SUPPLEMENT

I. Statistical Modeling of Lobe Effects of Resting CBF

We included lobe effects on the three coefficients of nonlinear mixed effect model to test if the change of resting gray matter CBF values with age differed significantly among the four lobes.

The model can be written as follows:

$$
\begin{aligned}
CBF_{ij} = \beta 0 &+ b1 * I(lobe = Frontal) + b2 * I(lobe = Temporal) + b3 * I(lobe = Parietal) \\
&+ \big(\beta 1 + b4 * I(lobe = Frontal) + b5 * I(lobe = Temporal) + b6 \\
&* \ I(lobe = Parietal)\big) \\
&* \exp\big(-\beta 2 * (age_{ij} - 6) - b7 * I(lobe = Frontal) * (age_{ij} - 6) - b8 \\
&* I(lobe = Temporal) * (age_{ij} - 6) - b9 * I(lobe = Parietal) * (age_{ij} - 6)\big) \\
&+ u_i + e_{ij}
\end{aligned}
$$

$where\ u_i \sim N(0, \sigma_u^2), e_{ij} \sim N(0, \sigma_e^2)$

and

$$I(lobe = Frontal) = \begin{cases} 1 & if\ lobe = Frontal \\ 0 & Otherwise \end{cases}$$
$$I(lobe = Temporal) = \begin{cases} 1 & if\ lobe = Temporal \\ 0 & Otherwise \end{cases}$$
$$I(lobe = Parietal) = \begin{cases} 1 & if\ lobe = Parietal \\ 0 & Otherwise \end{cases}$$

Coefficients $\beta 0, \beta 1, and\ \beta 2$ reflect the mature value, change over the age range (6 to 27 years), and exponential rate constant for the occipital lobe.

Parameters *b1* to *b3* model the 3 lobe effects on the $\beta 0$, parameters *b4* to *b6* model the 3 lobe effects on the $\beta 1$, parameters *b7* to *b9* model the 3 lobe effects on the $\beta 2$

1) When we fit lobe effects on all three coefficients: $\beta 0, \beta 1, and\ \beta 2$, only the Lobe effects on $\beta 0$ are significant ($p \leq 0.0001$ for all the lobes), i.e., all the other lobes had significant different $\beta 0$ than occipital lobe, but $\beta 1\ and\ \beta 2$ were not significantly different among the lobes.

2) Since no significant model effects were detected with $\beta 1\ and\ \beta 2$, we dropped the lobe effects on $\beta 1$, and fitted the model with lobe effects on $\beta 0\ and\ \beta 2$ only. With this reduced model, i.e. without parameters *b4*, *b5*, and *b6*, the lobe effects were significant on both coefficients

$\beta 0$ *and* $\beta 1$ (for $\beta 0$, p < 0.0001 for all the lobes; for $\beta 2$, p = 0.0088, p = 0.0273, and p = 0.0001 for Frontal, Temporal, and Parietal, respectively).

3) Then we dropped the lobe effects parameters on $\beta 2$, and fitted the model with lobe effects on $\beta 0$ *and* $\beta 1$ only. With this reduced model, i.e. without parameters *b7, b9*, and *b9*, the lobe effects were significant on both coefficients $\beta 0$ *and* $\beta 1$ (for $\beta 0$, p < 0.0001 for all the lobes; for $\beta 2$, p = 0.0241, p = 0.0317, and p = 0.0017 for Frontal, Temporal, and Parietal, respectively).

II. Statistical Modeling with Gender Effects

For the linear mixed-effect age models, the gender effects were added as:

$$y_{ij} = \beta_0 + \beta_1 * age_{ij} + b_1 * gender_i + b_2 * (gender_i * age_{ij}) + u_i + e_{ij}$$

where gender = 0 (female) or 1 (male), $u_i \sim N(0, \sigma_u^2), e_{ij} \sim N(0, \sigma_e^2)$, *i denotes the* i^{th} *subject and j denoted the* j^{th} *measurement for the* i^{th} *subject.*

Coefficients β_1 is the age effect; parameter b_1 reflects the gender effect, and b_2 reflects age gender interaction effect.

For the nonlinear mixed-effect age models, the gender effects were added as:

$$y_{ij} = \beta_0 + b_0 * gender + (\beta_1 + b_1 * gender) * \exp\left(-(age_{ij} - 6)/\beta_2 - b_2 * gender - b_3 * age_{ij} * gender\right) + u_i + e_{ij}$$

where gender = 0 (female) or 1 (male), $u_i \sim N(0, \sigma_u^2), e_{ij} \sim N(0, \sigma_e^2)$, *i denotes the* i^{th} *subject and j denoted the* j^{th} *measurement for the* i^{th} *subject.*

Coefficients β_0, β_1, and β_2, reflect the mature value, total change over the age range (6 to 27 years), and exponential rate constant (rate of change per year). Parameters b_0, b_1, and b_2 are the gender effects on β_0, β_1, and β_2; parameter b_3 is the age gender interaction effect for the model.

III. Estimate of the Coupling Parameter *k*

A heuristic model (Simon et. al., 2013) links changes in CBF (f) to changes in BOLD signal (b) as:

$$\frac{b(t)-b_0}{b_0} = M(1-\alpha_v-\lambda)\left(1-\frac{f_0}{f(t)}\right) = k(1-\frac{f_0}{f(t)})$$

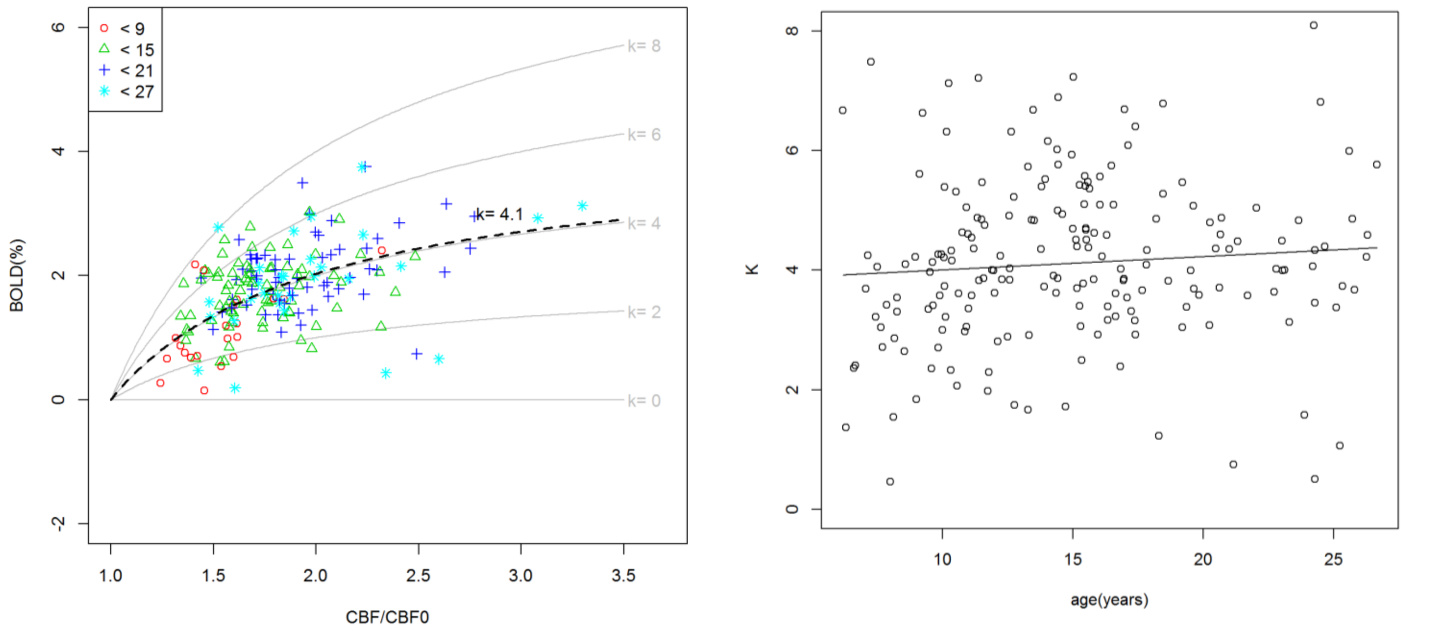
where *M* is a scaling factor related to imaging parameters and baseline physiological factors; α_v , is the power law exponent (Grubb's constant) relating CBV (*V*) to CBF $(V = f^{\alpha_v})$; and λ is the $CMRO_2$/CBF coupling ratio ($\lambda = \frac{\Delta CMRO_2/CMRO_{2_0}}{\Delta CBF/CBF_0}$) . These 3 unknown parameters can be combined into a single factor *k*, which is an apparent coupling parameter that scales BOLD signal to a nonlinear function of CBF change. We estimated the *k* parameter using the complete time courses of CBF and BOLD for each subject and tested age-effects on *k* with a linear mixed-effect model:

$$k_{ij} = \beta_0 + \beta_1 * age_{ij} + u_i + e_{ij}$$

where $u_i \sim N(0, \sigma_u^2), e_{ij} \sim N(0, \sigma_e^2)$, i denoted the i^{th} subject and j denoted the j^{th} measurement for the i^{th} subject.

The estimated *k* values and its relation to age are plotted below.

(A) **(B)**



(A) Scatter plot of peak BOLD (%) signal vs. fractional CBF changes. Data were color coded to reflect age groups for each participant. (B) Fitted *k* values *vs.* age. No significant age effect ($p = 0.84$) was detected for *k.*

- Simon, A.B., Griffeth, V.E., Wong, E.C., Buxton, R.B. (2013) A novel method of combining blood oxygenation and blood flow sensitive magnetic resonance imaging techniques to measure the cerebral blood flow and oxygen metabolism responses to an unknown neural stimulus. PloS one, 8:e54816.