdot \text{GDS}(t) \cdot \text{Currently married} \end{aligned}$$

Systemic inflammation

$$\begin{aligned} \text{TNF-alpha plasma} = & \theta_{45} + \\ & \theta_{46} \cdot \text{Mediterranean diet score}(t) + \\ & \theta_{47} \cdot \text{METs hours per week}(t) + \\ & \theta_{48} \cdot \text{Cortisol plasma}(t) + \\ & \theta_{49} \cdot \text{Fasting glucose}(t) + \\ & \theta_{50} \cdot \text{Morbidity score}(t) + \\ & \theta_{51} \cdot \text{BMI}(t) + \\ & \theta_{52} \cdot \text{Age}(t) + \\ & \theta_{53} \cdot \text{Male sex} + \\ & \theta_{54} \cdot \text{Morbidity score}(t) \cdot \text{BMI}(t) \end{aligned}$$

Brain perfusion

$$\begin{aligned} \text{Hippocampal cerebral blood flow} = & \theta_{55} + \\ & \theta_{56} \cdot \text{METs hours per week}(t) + \\ & \theta_{57} \cdot \text{WMH volume}(t) + \\ & \theta_{58} \cdot \text{Age}(t) + \\ & \theta_{59} \cdot \text{Male sex} \end{aligned}$$

Oxidative stress

$$\begin{aligned} \text{Superoxide dismutase plasma} = & \theta_{60} + \\ & \theta_{61} \cdot \text{Mediterranean diet score}(t) + \\ & \theta_{62} \cdot \text{Cortisol plasma}(t) + \\ & \theta_{63} \cdot \text{Smoking} + \\ & \theta_{64} \cdot \text{Alcohol abuse} + \\ & \theta_{65} \cdot \text{Age}(t) + \\ & \theta_{66} \cdot \text{Male sex} + \\ & \theta_{67} \cdot \text{Smoking} \cdot \text{Alcohol abuse} \end{aligned}$$

Neuroinflammation

$$\begin{aligned} \text{TNF-alpha csf} = & \theta_{68} + \\ & \theta_{69} \cdot \text{Mediterranean diet score}(t) + \\ & \theta_{70} \cdot \text{TNF-alpha plasma}(t) + \\ & \theta_{71} \cdot \text{Superoxide dismutase plasma}(t) + \\ & \theta_{72} \cdot \text{A-beta csf}(t) + \\ & \theta_{73} \cdot \text{Traumatic brain injury} + \\ & \theta_{74} \cdot \text{Age}(t) + \\ & \theta_{75} \cdot \text{Male sex} + \\ & \theta_{76} \cdot \text{A-beta csf}(t) \cdot \text{Traumatic brain injury} \end{aligned}$$

Neuronal connectivity

$$\begin{aligned} \text{DMN connectivity anterior-posterior ratio} = & \theta_{77} + \\ & \theta_{78} \cdot \text{METs hours per week}(t) + \\ & \theta_{79} \cdot \text{PSQI}(t) + \\ & \theta_{80} \cdot \text{FDG-PET}(t) + \\ & \theta_{81} \cdot \text{Age}(t) + \\ & \theta_{82} \cdot \text{Male sex} \end{aligned}$$

Diabetes

$$\begin{aligned} \text{Fasting glucose} = & \theta_{83} + \\ & \theta_{84} \cdot \text{Mediterranean diet score}(t) + \\ & \theta_{85} \cdot \text{BMI}(t) + \\ & \theta_{86} \cdot \text{Age}(t) + \\ & \theta_{87} \cdot \text{Male sex} \end{aligned}$$

Dyslipidaemia

$$\begin{aligned} \text{Total cholesterol} = & \theta_{88} + \\ & \theta_{89} \cdot \text{Mediterranean diet score}(t) + \\ & \theta_{90} \cdot \text{Fasting glucose}(t) + \\ & \theta_{91} \cdot \text{BMI}(t) + \\ & \theta_{92} \cdot \text{ApoE-4 alleles} + \\ & \theta_{93} \cdot \text{Age}(t) + \\ & \theta_{94} \cdot \text{Male sex} + \\ & \theta_{95} \cdot \text{BMI}(t) \cdot \text{ApoE-4 alleles} \end{aligned}$$

STOCKS

Cognitive functioning

$$\begin{aligned} \frac{\text{dADAS-cog-13}}{\text{dt}} = & \theta_{96} + \\ & \theta_{97} \cdot \text{PSQI}(t) + \\ & \theta_{98} \cdot \text{Hippocampal cerebral blood flow}(t) + \\ & \theta_{99} \cdot \text{DMN connectivity anterior-posterior ratio}(t) + \\ & \theta_{100} \cdot \text{FDG-PET}(t) + \\ & \theta_{101} \cdot \text{GDS}(t) + \\ & \theta_{102} \cdot \text{Hearing impairment} + \\ & \theta_{103} \cdot \text{Age}(t) + \\ & \theta_{104} \cdot \text{PSQI}(t) \cdot \text{FDG-PET}(t) + \\ & \theta_{105} \cdot \text{PSQI}(t) \cdot \text{GDS}(t) + \\ & \theta_{106} \cdot \text{PSQI}(t) \cdot \text{Hearing impairment} + \\ & \theta_{107} \cdot \text{Hippocampal cerebral blood flow}(t) \cdot \text{FDG-PET}(t) + \\ & \theta_{108} \cdot \text{FDG-PET}(t) \cdot \text{GDS}(t) + \\ & \theta_{109} \cdot \text{FDG-PET}(t) \cdot \text{Hearing impairment} + \\ & \theta_{110} \cdot \text{GDS}(t) \cdot \text{Hearing impairment} \end{aligned}$$

Neuronal dysfunction

$$\begin{aligned} \frac{d\text{FDG-PET}}{dt} = & \theta_{111} + \\ & \theta_{112} \cdot \text{Mediterranean diet score}(t) + \\ & \theta_{113} \cdot \text{Hippocampal cerebral blood flow}(t) + \\ & \theta_{114} \cdot \text{Superoxide dismutase plasma}(t) + \\ & \theta_{115} \cdot \text{TNF-alpha csf}(t) + \\ & \theta_{116} \cdot \text{WMH volume}(t) + \\ & \theta_{117} \cdot \text{A-beta csf}(t) + \\ & \theta_{118} \cdot \text{P Tau csf}(t) + \\ & \theta_{119} \cdot \text{Smoking} + \\ & \theta_{120} \cdot \text{Alcohol abuse} + \\ & \theta_{121} \cdot \text{Traumatic brain injury} + \\ & \theta_{122} \cdot \text{Age}(t) + \\ & \theta_{123} \cdot \text{Mediterranean diet score}(t) \cdot \text{Superoxide dismutase plasma}(t) + \\ & \theta_{124} \cdot \text{Mediterranean diet score}(t) \cdot \text{TNF-alpha csf}(t) + \\ & \theta_{125} \cdot \text{Mediterranean diet score}(t) \cdot \text{WMH volume}(t) + \\ & \theta_{126} \cdot \text{Mediterranean diet score}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{127} \cdot \text{Hippocampal cerebral blood flow}(t) \cdot \text{WMH volume}(t) + \\ & \theta_{128} \cdot \text{Superoxide dismutase plasma}(t) \cdot \text{TNF-alpha csf}(t) + \\ & \theta_{129} \cdot \text{Superoxide dismutase plasma}(t) \cdot \text{WMH volume}(t) + \\ & \theta_{130} \cdot \text{Superoxide dismutase plasma}(t) \cdot \text{Smoking} + \\ & \theta_{131} \cdot \text{Superoxide dismutase plasma}(t) \cdot \text{Alcohol abuse} + \\ & \theta_{132} \cdot \text{Superoxide dismutase plasma}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{133} \cdot \text{TNF-alpha csf}(t) \cdot \text{WMH volume}(t) + \\ & \theta_{134} \cdot \text{TNF-alpha csf}(t) \cdot \text{A-beta csf}(t) + \\ & \theta_{135} \cdot \text{TNF-alpha csf}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{136} \cdot \text{WMH volume}(t) \cdot \text{Smoking} + \\ & \theta_{137} \cdot \text{WMH volume}(t) \cdot \text{Alcohol abuse} + \\ & \theta_{138} \cdot \text{A-beta csf}(t) \cdot \text{Alcohol abuse} + \\ & \theta_{139} \cdot \text{A-beta csf}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{140} \cdot \text{P Tau csf}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{141} \cdot \text{Smoking} \cdot \text{Alcohol abuse} + \\ & \theta_{142} \cdot \text{Smoking} \cdot \text{Traumatic brain injury} \end{aligned}$$

Cerebral endothelial dysfunction

$$\begin{aligned} \frac{d\text{WMH volume}}{dt} = & \theta_{143} + \theta_{144} \cdot \text{Mediterranean diet score}(t) + \theta_{145} \cdot \text{TNF-alpha plasma}(t) + \\ & \theta_{146} \cdot \text{Hippocampal cerebral blood flow}(t) + \\ & \theta_{147} \cdot \text{Superoxide dismutase plasma}(t) + \\ & \theta_{148} \cdot \text{Fasting glucose}(t) + \theta_{149} \cdot \text{Total cholesterol}(t) + \\ & \theta_{150} \cdot \text{A-beta csf}(t) + \theta_{151} \cdot \text{Pulse pressure}(t) + \\ & \theta_{152} \cdot \text{Smoking} + \theta_{153} \cdot \text{Traumatic brain injury} + \\ & \theta_{154} \cdot \text{ApoE-4 alleles} + \theta_{155} \cdot \text{Age}(t) + \\ & \theta_{156} \cdot \text{Mediterranean diet score}(t) \cdot \text{TNF-alpha plasma}(t) + \\ & \theta_{157} \cdot \text{Mediterranean diet score}(t) \cdot \text{Hippocampal cerebral blood flow}(t) + \\ & \theta_{158} \cdot \text{Mediterranean diet score}(t) \cdot \text{Superoxide dismutase plasma}(t) + \\ & \theta_{159} \cdot \text{Mediterranean diet score}(t) \cdot \text{Total cholesterol}(t) + \\ & \theta_{160} \cdot \text{Mediterranean diet score}(t) \cdot \text{A-beta csf}(t) + \\ & \theta_{161} \cdot \text{Mediterranean diet score}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{162} \cdot \text{Mediterranean diet score}(t) \cdot \text{ApoE-4 alleles} + \\ & \theta_{163} \cdot \text{TNF-alpha plasma}(t) \cdot \text{Hippocampal cerebral blood flow}(t) + \\ & \theta_{164} \cdot \text{TNF-alpha plasma}(t) \cdot \text{Superoxide dismutase plasma}(t) + \\ & \theta_{165} \cdot \text{TNF-alpha plasma}(t) \cdot \text{Total cholesterol}(t) + \\ & \theta_{166} \cdot \text{TNF-alpha plasma}(t) \cdot \text{A-beta csf}(t) + \\ & \theta_{167} \cdot \text{TNF-alpha plasma}(t) \cdot \text{Pulse pressure}(t) + \\ & \theta_{168} \cdot \text{TNF-alpha plasma}(t) \cdot \text{Smoking} + \\ & \theta_{169} \cdot \text{TNF-alpha plasma}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{170} \cdot \text{TNF-alpha plasma}(t) \cdot \text{ApoE-4 alleles} + \\ & \theta_{171} \cdot \text{Hippocampal cerebral blood flow}(t) \cdot \text{Superoxide dismutase plasma}(t) + \\ & \theta_{172} \cdot \text{Hippocampal cerebral blood flow}(t) \cdot \text{Total cholesterol}(t) + \\ & \theta_{173} \cdot \text{Hippocampal cerebral blood flow}(t) \cdot \text{A-beta csf}(t) + \\ & \theta_{174} \cdot \text{Hippocampal cerebral blood flow}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{175} \cdot \text{Hippocampal cerebral blood flow}(t) \cdot \text{ApoE-4 alleles} + \\ & \theta_{176} \cdot \text{Superoxide dismutase plasma}(t) \cdot \text{Total cholesterol}(t) + \\ & \theta_{177} \cdot \text{Superoxide dismutase plasma}(t) \cdot \text{A-beta csf}(t) + \\ & \theta_{178} \cdot \text{Superoxide dismutase plasma}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{179} \cdot \text{Superoxide dismutase plasma}(t) \cdot \text{ApoE-4 alleles} + \\ & \theta_{180} \cdot \text{Fasting glucose}(t) \cdot \text{A-beta csf}(t) + \\ & \theta_{181} \cdot \text{Total cholesterol}(t) \cdot \text{A-beta csf}(t) + \\ & \theta_{182} \cdot \text{Total cholesterol}(t) \cdot \text{Pulse pressure}(t) + \\ & \theta_{183} \cdot \text{Total cholesterol}(t) \cdot \text{Smoking} + \\ & \theta_{184} \cdot \text{Total cholesterol}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{185} \cdot \text{Total cholesterol}(t) \cdot \text{ApoE-4 alleles} + \\ & \theta_{186} \cdot \text{A-beta csf}(t) \cdot \text{Pulse pressure}(t) + \\ & \theta_{187} \cdot \text{A-beta csf}(t) \cdot \text{ApoE-4 alleles} + \\ & \theta_{188} \cdot \text{Pulse pressure}(t) \cdot \text{Smoking} + \\ & \theta_{189} \cdot \text{Pulse pressure}(t) \cdot \text{Traumatic brain injury} + \\ & \theta_{190} \cdot \text{Pulse pressure}(t) \cdot \text{ApoE-4 alleles} + \\ & \theta_{191} \cdot \text{Smoking} \cdot \text{Traumatic brain injury} + \\ & \theta_{192} \cdot \text{Smoking} \cdot \text{ApoE-4 alleles} + \\ & \theta_{193} \cdot \text{Traumatic brain injury} \cdot \text{ApoE-4 alleles} \end{aligned}$$

Amyloid beta burden

$$\begin{aligned}\frac{dA\text{-beta csf}}{dt} = & \theta_{194} + \\ & \theta_{195} \cdot \text{TNF-alpha csf}(t) + \\ & \theta_{196} \cdot \text{Fasting glucose}(t) + \\ & \theta_{197} \cdot \text{WMH volume}(t) + \\ & \theta_{198} \cdot \text{ApoE-4 alleles} + \\ & \theta_{199} \cdot \text{Age}(t) + \\ & \theta_{200} \cdot \text{TNF-alpha csf}(t) \cdot \text{WMH volume}(t) + \\ & \theta_{201} \cdot \text{TNF-alpha csf}(t) \cdot \text{ApoE-4 alleles} + \\ & \theta_{202} \cdot \text{WMH volume}(t) \cdot \text{ApoE-4 alleles}\end{aligned}$$

Morbidity burden

$$\begin{aligned}\frac{d\text{Morbidity score}}{dt} = & \theta_{203} + \\ & \theta_{204} \cdot \text{Mediterranean diet score}(t) + \\ & \theta_{205} \cdot \text{METs hours per week}(t) + \\ & \theta_{206} \cdot \text{PSQI}(t) + \\ & \theta_{207} \cdot \text{TNF-alpha plasma}(t) + \\ & \theta_{208} \cdot \text{Fasting glucose}(t) + \\ & \theta_{209} \cdot \text{Total cholesterol}(t) + \\ & \theta_{210} \cdot \text{BMI}(t) + \\ & \theta_{211} \cdot \text{Currently married} + \\ & \theta_{212} \cdot \text{Alcohol abuse} + \\ & \theta_{213} \cdot \text{Age}(t)\end{aligned}$$

Depressive symptoms

$$\begin{aligned}\frac{d\text{GDS}}{dt} = & \theta_{214} + \\ & \theta_{215} \cdot \text{METs hours per week}(t) + \\ & \theta_{216} \cdot \text{PSQI}(t) + \\ & \theta_{217} \cdot \text{Cortisol plasma}(t) + \\ & \theta_{218} \cdot \text{ADAS-cog-13}(t) + \\ & \theta_{219} \cdot \text{Currently married} + \\ & \theta_{220} \cdot \text{Age}(t) + \\ & \theta_{221} \cdot \text{METs hours per week}(t) \cdot \text{Cortisol plasma}(t) + \\ & \theta_{222} \cdot \text{METs hours per week}(t) \cdot \text{ADAS-cog-13}(t) + \\ & \theta_{223} \cdot \text{METs hours per week}(t) \cdot \text{Currently married} + \\ & \theta_{224} \cdot \text{PSQI}(t) \cdot \text{Cortisol plasma}(t) + \\ & \theta_{225} \cdot \text{PSQI}(t) \cdot \text{ADAS-cog-13}(t) + \\ & \theta_{226} \cdot \text{Cortisol plasma}(t) \cdot \text{ADAS-cog-13}(t) + \\ & \theta_{227} \cdot \text{Cortisol plasma}(t) \cdot \text{Currently married} + \\ & \theta_{228} \cdot \text{ADAS-cog-13}(t) \cdot \text{Currently married}\end{aligned}$$

Obesity

$$\begin{aligned}\frac{d\text{BMI}}{dt} = & \theta_{229} + \\ & \theta_{230} \cdot \text{Mediterranean diet score}(t) + \\ & \theta_{231} \cdot \text{METs hours per week}(t) + \\ & \theta_{232} \cdot \text{Age}(t)\end{aligned}$$

Blood pressure

$$\begin{aligned}\frac{d\text{Pulse pressure}}{dt} = & \theta_{233} + \\ & \theta_{234} \cdot \text{Mediterranean diet score}(t) + \\ & \theta_{235} \cdot \text{METs hours per week}(t) + \\ & \theta_{236} \cdot \text{Cortisol plasma}(t) + \\ & \theta_{237} \cdot \text{BMI}(t) + \\ & \theta_{238} \cdot \text{Currently married} + \\ & \theta_{239} \cdot \text{Age}(t) + \\ & \theta_{240} \cdot \text{Mediterranean diet score}(t) \cdot \text{Cortisol plasma}(t) + \\ & \theta_{241} \cdot \text{Mediterranean diet score}(t) \cdot \text{Currently married} + \\ & \theta_{242} \cdot \text{Cortisol plasma}(t) \cdot \text{BMI}(t) + \\ & \theta_{243} \cdot \text{Cortisol plasma}(t) \cdot \text{Currently married} + \\ & \theta_{244} \cdot \text{BMI}(t) \cdot \text{Currently married}\end{aligned}$$

Tau burden

$$\begin{aligned}\frac{d\text{P Tau csf}}{dt} = & \theta_{245} + \\ & \theta_{246} \cdot \text{Superoxide dismutase plasma}(t) + \\ & \theta_{247} \cdot \text{TNF-alpha csf}(t) + \\ & \theta_{248} \cdot \text{A-beta csf}(t) + \\ & \theta_{249} \cdot \text{ApoE-4 alleles} + \\ & \theta_{250} \cdot \text{Age}(t)\end{aligned}$$