Impaired cerebrovascular reactivity in pediatric sickle cell disease using diffuse correlation spectroscopy: supplement

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IMPAIRED CEREBROVASCULAR REACTIVITY IN PEDIATRIC SICKLE CELL DISEASE USING DIFFUSE CORRELATION SPECTROSCOPY: SUPPLEMENTAL DOCUMENT

Graphical User Interface to facilitate breath-holding. A graphical user interface (GUI) functioning as a rudimentary video game was developed in MATLAB to provide the participant end-user with a visual guide to facilitate the breath-hold examination. The GUI was designed to visually and functionally mimic a mechanical metronome to facilitate paced breathing prior to and after each breath hold (**Fig. S1**) in addition to help the participant prepare for and to time the duration of the end-expiration breath hold (**Fig. S2**). The choice of a mechanical metronome as the visual display to the end-user was designed to provide a relatable experience for children who have exposure to practicing a musical instrument.
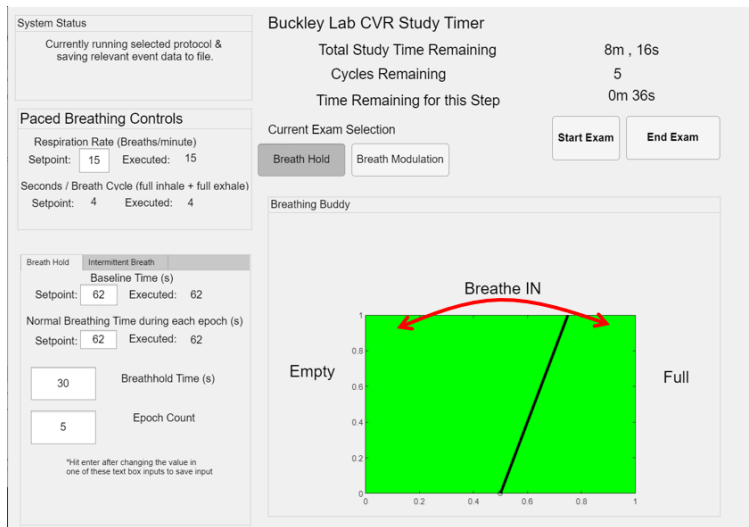

Fig. S1. "Breathing Buddy" Graphical User Interface during paced breathing. A visual depiction of the end-user interface used to guide participants in the breath-hold exam is provided for reference. User inputs are provided on the left-hand panel to control various exam parameters. Participants are instructed to watch the "Breathing Buddy" panel in the bottom right. The thick black line in this panel swings back and forth (red arrow, akin to a metronome) during the paced breathing portion of the breath-hold exam.
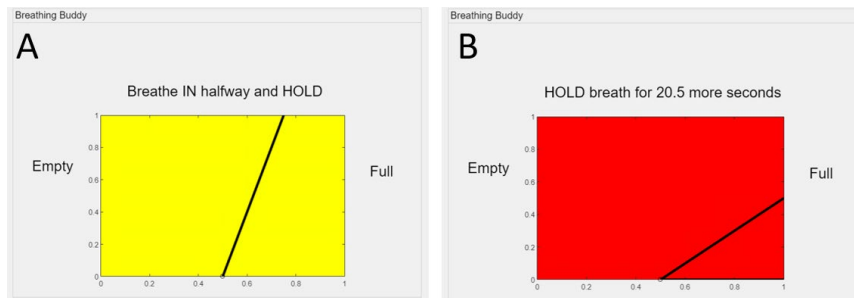

Fig. S2. "Breathing Buddy" Graphical User Interface during breath-hold state. A visual depiction of the end-user interface used to guide participants A) immediately before and B) during the breath-hold state.

Representative breath-hold timeseries. Fig. S3 shows representative vital sign data, including arterial blood pressure, heart rate, and transcutaneous oxygen saturation, during the breath-hold paradigm for the same participant depicted in Fig. 1.
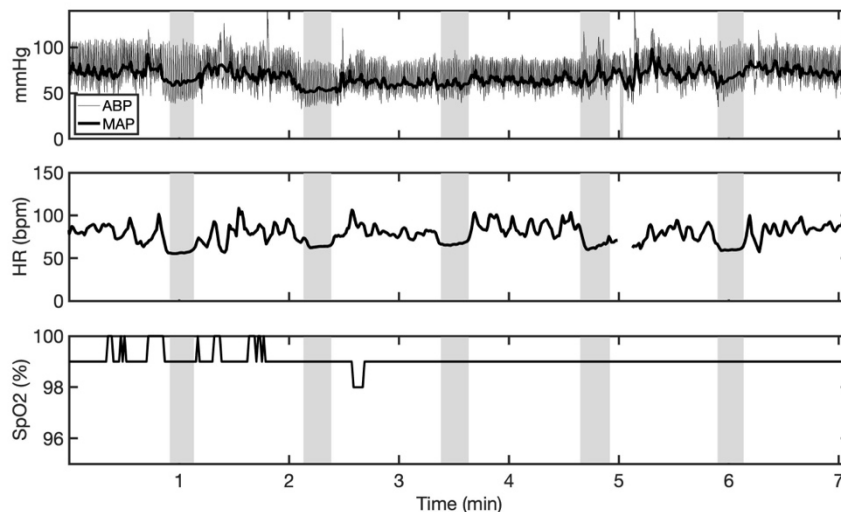

Fig. S3 Representative vital sign timeseries during breath-hold. A) Arterial blood pressure (ABP), mean arterial pressure (MAP, top panel), heart rate (HR, middle panel), and transcutaneous oxygen saturation (SpO2) as a function of time during the roughly 7 min breath-hold paradigm. Grey shaded rectangles denote the 5 breath hold epochs.

Summary of associations between CVR and demographic/hematologic factors. Table S1 provides a summary of the associations between CVR and demographic factors for the entire cohort (control and SCD children). Table S2 provides a summary of the associations between CVR and hematologic factors for SCD participants.

Table S1. Bivariable analysis of breath-hold CVR and demographic factors[a]

	Full Dataset		**Subset Dataset- BFI(ρ_{short}) < BFI(ρ_{long})**	
	Estimate (95% CI)	r, p	Estimate (95% CI)	r, p
Age (years)	-0.14 (-0.33, 0.05)	-0.31, 0.15	-0.28 (-0.53, 0.08)	-0.39, 0.13
Sex	0.37 (-0.83, 1.56)	0.14, 0.52	0.34 (-1.08, 1.76)	0.14, 0.61

[a]Associations are presented in terms of the slope estimate for the line of best fit with 95% confidence intervals, along with Pearson's correlation coefficient (r) and p-values. Analysis was performed on the entire dataset (N = 23), and a sensitivity analysis on the subset with BFI(ρ_{short}) < BFI(ρ_{long}), indicative of enhanced brain sensitivity (N = 16).

Table S2. Bivariable analysis of breath-hold CVR and hematological factors within the sickle cell group.

	Full Dataset		**Subset Dataset - BFI(ρ_{short}) < BFI(ρ_{long})**	
	Estimate (95% CI)	r, p	Estimate (95% CI)	r, p
Hemoglobin	-0.06 (-0.51, 0.40)	-0.10, 0.78	-0.02 (-0.55, 0.51)	-0.04, 0.92
Hematocrit	-0.03 (-0.18, 0.12)	-0.14, 0.70	-0.02 (-0.18, 0.14)	-0.13, 0.78
Reticulocytes	-0.05 (-0.13 0.02)	-0.53, 0.15	**-0.06 (-0.10, -0.02)**	**-0.90, 0.01**
Fetal hemoglobin	-0.04 (-0.13, 0.04)	-0.38, 0.28	-0.01 (-0.10, 0.08)	-0.12, 0.80
Sickle hemoglobin	-0.01 (-0.11, 0.09)	-0.07, 0.86	0.01 (-0.14, 0.16)	0.12, 0.82

Associations are presented in terms of the slope estimate for the line of best fit with 95% confidence intervals, along with Pearson correlation coefficient (r) and p-values. Analysis was performed on the entire sickle group (N = 10), and a sensitivity analysis on the subset of individuals with BFI(ρ_{short}) < BFI(ρ_{long}), indicative of enhanced brain sensitivity (N= 7). Bolded text indicates statistical significance; $p < 0.05$.