

**Concept Paper Form**

<b>Provisional Paper Title:</b> Association of age 3 brain health with age 45 physical function
<b>Proposing Author:</b> J. Kathy Xie
<b>Author's Email:</b> kathy.xie@duke.edu
<b>P.I. Sponsor:</b> Terrie Moffitt, Avshalom Caspi (if the proposing author is a student or colleague of an original PI)
<b>Today's Date:</b> 7/16/2023

**Addendum:**

The concept paper for this project, posted on December 10, 2022, proposed the following secondary analysis:

*We will assess the association between age 3 brain health composite and age 45 VO2 max (maximum mL oxygen per kg body weight per minute when under respiratory exertion), a test of aerobic capacity that does not tap into brain function, as a negative control. We hypothesize that this association will be weaker than that between age 3 brain health and age 45 physical function.*

We examined the results of this analysis alongside findings from a previous Dunedin Study manuscript (Belsky et al., 2015), presented in the table below.

<b>Table 1.</b> Childhood cognition variables of interest and their associations ( $\beta$ ) with physical outcomes. Estimates are residualized for sex. Asterisk (*) denotes statistical significance.		
	<b>Age-3 brain health</b> (Xie et al., <i>in prep</i> )	<b>Childhood IQ ages 7-13</b> (Belsky et al., 2015)
Physical function factor	0.27*	0.39*
VO <sub>2</sub> max	0.05	0.10*

The section of the table bordered in red indicates the preregistered analysis for our current project. Findings were consistent with our hypothesis, as the association between age-3 brain health and age-45 physical function was (1) statistically significant and (2) more than 5x stronger than its association with age-45 VO<sub>2</sub> max (which was not significant).

The paper by Belsky and colleagues used a different childhood cognition variable, but this variable nonetheless had a similar pattern of associations with our age-45 outcomes of interest. That is, the association between childhood IQ and age-45 physical function was almost 4x stronger than its association with age-45 VO<sub>2</sub> max.

However, the association between childhood IQ and VO<sub>2</sub> max reported by Belsky and colleagues *was statistically significant* (boxes shaded in orange). Because we did not/do not plan to include the childhood IQ variable in our analyses, and did not want to report findings that, without inclusion of the childhood IQ variable and the Table 1 above, would appear to contradict previously reported results, we decided to omit the analysis involving VO<sub>2</sub> max from this project.

**Reference:**

Belsky, D. W., Caspi, A., Israel, S., Blumenthal, J. A., Poulton, R., & Moffitt, T. E. (2015). Cardiorespiratory fitness and cognitive function in midlife: Neuroprotection or neuroselection? *Annals of Neurology*, 77(4), 607–617. <https://doi.org/10.1002/ana.24356>