Prenatal exposure to organophosphate pesticides and functional neuroimaging in adolescents living in proximity to pesticide application

Supporting Information

1. fNIRS Tasks:

a) *Wisconsin Card Sorting Test (13 min)(1)*: *Wisconsin Card Sorting Test (13 min)(1)*: Assesses cognitive flexibility and executive function. Participants were asked to determine an implicit rule that governs how cards should be sorted (2). They were presented four fixed reference cards situated evenly along the bottom half of the computer screen, each containing a different configuration of geometric figures. Specifically, each reference card contained a unique shape (dot, star, cross, or triangle), number (1-4), and color (red, blue, yellow, or green) of figures. The configuration of each reference card was fixed, and did not vary across participants. On each 'match' trial, a new test card was presented in the top center portion of the screen, and participants had to match the test card to a reference card based on an unstated criterion (i.e., matching on shape, number, or color). In this condition, the test card was never a perfect match with any reference card configuration. Participants received auditory feedback (right or wrong) through which they had to deduce the sorting rule. Participants were given 15 trials per block to identify and correctly respond to the rule six times in a row, and the rule was pseudo-randomly changed after each block. In the control (exact match) condition, the test card was identical to one of the four fixed reference cards and the participant indicated the card with the exact match. Furthermore, in this condition participants had to correctly respond to the exact match sorting rule eight times in a row.

b) *Sternberg working memory task* (14 min)(3): Assesses letter-retrieval working memory. In each trial, a string of 7 or 8 consonant letters was presented for 2 s (encoding phase) followed by an interstimulus interval (6 s, maintenance phase). Then, a single inquiry letter was presented on

the screen for 6 s (inquiry phase) and the participant was asked to respond if the inquiry letter was included in the original set (recall phase). There were 15 26 s trials for the 7- and 8-letter strings.

c) *Visuospatial N-back working memory task (8 min)*: Assesses visuospatial working memory. The stimulus, the letter O, was presented in one of 9 locations in a 3x3 matrix. In the 1-back task condition, participants were instructed to respond if the stimulus was presented in the same location as the previous trial; in the 2-back condition, they responded if the stimulus was in the same location as in two trials previously. The 1-back and 2-back tasks were presented in separate blocks alternating with a control condition in which the participant was instructed to respond if the stimulus appeared in the center of the screen. The stimulus never appeared in the center location in non-control blocks. There were 3 1-back, 3 2-back and 6 control blocks, each 34 s, interleaved between twelve 2 s instruction epochs and 3 16 s rest epochs.

d) *Go/No-Go task (10 min)*: Assesses sustained attention and response inhibition. A letter was presented for 250 ms, followed by a jittered interstimulus interval (1 to 12 s). Participants were instructed to press a button (Go trial) when any letter appeared except for “X”, for which they were instructed to withhold (inhibit) a response (No-Go trial). The letter X occurs in 20% of 375 total trials.

e) *Pyramids and Palm Trees (4) (11 min)*: Assesses verbal comprehension. Participants were shown a triad of words on a screen, arranged in a triangle. In the test (meaning) condition, participants decided which of the two words at the bottom was semantically related to the word at the top. In the control (size) condition, all three words were the same but differ in size. Specifically, the two words on the bottom of the pyramid were either 6% or 12% larger or smaller than the top word. Participants had to determine which of the two words at the bottom was closest in size to the word at the top. The task consisted of 12 blocks that alternated between test and control conditions, each containing 9 trials (3 s per trial, separated by a 0.5 s inter-trial interval). Task blocks were separated by a jittered inter-block interval between 14 and 17 s.

f) *Dynamic social gesture task (16 min)*: Assesses neural response to social gestures. This task was comprised of 100 short (2 s) color video clips of a live actor either performing a social gesture (i.e., friendly wave, handshake, beckoning, joint attention, or imploring) or a nonsocial gesture (i.e., rubbing hand on table, reaching for a cup, brushing off a table, looking at a book, and looking at arms) while seated and oriented towards the viewer. Stimuli were presented at the center of a viewing screen. As an attentional cover task, the participants were asked to press a button when they saw a white dot at the center of the screen turn red. Each clip was followed by a jittered interstimulus interval (500 to 9500 msec).

2. fNIRS data acquisition and preprocessing.

We generated all tasks using Matlab 2014b Psychtoolbox-3, with trial order and timing optimized to maximize detectable changes in hemodynamic response using OptSeq2,180. Tasks were presented on a MacBook Pro connected to a 20” LED monitor. Task responses were collected via button presses on a standard keyboard. We recorded hemodynamic activity using the NIRScout (NIRx, Germany) with a sampling frequency of 3.906 Hz. We assessed patterns of brain activation during each task of interest using a generalized linear model (GLM) approach, which has been well established for analysis of block and event-related fNIRS designs (5, 6). Following acquisition, we uploaded raw fNIRS data to a HIPAA-compliant database for processing and cleaning. All data were subject to the data preprocessing pipeline outlined by Brigadoi and colleagues (7) using the Homer2 Matlab package. First, we corrected all optical density data for motion artifacts using a wavelet motion correction procedure. Next, we bandpass filtered optical density data between 0.01 and 0.5 Hz to remove artifacts related to physiological fluctuations such as cardiac pulsation and respiratory signals. Using these correction methods we demonstrated adequate sampling of heart rate and hemodynamic activity and showed that filtering removed nuisance signals (see Figure S3). We also demonstrated exemplar hemodynamic activation in relation to OP pesticide exposure across

performance (see Figure S4 for activation patterns in an individual with high performance and another individual with low performance on the Wisconsin Card Sort Task).

Technical issues with data collection included: 1) failure of the task computer to present the task, 2) failure of the task computer to record the performance data, and 3) failure of the fNIRS device to record the fNIRS data correctly. These technical issues resulted in the following task-specific exclusions: n=3 for the Wisconsin Card Sorting Test, n=5 for the Sternberg working memory task, n=1 for the visuospatial N-back, n=1 for the Go/No-Go, and n=1 for Pyramids and Palm Trees; there were no exclusions for the Dynamic Social Gestures task. Following further data cleaning, individual fNIRS channels were rejected for the following reasons: 1) correlation between oxygenated (HbO) and deoxygenated hemoglobin (HbR) (8); 2) change in signal to noise ratio (SNR) measured by the Homer2 'enPruneChannels' function (i.e., ±2 SD change in SNR); or 3) critically low signal quality based on NIRx calibration methods (i.e., >10% of scan demonstrating high (>2.5) or low (<0.03) signal voltage or >7.5 SNR). In 3 cases, these quality control criteria resulted in removal of all channels for a given task (n=2 for the Sternberg working memory task and n=1 for the Dynamic Social Gestures task). In all other cases, data were excluded at the level of the region of interest (task-specific sample sizes are listed in each table).

We converted filtered optical density data to HbO and HbR values using the modified Beers-Lambert law. The onset and duration of each condition of interest were submitted to the GLM procedure as predictor variables used to estimate standardized beta (β) coefficients for each condition across each channel. The sign and magnitude of each β coefficient provides an indicator of the direction (positive/negative) and intensity of blood oxygen level dependent change (i.e., brain activity) that occurs during each condition. We estimated β coefficients for all task and control conditions. In order to capture the brain activation unique to the task demands, and thus not expected to be present in signals corresponding to the control conditions, we made contrasts between each β coefficient and its corresponding control. We employed functional

localization at the individual participant level to select regions of interest among the 36 measurement channels (9, 10). Specifically, within each channel cluster, we selected and submitted for group-level analysis the channel with the greatest contrast value. This procedure allows for individual variation in the location of task-responsive brain regions across participants and reduces the risk of committing Type II errors due to averaging across non-responsive channels.

Table S1. Adjusted[a] associations for a 10-fold increase in **acephate** use within a 1-km radius of maternal residence during pregnancy and fNIRS brain activation by task and region of interest for participants with fNIRS data in the CHAM2 study, enrolled 2009 in Salinas Valley, California.

Region (Localization cluster)	Wisconsin Card Sort (Cognitive Flexibility)			Sternberg (Letter-retrieval WM)			N-back (Visuospatial WM)			Go/No-Go (Attention/Impulsivity)			Pyramids & Palm Trees (Semantic Language)			Social Gestures (Social Cognition)		
	N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]	
Left hemisphere																		
Inferior frontal pole (1)	91	-4.06	(-8.92, 0.79)	87	1.17	(-2.72, 5.07)	93	-0.09	(-3.68, 3.49)	94	-0.66	(-3.77, 2.45)	93	2.38	(-0.74, 5.50)	91	-0.86	(-2.64, 0.91)
Superior frontal pole (2)	89	-2.48	(-6.75, 1.79)	80	3.69	(-0.22, 7.60)	86	0.16	(-3.17, 3.48)	83	-0.19	(-3.24, 2.85)	90	0.81	(-2.29, 3.92)	90	-1.40	(-3.20, 0.39)
Broca's/BA 44/45 (3)	90	-1.18	(-6.51, 4.14)	85	2.92	(-0.65, 6.49)	90	1.78	(-2.55, 6.11)	92	1.24	(-2.08, 4.57)	91	1.51	(-1.67, 4.68)	92	0.66	(-1.16, 2.47)
Dorsolateral PFC (4)	90	-1.99	(-6.86, 2.88)	85	2.99	(-0.71, 6.69)	88	0.85	(-2.66, 4.36)	92	-1.12	(-3.89, 1.65)	90	0.51	(-2.33, 3.34)	92	-0.66	(-2.33, 1.01)
Broca's/BA 44 and 6 (5)	92	-1.83	(-7.24, 3.58)	88	0.60	(-3.06, 4.26)	92	1.43	(-3.19, 6.05)	93	-0.02	(-3.35, 3.30)	94	1.49	(-1.51, 4.49)	94	-0.23	(-1.88, 1.42)
Superior/inferior temporal /postcentral gyrus (6)	92	-1.09	(-6.21, 4.02)	88	1.24	(-1.53, 4.01)	93	0.86	(-3.71, 5.42)	94	-1.61	(-4.70, 1.48)	93	2.50	(-0.70, 5.70)	93	-0.28	(-2.16, 1.60)
Inferior parietal lobule (7)	92	-1.52	(-5.44, 2.41)	88	1.83	(-2.34, 6.01)	91	2.82	(-0.28, 5.92)	92	-1.54	(-4.16, 1.09)	92	1.28	(-1.23, 3.78)	94	-1.08	(-2.81, 0.64)
Superior parietal lobule (8)	87	-1.13	(-5.21, 2.96)	81	4.38	(-0.01, 8.77)	86	2.01	(-0.72, 4.74)	85	0.07	(-2.73, 2.87)	83	0.10	(-2.18, 2.38)	84	-1.17	(-2.75, 0.42)
Right hemisphere																		
Inferior frontal pole (9)	92	-3.75	(-8.77, 1.26)	87	2.57	(-1.69, 6.84)	93	-1.90	(-5.82, 2.02)	93	-1.26	(-4.20, 1.69)	94	1.35	(-1.60, 4.30)	93	0.05	(-1.62, 1.73)
Broca's/BA 44/45 (10)	91	-1.36	(-6.79, 4.08)	84	1.42	(-2.17, 5.02)	93	0.93	(-3.25, 5.10)	92	-0.55	(-3.75, 2.65)	91	0.98	(-2.42, 4.38)	91	0.31	(-1.60, 2.23)
Superior frontal pole /dorsolateral PFC (11)	90	-1.22	(-5.50, 3.05)	82	1.31	(-2.67, 5.30)	92	1.64	(-1.69, 4.96)	93	-1.23	(-4.08, 1.63)	92	0.49	(-2.17, 3.15)	84	-1.23	(-2.85, 0.38)
Premotor/somatosensory cortex (12)	92	-1.69	(-6.63, 3.24)	87	1.67	(-2.18, 5.52)	94	1.04	(-2.65, 4.73)	93	-0.92	(-3.75, 1.91)	94	1.52	(-1.50, 4.55)	94	-0.81	(-2.57, 0.94)
Posterior superior/middle temporal sulcus (13)	92	-3.67	(-8.34, 0.99)	88	2.71	(-0.29, 5.70)	93	1.29	(-1.97, 4.55)	94	-0.34	(-3.27, 2.60)	94	0.00	(-2.93, 2.93)	94	-0.54	(-2.26, 1.18)
Inferior parietal lobule (14)	90	-1.76	(-5.38, 1.87)	87	0.65	(-3.33, 4.63)	93	1.53	(-1.84, 4.89)	93	-1.93	(-4.81, 0.96)	93	-0.15	(-2.72, 2.43)	94	-1.60	(-3.23, 0.03)
Superior parietal lobule (15)	85	-1.09	(-5.04, 2.86)	73	3.09	(-1.85, 8.02)	84	0.13	(-3.14, 3.40)	85	0.70	(-2.09, 3.49)	85	-0.43	(-2.68, 1.82)	87	-1.23	(-2.74, 0.29)

Abbreviations: BA=Brodmann Areas, PFC=prefrontal cortex, WM=Working Memory

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)

*non-FDR corrected p<0.05 †FDR-corrected p<0.05

Table S2. Adjusted[a] associations for a 10-fold increase in **chlorpyrifos** use within a 1-km radius of maternal residence during pregnancy and fNIRS brain activation by task and region of interest for participants with fNIRS data in the CHAM2 study, enrolled 2009 in Salinas Valley, California.

Region (Localization cluster)	Wisconsin Card Sort (Cognitive Flexibility)		Sternberg (Letter-retrieval WM)		N-back (Visuospatial WM)		Go/No-Go (Attention/Impulsivity)		Pyramids & Palm Trees (Semantic Language)		Social Gestures (Social Cognition)	
	N	Beta (95% CI)[a]	N	Beta (95% CI)[a]	N	Beta (95% CI)[a]	N	Beta (95% CI)[a]	N	Beta (95% CI)[a]	N	Beta (95% CI)[a]
Left hemisphere												
Inferior frontal pole (1)	91	-3.57 (-8.75, 1.61)	87	-1.57 (-5.64, 2.51)	93	-2.70 (-6.44, 1.03)	94	-2.29 (-5.49, 0.91)	93	-0.84 (-4.16, 2.49)	91	-0.83 (-2.73, 1.06)
Superior frontal pole (2)	89	-3.27 (-7.80, 1.27)	80	1.69 (-2.59, 5.97)	86	-2.87 (-6.25, 0.51)	83	-1.45 (-4.66, 1.76)	90	-2.18 (-5.45, 1.08)	90	-1.09 (-2.97, 0.78)
Broca's/BA 44/45 (3)	90	-2.56 (-8.20, 3.08)	85	2.67 (-0.91, 6.25)	90	1.02 (-3.54, 5.58)	92	-0.03 (-3.52, 3.46)	91	0.20 (-3.18, 3.58)	92	0.60 (-1.29, 2.50)
Dorsolateral PFC (4)	90	-3.39 (-8.50, 1.72)	85	2.11 (-1.81, 6.02)	88	-2.24 (-5.98, 1.49)	92	-0.04 (-2.94, 2.86)	90	0.68 (-2.31, 3.67)	92	-0.63 (-2.38, 1.11)
Broca's/BA 44 and 6 (5)	92	-3.32 (-9.02, 2.38)	88	2.17 (-1.62, 5.96)	92	1.15 (-3.65, 5.96)	93	0.66 (-2.80, 4.12)	94	0.27 (-2.90, 3.43)	94	0.07 (-1.65, 1.80)
Superior/inferior temporal /postcentral gyrus (6)	92	-3.39 (-8.76, 1.98)	88	1.12 (-1.77, 4.00)	93	-0.53 (-5.31, 4.25)	94	-0.21 (-3.45, 3.02)	93	0.45 (-2.95, 3.85)	93	1.21 (-0.70, 3.13)
Inferior parietal lobule (7)	92	-2.70 (-6.83, 1.43)	88	0.34 (-4.03, 4.71)	91	-0.56 (-3.88, 2.76)	92	0.16 (-2.58, 2.90)	92	-0.32 (-2.96, 2.32)	94	-0.94 (-2.75, 0.86)
Superior parietal lobule (8)	87	-0.84 (-5.10, 3.42)	81	1.91 (-2.70, 6.52)	86	-0.64 (-3.56, 2.29)	85	1.74 (-1.12, 4.60)	83	-0.70 (-3.16, 1.76)	84	-0.33 (-2.02, 1.36)
Right hemisphere												
Inferior frontal pole (9)	92	-4.12 (-9.42, 1.18)	87	1.58 (-2.92, 6.08)	93	-5.02 (-9.02, -1.03)*	93	-1.06 (-4.12, 2.00)	94	-0.48 (-3.60, 2.63)	93	0.39 (-1.36, 2.14)
Broca's/BA 44/45 (10)	91	-2.96 (-8.70, 2.78)	84	2.62 (-1.27, 6.51)	93	-1.38 (-5.77, 3.00)	92	-1.24 (-4.57, 2.09)	91	0.49 (-3.11, 4.08)	91	1.11 (-0.88, 3.10)
Superior frontal pole /dorsolateral PFC (11)	90	-2.12 (-6.65, 2.41)	82	-0.56 (-4.93, 3.81)	92	-2.09 (-5.67, 1.50)	93	-2.48 (-5.43, 0.46)	92	-0.45 (-3.34, 2.43)	84	0.25 (-1.44, 1.94)
Premotor/somatosensory cortex (12)	92	-1.75 (-6.97, 3.48)	87	1.38 (-2.78, 5.55)	94	-4.92 (-8.65, -1.19)*	93	-0.74 (-3.70, 2.22)	94	0.89 (-2.30, 4.07)	94	0.11 (-1.74, 1.95)
Posterior superior/middle temporal sulcus (13)	92	-3.39 (-8.34, 1.56)	88	2.92 (-0.20, 6.04)	93	-0.55 (-3.98, 2.89)	94	0.44 (-2.61, 3.50)	94	-1.52 (-4.58, 1.54)	94	0.41 (-1.39, 2.20)
Inferior parietal lobule (14)	90	-1.98 (-5.79, 1.83)	87	0.40 (-3.77, 4.57)	93	-0.58 (-4.13, 2.97)	93	-0.66 (-3.68, 2.35)	93	-2.96 (-5.59, -0.33)*	94	-0.36 (-2.09, 1.38)
Superior parietal lobule (15)	85	0.49 (-3.68, 4.66)	73	-0.42 (-5.75, 4.91)	84	-1.77 (-5.21, 1.66)	85	1.71 (-1.12, 4.54)	85	-1.55 (-3.94, 0.83)	87	-1.09 (-2.68, 0.51)

Abbreviations: BA=Brodmann Areas, PFC=prefrontal cortex, WM=Working Memory

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)

*non-FDR corrected p<0.05 †FDR-corrected p<0.05

Table S3. Adjusted[a] associations for a 10-fold increase in **diazinon** use within a 1-km radius of maternal residence during pregnancy and fNIRS brain activation by task and region of interest for participants with fNIRS data in the CHAM2 study, enrolled 2009 in Salinas Valley, California.

Region (Localization cluster)	Wisconsin Card Sort (Cognitive Flexibility)			Sternberg (Letter-retrieval WM)			N-back (Visuospatial WM)			Go/No-Go (Attention/Impulsivity)			Pyramids & Palm Trees (Semantic Language)			Social Gestures (Social Cognition)		
	N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]	
Left hemisphere																		
Inferior frontal pole (1)	91	-5.37	(-9.59, -1.15)*	87	-1.90	(-5.38, 1.59)	93	-2.00	(-5.17, 1.17)	94	-1.43	(-4.17, 1.30)	93	-0.23	(-3.05, 2.59)	91	-0.52	(-2.12, 1.09)
Superior frontal pole (2)	89	-2.85	(-6.63, 0.94)	80	1.82	(-1.86, 5.50)	86	-1.11	(-4.05, 1.82)	83	-0.69	(-3.45, 2.08)	90	-1.70	(-4.45, 1.06)	90	-1.30	(-2.89, 0.29)
Broca's/BA 44/45 (3)	90	-3.34	(-8.05, 1.37)	85	1.65	(-1.51, 4.81)	90	0.18	(-3.67, 4.03)	92	0.58	(-2.37, 3.52)	91	-0.35	(-3.22, 2.52)	92	0.81	(-0.81, 2.42)
Dorsolateral PFC (4)	90	-4.33	(-8.56, -0.10)*	85	0.97	(-2.41, 4.35)	88	-1.69	(-4.79, 1.41)	92	-0.47	(-2.92, 1.98)	90	-0.71	(-3.17, 1.75)	92	-0.12	(-1.61, 1.37)
Broca's/BA 44 and 6 (5)	92	-4.00	(-8.74, 0.73)	88	0.88	(-2.41, 4.17)	92	-0.01	(-4.10, 4.09)	93	0.21	(-2.74, 3.15)	94	-0.14	(-2.83, 2.56)	94	0.32	(-1.15, 1.78)
Superior/inferior temporal /postcentral gyrus (6)	92	-3.34	(-7.83, 1.14)	88	1.35	(-1.13, 3.83)	93	-2.24	(-6.30, 1.82)	94	-0.72	(-3.46, 2.02)	93	0.27	(-2.63, 3.17)	93	0.87	(-0.77, 2.52)
Inferior parietal lobule (7)	92	-1.72	(-5.19, 1.76)	88	1.56	(-2.19, 5.32)	91	1.96	(-0.83, 4.75)	92	-0.09	(-2.42, 2.24)	92	-0.73	(-2.97, 1.51)	94	-1.23	(-2.76, 0.29)
Superior parietal lobule (8)	87	-1.11	(-4.70, 2.49)	81	3.90	(-0.08, 7.88)	86	0.93	(-1.52, 3.39)	85	0.54	(-1.92, 3.00)	83	-1.16	(-3.17, 0.85)	84	-1.05	(-2.48, 0.37)
Right hemisphere																		
Inferior frontal pole (9)	92	-5.21	(-9.58, -0.85)*	87	-0.20	(-4.07, 3.67)	93	-3.77	(-7.22, -0.32)*	93	-0.85	(-3.48, 1.78)	94	0.42	(-2.22, 3.06)	93	0.16	(-1.33, 1.65)
Broca's/BA 44/45 (10)	91	-3.32	(-8.10, 1.46)	84	-0.45	(-3.87, 2.97)	93	-0.33	(-4.07, 3.40)	92	-1.08	(-3.91, 1.75)	91	0.40	(-2.66, 3.46)	91	1.15	(-0.55, 2.84)
Superior frontal pole /dorsolateral PFC (11)	90	-2.12	(-5.89, 1.65)	82	-1.61	(-5.37, 2.15)	92	-1.14	(-4.25, 1.96)	93	-1.61	(-4.12, 0.90)	92	-0.58	(-2.95, 1.79)	84	-0.76	(-2.20, 0.68)
Premotor/somatosensory cortex (12)	92	-2.31	(-6.67, 2.06)	87	-0.21	(-3.84, 3.43)	94	-1.99	(-5.25, 1.27)	93	-0.54	(-3.05, 1.97)	94	1.05	(-1.65, 3.76)	94	-0.20	(-1.77, 1.36)
Posterior superior/middle temporal sulcus (13)	92	-3.97	(-8.08, 0.14)	88	1.71	(-1.01, 4.43)	93	0.28	(-2.63, 3.20)	94	0.21	(-2.38, 2.81)	94	-1.11	(-3.71, 1.49)	94	-0.16	(-1.69, 1.37)
Inferior parietal lobule (14)	90	-2.17	(-5.36, 1.02)	87	-0.08	(-3.67, 3.51)	93	0.43	(-2.58, 3.44)	93	-1.05	(-3.61, 1.51)	93	-1.60	(-3.87, 0.67)	94	-1.33	(-2.78, 0.13)
Superior parietal lobule (15)	85	-0.11	(-3.60, 3.37)	73	1.81	(-2.81, 6.43)	84	-1.41	(-4.48, 1.66)	85	0.96	(-1.45, 3.38)	85	-1.45	(-3.48, 0.58)	87	-1.96	(-3.26, -0.67)*

Abbreviations: BA=Brodmann Areas, PFC=prefrontal cortex, WM=Working Memory

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)

*non-FDR corrected p<0.05 †FDR-corrected p<0.05

Table S4. Adjusted[a] associations for a 10-fold increase in **malathion** use within a 1-km radius of maternal residence during pregnancy and fNIRS brain activation by task and region of interest for participants with fNIRS data in the CHAM2 study, enrolled 2009 in Salinas Valley, California.

Region (Localization cluster)	Wisconsin Card Sort (Cognitive Flexibility)			Sternberg (Letter-retrieval WM)			N-back (Visuospatial WM)			Go/No-Go (Attention/Impulsivity)			Pyramids & Palm Trees (Semantic Language)			Social Gestures (Social Cognition)		
	N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]	
Left hemisphere																		
Inferior frontal pole (1)	91	-4.21	(-8.45, 0.03)	87	-2.14	(-5.61, 1.33)	93	-2.60	(-5.71, 0.51)	94	-2.10	(-4.89, 0.70)	93	-1.10	(-3.88, 1.68)	91	0.38	(-1.20, 1.95)
Superior frontal pole (2)	89	-0.75	(-4.51, 3.01)	80	0.23	(-3.55, 4.01)	86	-2.18	(-5.01, 0.66)	83	-1.86	(-4.67, 0.95)	90	-3.23	(-5.90, -0.57)*	90	-0.93	(-2.50, 0.64)
Broca's/BA 44/45 (3)	90	-3.79	(-8.42, 0.84)	85	0.05	(-3.02, 3.11)	90	-1.94	(-5.72, 1.83)	92	-0.73	(-3.76, 2.30)	91	-0.58	(-3.40, 2.23)	92	0.79	(-0.79, 2.38)
Dorsolateral PFC (4)	90	-1.06	(-5.35, 3.24)	85	0.53	(-2.84, 3.90)	88	-1.84	(-4.98, 1.30)	92	-1.30	(-3.81, 1.21)	90	-1.91	(-4.30, 0.48)	92	0.53	(-0.93, 1.99)
Broca's/BA 44 and 6 (5)	92	-2.94	(-7.65, 1.78)	88	0.25	(-3.03, 3.54)	92	-1.28	(-5.30, 2.75)	93	0.16	(-2.83, 3.16)	94	-0.77	(-3.42, 1.88)	94	0.84	(-0.60, 2.28)
Superior/inferior temporal /postcentral gyrus (6)	92	-2.10	(-6.56, 2.36)	88	1.22	(-1.25, 3.70)	93	-2.80	(-6.77, 1.17)	94	-1.25	(-4.07, 1.56)	93	-0.23	(-3.09, 2.63)	93	1.25	(-0.36, 2.87)
Inferior parietal lobule (7)	92	-0.81	(-4.26, 2.64)	88	1.42	(-2.32, 5.16)	91	1.33	(-1.43, 4.09)	92	-1.56	(-3.96, 0.83)	92	-1.73	(-3.93, 0.47)	94	0.33	(-1.20, 1.85)
Superior parietal lobule (8)	87	-0.33	(-4.14, 3.47)	81	2.48	(-1.55, 6.50)	86	-0.23	(-2.68, 2.23)	85	-1.56	(-4.07, 0.95)	83	-1.65	(-3.67, 0.37)	84	-1.34	(-2.80, 0.12)
Right hemisphere																		
Inferior frontal pole (9)	92	-3.19	(-7.59, 1.21)	87	-2.29	(-6.12, 1.54)	93	-2.28	(-5.69, 1.14)	93	-1.39	(-4.05, 1.27)	94	0.22	(-2.39, 2.83)	93	0.56	(-0.91, 2.03)
Broca's/BA 44/45 (10)	91	-3.69	(-8.39, 1.01)	84	-1.33	(-4.56, 1.90)	93	-2.35	(-6.00, 1.29)	92	-1.44	(-4.33, 1.44)	91	1.00	(-2.00, 4.00)	91	1.11	(-0.56, 2.77)
Superior frontal pole /dorsolateral PFC (11)	90	-1.62	(-5.58, 2.34)	82	-1.63	(-5.47, 2.21)	92	-1.66	(-4.59, 1.27)	93	-2.94	(-5.64, -0.24)*	92	-2.82	(-5.15, -0.49)*	84	-1.89	(-3.38, -0.40)*
Premotor/somatosensory cortex (12)	92	-2.69	(-6.99, 1.60)	87	-0.83	(-4.31, 2.65)	94	-2.14	(-5.35, 1.07)	93	-1.23	(-3.80, 1.33)	94	-0.86	(-3.54, 1.81)	94	0.30	(-1.24, 1.85)
Posterior superior/middle temporal sulcus (13)	92	-1.55	(-5.68, 2.59)	88	0.55	(-2.18, 3.29)	93	-0.70	(-3.59, 2.19)	94	-1.18	(-3.84, 1.48)	94	0.27	(-2.31, 2.85)	94	0.62	(-0.88, 2.13)
Inferior parietal lobule (14)	90	-1.00	(-4.19, 2.20)	87	0.01	(-3.56, 3.57)	93	-0.48	(-3.47, 2.50)	93	-1.89	(-4.50, 0.73)	93	-1.45	(-3.71, 0.81)	94	0.18	(-1.29, 1.64)
Superior parietal lobule (15)	85	-0.10	(-3.61, 3.40)	73	1.43	(-2.89, 5.75)	84	-0.65	(-3.36, 2.06)	85	-1.26	(-3.75, 1.23)	85	-1.98	(-3.89, -0.07)*	87	-1.25	(-2.59, 0.09)

Abbreviations: BA=Brodmann Areas, PFC=prefrontal cortex, WM=Working Memory

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)

*non-FDR corrected p<0.05 †FDR-corrected p<0.05

Table S5. Adjusted[a] associations for a 10-fold increase in **oxydemeton-methyl** use within a 1-km radius of maternal residence during pregnancy and fNIRS brain activation by task and region of interest for participants with fNIRS data in the CHAM2 study, enrolled 2009 in Salinas Valley, California.

Region (Localization cluster)	Wisconsin Card Sort (Cognitive Flexibility)			Sternberg (Letter-retrieval WM)			N-back (Visuospatial WM)			Go/No-Go (Attention/Impulsivity)			Pyramids & Palm Trees (Semantic Language)			Social Gestures (Social Cognition)		
	N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]		N	Beta (95% CI)[a]	
Left hemisphere																		
Inferior frontal pole (1)	91	-3.50	(-8.78, 1.77)	87	-0.06	(-4.39, 4.26)	93	-1.50	(-5.39, 2.39)	94	-1.79	(-5.13, 1.54)	93	0.39	(-3.05, 3.83)	91	-0.81	(-2.74, 1.12)
Superior frontal pole (2)	89	-2.00	(-6.64, 2.63)	80	3.33	(-1.33, 8.00)	86	-0.74	(-4.26, 2.78)	83	-1.08	(-4.49, 2.34)	90	-1.08	(-4.46, 2.30)	90	-1.19	(-3.16, 0.77)
Broca's/BA 44/45 (3)	90	-1.76	(-7.51, 3.99)	85	2.43	(-1.48, 6.34)	90	-0.37	(-5.05, 4.31)	92	0.88	(-2.70, 4.47)	91	0.47	(-3.01, 3.95)	92	1.07	(-0.89, 3.03)
Dorsolateral PFC (4)	90	-2.53	(-7.77, 2.72)	85	2.34	(-1.78, 6.47)	88	-2.10	(-5.85, 1.65)	92	-0.92	(-3.90, 2.07)	90	0.24	(-2.80, 3.28)	92	-0.38	(-2.19, 1.43)
Broca's/BA 44 and 6 (5)	92	-2.41	(-8.24, 3.43)	88	1.05	(-3.00, 5.10)	92	0.43	(-4.56, 5.42)	93	0.21	(-3.39, 3.81)	94	0.69	(-2.59, 3.97)	94	0.17	(-1.62, 1.96)
Superior/inferior temporal /postcentral gyrus (6)	92	-1.44	(-6.96, 4.08)	88	0.71	(-2.36, 3.78)	93	-1.06	(-6.03, 3.90)	94	-0.61	(-3.96, 2.74)	93	2.34	(-1.15, 5.83)	93	0.40	(-1.62, 2.41)
Inferior parietal lobule (7)	92	-1.75	(-5.98, 2.48)	88	2.18	(-2.43, 6.79)	91	1.84	(-1.55, 5.23)	92	-1.32	(-4.15, 1.50)	92	-0.14	(-2.87, 2.60)	94	-1.37	(-3.23, 0.49)
Superior parietal lobule (8)	87	-0.63	(-5.00, 3.73)	81	5.31	(0.55, 10.08)*	86	1.40	(-1.59, 4.39)	85	0.63	(-2.36, 3.61)	83	-1.15	(-3.58, 1.28)	84	-1.17	(-2.89, 0.55)
Right hemisphere																		
Inferior frontal pole (9)	92	-3.77	(-9.20, 1.65)	87	1.17	(-3.59, 5.93)	93	-3.78	(-7.99, 0.43)	93	-2.20	(-5.36, 0.95)	94	-0.18	(-3.41, 3.05)	93	0.13	(-1.68, 1.95)
Broca's/BA 44/45 (10)	91	-2.09	(-7.94, 3.77)	84	0.82	(-3.20, 4.83)	93	-0.50	(-5.04, 4.05)	92	-1.58	(-5.00, 1.84)	91	-0.58	(-4.29, 3.13)	91	1.24	(-0.82, 3.29)
Superior frontal pole /dorsolateral PFC (11)	90	-0.99	(-5.60, 3.62)	82	-0.63	(-5.09, 3.84)	92	1.02	(-2.63, 4.67)	93	-1.98	(-5.05, 1.08)	92	-0.23	(-3.13, 2.66)	84	-1.04	(-2.79, 0.71)
Premotor/somatosensory cortex (12)	92	-2.90	(-8.21, 2.41)	87	1.53	(-2.77, 5.82)	94	-1.53	(-5.54, 2.47)	93	-1.35	(-4.40, 1.69)	94	0.65	(-2.66, 3.95)	94	-0.23	(-2.14, 1.69)
Posterior superior/middle temporal sulcus (13)	92	-3.27	(-8.33, 1.79)	88	3.07	(-0.24, 6.38)	93	0.48	(-3.08, 4.03)	94	-1.01	(-4.17, 2.15)	94	-0.34	(-3.53, 2.85)	94	0.37	(-1.50, 2.23)
Inferior parietal lobule (14)	90	-1.99	(-5.88, 1.89)	87	1.46	(-2.93, 5.85)	93	1.01	(-2.65, 4.68)	93	-2.59	(-5.68, 0.49)	93	-1.55	(-4.33, 1.23)	94	-1.12	(-2.91, 0.67)
Superior parietal lobule (15)	85	-0.17	(-4.41, 4.07)	73	2.59	(-3.21, 8.39)	84	-0.39	(-4.26, 3.48)	85	0.24	(-2.70, 3.18)	85	-1.87	(-4.41, 0.66)	87	-1.62	(-3.25, 0.00)

Abbreviations: BA=Brodmann Areas, PFC=prefrontal cortex, WM=Working Memory

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)

*non-FDR corrected p<0.05 †FDR-corrected p<0.05

Table S6. Distributions of test performance and their adjusted[a] associations with a 10-fold increase in total OP pesticide use within a 1-km radius of maternal residence during pregnancy, for the six tasks administered during fNIRS in the CHAM2 study (n=95), enrolled 2009 in Salinas Valley, California.

		Percentile			Total OP pesticide use
Domain/Task	N	25th	50th	75th	β[a] (95% CI)
Wisconsin Card Sorting Test (Cognitive Flexibility)					
Total errors	92	17	24	32	0.03 (-3.48, 3.55)
Perseverative errors	92	1	2	3	-0.13 (-0.76, 0.51)
Sternberg (Letter Retrieval Working Memory)					
Accuracy	90	0.68	0.77	0.83	-0.01 (-0.05, 0.03)
Reaction time	90	1.35	1.65	2.04	0.25 (0.06, 0.45)*
N-back (Visuospatial Working Memory)					
Accuracy	94	0.73	0.79	0.81	0.01 (-0.01,0.03)
Reaction time	94	0.49	0.56	0.66	0.01 (-0.04,0.05)
Go/No-Go (Attention/Impulsivity)					
Errors of omission	94	6	12	26	-0.96 (-3.09, 1.17)
Errors of commission	94	9	11	18	3.21 (-2.38, 8.80)
Reaction time	94	0.37	0.40	0.43	0.00 (-0.02, 0.02)
D prime	91	1.27	1.97	2.42	0.03 (-0.25, 0.30)
Pyramids and Palm Trees (Semantic Language)					
Accuracy	94	0.70	0.76	0.81	-0.01 (-0.04,0.02)
Reaction time	94	1.77	1.91	2.02	-0.03 (-0.09,0.04)
Dynamic Social Gestures					
Accuracy	95	0.93	0.96	0.99	0.00 (-0.02, 0.01)
Reaction time	95	4.85	5.02	5.20	0.07 (0.00, 0.15)

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)
*non-FDR corrected p<0.05

Table S7. Adjusted[a] associations for a 10-fold increase in total OP pesticide use within a 1-km radius of maternal residence during pregnancy and fNIRS brain activation during the Sternberg letter retrieval working memory and the N-back visuospatial working memory tasks, stratified by test performance [dichotomized at the median for accuracy (0.77 for the Sternberg and 0.79 for the N-back)], by region of interest for participants with fNIRS data in the CHAM2 study, enrolled 2009 in Salinas Valley, California.

	Sternberg Letter Retrieval Working Memory (Accuracy)						N-back Visuospatial Working Memory (Accuracy)					
	High Performers			Low Performers			High Performers			Low Performers		
Region (Localization cluster)	N	Beta (95% CI)		N	Beta (95% CI)		N	Beta (95% CI)		N	Beta (95% CI)	
Left hemisphere												
Inferior frontal pole (1)	42	-0.39	(-5.32, 4.54)	45	0.97	(-3.14, 5.08)	40	-3.11	(-7.78, 1.55)	53	-1.96	(-5.65, 1.73)
Superior frontal pole (2)	40	0.59	(-3.74, 4.92)	40	6.09	(1.38, 10.81)*	38	-1.41	(-6.35, 3.53)	48	-0.20	(-3.13, 2.74)
Broca's/BA 44/45 (3)	42	0.42	(-4.38, 5.22)	43	2.72	(-0.66, 6.10)	37	-2.64	(-8.52, 3.24)	53	0.52	(-3.78, 4.83)
Dorsolateral PFC (4)	42	2.17	(-2.28, 6.61)	43	4.08	(-0.10, 8.27)	39	-1.27	(-5.87, 3.33)	49	-2.04	(-5.97, 1.88)
Broca's/BA 44 and 6 (5)	42	1.78	(-2.97, 6.52)	46	0.24	(-3.76, 4.23)	38	-3.59	(-10.10, 2.92)	54	2.24	(-2.25, 6.73)
Superior/inferior temporal /postcentral gyrus (6)	42	1.80	(-1.03, 4.63)	46	0.49	(-2.90, 3.87)	39	-4.54	(-11.11, 2.04)	54	0.44	(-4.02, 4.91)
Inferior parietal lobule (7)	42	3.90	(-1.30, 9.09)	46	1.67	(-3.03, 6.37)	38	3.04	(-1.33, 7.40)	53	1.33	(-1.91, 4.58)
Superior parietal lobule (8)	39	4.63	(-0.90, 10.15)	42	4.82	(0.12, 9.53)*	36	2.17	(-2.27, 6.61)	50	-0.16	(-2.80, 2.48)
Right hemisphere												
Inferior frontal pole (9)	42	-0.05	(-5.17, 5.07)	45	2.10	(-2.69, 6.90)	40	-0.91	(-6.95, 5.14)	53	-2.96	(-6.38, 0.46)
Broca's/BA 44/45 (10)	41	-1.56	(-6.70, 3.58)	43	2.11	(-1.40, 5.63)	40	-4.42	(-10.41, 1.58)	53	1.67	(-2.54, 5.89)
Superior frontal pole /dorsolateral PFC (11)	38	0.09	(-4.31, 4.49)	44	0.63	(-4.02, 5.27)	39	-0.52	(-5.74, 4.71)	53	-0.24	(-3.36, 2.88)
Premotor/somatosensory cortex (12)	41	0.99	(-4.07, 6.04)	46	1.97	(-2.11, 6.05)	40	-3.77	(-8.99, 1.45)	54	-0.24	(-3.77, 3.29)
Posterior superior/middle temporal sulcus (13)	42	1.99	(-2.35, 6.33)	46	3.57	(0.90, 6.24)*	39	-1.66	(-6.63, 3.31)	54	0.32	(-2.90, 3.53)
Inferior parietal lobule (14)	42	1.57	(-3.59, 6.73)	45	2.42	(-1.72, 6.57)	39	0.53	(-4.24, 5.29)	54	-0.36	(-3.69, 2.97)
Superior parietal lobule (15)	36	1.46	(-3.91, 6.83)	37	4.34	(-2.26, 10.94)	37	0.12	(-3.75, 3.99)	47	-2.34	(-5.83, 1.16)

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)

*non-FDR corrected p<0.05 †FDR-corrected p<0.05

Table S8. Adjusted[a] associations for a 10-fold increase in total OP pesticide use within a 1-km radius of maternal residence during pregnancy and fNIRS brain activation during the Go/No-Go Task, stratified by test performance [dichotomized at the median for errors of omission (median=12) and errors of commission (median=11)], by region of interest for participants with fNIRS data in the CHAM2 study, enrolled 2009 in Salinas Valley, California.

	Errors of Omission						Errors of Commission					
	High Performers			Low Performers			High Performers			Low Performers		
Region (Localization cluster)	N	Beta (95% CI)		N	Beta (95% CI)		N	Beta (95% CI)		N	Beta (95% CI)	
Left hemisphere												
Inferior frontal pole (1)	46	-0.25	(-3.62, 3.12)	48	-2.35	(-5.93, 1.24)	40	0.18	(-4.35, 4.71)	54	-2.70	(-5.03, -0.38)*
Superior frontal pole (2)	41	1.42	(-2.27, 5.10)	42	-3.20	(-6.28, -0.13)*	38	1.68	(-2.90, 6.26)	45	-1.83	(-4.06, 0.40)
Broca's/BA 44/45 (3)	46	1.48	(-2.47, 5.43)	46	-0.26	(-3.80, 3.27)	40	2.11	(-2.63, 6.85)	52	-1.53	(-4.25, 1.20)
Dorsolateral PFC (4)	45	-1.36	(-4.23, 1.50)	47	-1.13	(-4.16, 1.90)	40	0.42	(-3.28, 4.12)	52	-1.82	(-4.15, 0.52)
Broca's/BA 44 and 6 (5)	45	0.34	(-3.99, 4.67)	48	-0.27	(-3.59, 3.06)	40	2.33	(-2.05, 6.71)	53	-1.99	(-5.04, 1.06)
Superior/inferior temporal /postcentral gyrus (6)	46	-2.05	(-5.73, 1.63)	48	-0.42	(-3.81, 2.96)	40	0.90	(-3.10, 4.90)	54	-2.51	(-5.43, 0.41)
Inferior parietal lobule (7)	45	0.09	(-2.82, 3.00)	47	-1.82	(-4.40, 0.76)	40	-1.63	(-4.94, 1.68)	52	-0.19	(-2.51, 2.14)
Superior parietal lobule (8)	44	1.11	(-2.22, 4.45)	41	-2.68	(-5.51, 0.16)	36	0.31	(-3.70, 4.32)	49	-0.24	(-2.79, 2.32)
Right hemisphere												
Inferior frontal pole (9)	46	0.49	(-3.22, 4.20)	46	-2.38	(-5.12, 0.36)	40	0.27	(-4.03, 4.58)	53	-1.88	(-4.13, 0.37)
Broca's/BA 44/45 (10)	45	-0.34	(-3.76, 3.08)	46	-0.75	(-4.38, 2.88)	39	-0.32	(-4.56, 3.92)	53	-1.67	(-4.52, 1.18)
Superior frontal pole /dorsolateral PFC (11)	46	-0.01	(-3.27, 3.24)	45	-3.54	(-6.42, -0.66)*	40	-0.65	(-4.74, 3.45)	53	-2.65	(-4.89, -0.40)*
Premotor/somatosensory cortex (12)	46	-0.08	(-3.11, 2.94)	46	-1.98	(-5.14, 1.19)	40	0.03	(-3.81, 3.86)	53	-1.76	(-4.27, 0.76)
Posterior superior/middle temporal sulcus (13)	46	0.51	(-2.98, 4.00)	46	-1.07	(-4.23, 2.09)	40	-0.52	(-4.71, 3.68)	54	-0.18	(-2.73, 2.37)
Inferior parietal lobule (14)	46	0.71	(-2.56, 3.98)	45	-4.51	(-7.48, -1.54)*	40	-1.24	(-4.89, 2.41)	53	-1.90	(-4.52, 0.71)
Superior parietal lobule (15)	41	2.66	(-0.24, 5.57)	43	-3.35	(-6.10, -0.61)*	35	-0.64	(-4.78, 3.51)	50	0.28	(-1.86, 2.43)

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)

*non-FDR corrected p<0.05 †FDR-corrected p<0.05

Table S9. Adjusted[a] associations for a 10-fold increase in total OP pesticide use within a 1 km radius of maternal residence during pregnancy and fNIRS brain activation during the Pyramids and Palm Trees task, stratified by test performance [dichotomized at the median for Pyramids and Palm Trees accuracy (0.76%)], by region of interest for participants with fNIRS data in the CHAM2 study, enrolled 2009 in Salinas Valley, California.

	Pyramids and Palm Trees Accuracy (Semantic Language)					
	High Performers			Low Performers		
Region (Localization cluster)	N	Beta (95% CI)		N	Beta (95% CI)	
Left hemisphere						
Inferior frontal pole (1)	46	1.08	(-1.98, 4.13)	47	-0.52	(-4.36, 3.32)
Superior frontal pole (2)	45	-0.69	(-3.18, 1.80)	45	-1.79	(-6.33, 2.75)
Broca's/BA 44/45 (3)	44	1.15	(-1.94, 4.24)	47	-0.56	(-4.54, 3.41)
Dorsolateral PFC (4)	44	-0.59	(-2.79, 1.62)	46	-0.38	(-4.08, 3.32)
Broca's/BA 44 and 6 (5)	46	1.16	(-1.91, 4.23)	48	-1.91	(-5.43, 1.62)
Superior/inferior temporal /postcentral gyrus (6)	46	1.86	(-1.30, 5.01)	47	0.61	(-3.41, 4.63)
Inferior parietal lobule (7)	46	-0.92	(-3.25, 1.41)	46	-0.53	(-3.56, 2.51)
Superior parietal lobule (8)	41	-1.62	(-3.80, 0.56)	42	-1.18	(-3.68, 1.33)
Right hemisphere						
Inferior frontal pole (9)	46	0.68	(-2.42, 3.78)	48	-0.91	(-4.28, 2.47)
Broca's/BA 44/45 (10)	44	0.53	(-3.09, 4.14)	47	0.03	(-4.18, 4.25)
Superior frontal pole /dorsolateral PFC (11)	45	-0.36	(-2.63, 1.90)	47	-2.94	(-6.64, 0.76)
Premotor/somatosensory cortex (12)	46	1.01	(-1.86, 3.87)	48	-1.73	(-5.74, 2.29)
Posterior superior/middle temporal sulcus (13)	46	-1.12	(-3.92, 1.68)	48	-0.07	(-3.82, 3.68)
Inferior parietal lobule (14)	46	-1.67	(-4.15, 0.81)	47	-1.15	(-4.22, 1.91)
Superior parietal lobule (15)	40	-1.52	(-3.67, 0.63)	45	-1.31	(-3.86, 1.24)

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)
*non-FDR corrected p<0.05 †FDR-corrected p<0.05

Table S10. Sex-specific adjusted[a] associations for a 10-fold increase in total OP pesticide use within a 1-km radius of maternal residence during pregnancy and fNIRS brain activation by region of interest for cognitive flexibility/working memory tasks among participants with fNIRS data in the CHAM2 study, enrolled 2009 in Salinas Valley, California.

Region (Localization cluster)	Wisconsin Card Sort (Cognitive Flexibility)					Sternberg (Letter-retrieval Working Memory)					N-back (Visuospatial Working Memory)				
	Males		Females			Males		Females			Males		Females		
	N	Beta (95% CI)	Beta (95% CI)		p[b]	N	Beta (95% CI)	Beta (95% CI)		p[b]	N	Beta (95% CI)	Beta (95% CI)		p[b]
Left hemisphere															
Inferior frontal pole (1)	91	-3.58 (-8.72, 1.56)	-5.59	(-10.00, -1.17)*	0.55	87	-0.04 (-4.12, 4.04)	-1.08 (-4.94, 2.78)		0.71	93	-2.50 (-6.35, 1.36)	-2.11	(-5.39, 1.18)	0.88
Superior frontal pole (2)	89	-0.72 (-5.43, 3.99)	-2.55	(-6.53, 1.44)	0.55	80	1.78 (-2.46, 6.03)	2.74 (-1.33, 6.82)		0.74	86	0.27 (-3.34, 3.89)	-2.87	(-5.83, 0.10)	0.18
Broca's/BA 44/45 (3)	90	-0.95 (-6.66, 4.77)	-4.46	(-9.39, 0.47)	0.34	85	2.44 (-1.08, 5.96)	0.73 (-2.76, 4.22)		0.49	90	2.58 (-2.05, 7.21)	-1.91	(-5.87, 2.06)	0.14
Dorsolateral PFC (4)	90	0.86 (-4.33, 6.05)	-4.42	(-8.92, 0.08)	0.12	85	2.35 (-1.61, 6.32)	2.32 (-1.35, 5.99)		0.99	88	-0.79 (-4.52, 2.93)	-2.06	(-5.44, 1.31)	0.61
Broca's/BA 44 and 6 (5)	92	-2.57 (-8.36, 3.22)	-4.13	(-9.12, 0.85)	0.68	88	0.22 (-3.60, 4.03)	1.64 (-1.97, 5.25)		0.58	92	4.61 (-0.24, 9.47)	-2.70	(-6.84, 1.43)	**0.02**
Superior/inferior temporal /postcentral gyrus (6)	92	-1.18 (-6.68, 4.32)	-3.53	(-8.26, 1.20)	0.51	88	0.06 (-2.80, 2.93)	2.17 (-0.53, 4.88)		0.28	93	2.46 (-2.41, 7.33)	-3.67	(-7.82, 0.49)	**0.05**
Inferior parietal lobule (7)	92	-1.49 (-5.74, 2.75)	-2.05	(-5.70, 1.61)	0.84	88	1.20 (-3.13, 5.53)	2.85 (-1.24, 6.94)		0.58	91	2.46 (-0.93, 5.86)	0.90	(-2.02, 3.81)	0.48
Superior parietal lobule (8)	87	1.50 (-2.93, 5.93)	-1.96	(-5.75, 1.83)	0.23	81	3.16 (-1.29, 7.62)	4.76 (0.49, 9.03)*		0.60	86	1.41 (-1.59, 4.42)	-0.04	(-2.62, 2.54)	0.46
Right hemisphere															
Inferior frontal pole (9)	92	-4.63 (-9.97, 0.71)	-4.23	(-8.83, 0.36)	0.91	87	3.42 (-1.00, 7.85)	-1.53 (-5.71, 2.66)		0.10	93	-1.42 (-5.64, 2.80)	-3.73	(-7.30, -0.17)	0.39
Broca's/BA 44/45 (10)	91	-3.00 (-9.00, 2.99)	-2.89	(-7.91, 2.14)	0.98	84	0.96 (-3.07, 4.99)	0.05 (-3.42, 3.53)		0.73	93	1.89 (-2.69, 6.46)	-1.70	(-5.56, 2.15)	0.22
Superior frontal pole /dorsolateral PFC (11)	90	0.34 (-4.51, 5.19)	-2.33	(-6.30, 1.64)	0.39	82	1.39 (-3.33, 6.10)	-1.20 (-4.98, 2.58)		0.38	92	-0.17 (-3.98, 3.64)	-0.99	(-4.01, 2.04)	0.73
Premotor/somatosensory cortex (12)	92	-2.61 (-7.95, 2.72)	-2.22	(-6.81, 2.36)	0.91	87	1.60 (-2.61, 5.80)	0.61 (-3.10, 4.31)		0.72	94	0.01 (-3.99, 4.02)	-2.17	(-5.58, 1.24)	0.40
Posterior superior/middle temporal sulcus (13)	92	-2.07 (-7.14, 2.99)	-3.28	(-7.64, 1.07)	0.71	88	2.64 (-0.47, 5.76)	1.82 (-1.13, 4.76)		0.70	93	-0.18 (-3.74, 3.38)	0.33	(-2.70, 3.36)	0.82
Inferior parietal lobule (14)	90	0.56 (-3.30, 4.41)	-2.93	(-6.24, 0.38)	0.16	87	1.38 (-2.79, 5.55)	0.91 (-3.01, 4.84)		0.87	93	-0.21 (-3.89, 3.47)	0.27	(-2.86, 3.40)	0.84
Superior parietal lobule (15)	85	0.50 (-3.74, 4.75)	-0.40	(-4.13, 3.32)	0.74	73	2.40 (-2.62, 7.42)	2.35 (-2.91, 7.62)		0.99	84	-2.51 (-6.22, 1.20)	-0.03	(-3.01, 2.95)	0.29

Abbreviations: BA=Brodmann Areas, PFC=prefrontal cortex

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)

[b]Wald p-value for interaction by sex

*non-FDR corrected p<0.05 †FDR-corrected p<0.05

Table S11. Sex-specific adjusted[a] associations for a 10-fold increase in total OP pesticide use within a 1-km radius of maternal residence during pregnancy and fNIRS brain activation by region of interest for attention/impulsivity and social cognition among participants with fNIRS data in the CHAM2 study, enrolled 2009 in Salinas Valley, California.

	Go/No-Go (Attention/Impulsivity)					Dynamic Social Gestures (Social Cognition)				
		Males	Females				Males	Females		
Region (Localization cluster)	N	Beta (95% CI)	Beta (95% CI)		p[b]	N	Beta (95% CI)	Beta (95% CI)		p[b]
Left hemisphere										
Inferior frontal pole (1)	94	-2.50 (-5.84, 0.84)	-0.39	(-3.29, 2.51)	0.33	91	-1.25 (-3.20, 0.70)	0.18	(-1.45, 1.81)	0.25
Superior frontal pole (2)	83	-0.99 (-4.29, 2.30)	-0.29	(-3.32, 2.74)	0.75	90	-1.18 (-3.13, 0.77)	-1.29	(-2.97, 0.38)	0.93
Broca's/BA 44/45 (3)	92	-0.58 (-4.21, 3.05)	0.74	(-2.40, 3.88)	0.58	92	0.49 (-1.47, 2.45)	1.02	(-0.66, 2.69)	0.68
Dorsolateral PFC (4)	92	-1.03 (-4.12, 2.05)	-0.59	(-3.20, 2.01)	0.82	92	-0.80 (-2.70, 1.11)	0.32	(-1.22, 1.86)	0.36
Broca's/BA 44 and 6 (5)	93	-0.35 (-4.08, 3.39)	0.09	(-3.01, 3.19)	0.85	94	-0.18 (-1.97, 1.60)	0.80	(-0.72, 2.32)	0.39
Superior/inferior temporal /postcentral gyrus (6)	94	-0.88 (-4.24, 2.48)	-1.27	(-4.19, 1.64)	0.86	93	0.92 (-1.09, 2.93)	0.48	(-1.24, 2.20)	0.73
Inferior parietal lobule (7)	92	-0.26 (-3.10, 2.58)	-0.65	(-3.12, 1.81)	0.83	94	-1.20 (-3.08, 0.67)	-0.56	(-2.16, 1.03)	0.60
Superior parietal lobule (8)	85	0.27 (-2.82, 3.36)	-0.04	(-2.67, 2.60)	0.88	84	-1.22 (-3.01, 0.58)	-0.98	(-2.46, 0.49)	0.84
Right hemisphere										
Inferior frontal pole (9)	93	-1.65 (-4.85, 1.55)	-0.10	(-2.86, 2.66)	0.45	93	-0.79 (-2.59, 1.00)	1.12	(-0.40, 2.65)	0.10
Broca's/BA 44/45 (10)	92	-0.46 (-3.92, 3.00)	-1.06	(-4.05, 1.93)	0.79	91	0.59 (-1.54, 2.72)	1.18	(-0.57, 2.94)	0.67
Superior frontal pole /dorsolateral PFC (11)	93	-2.36 (-5.50, 0.79)	-0.89	(-3.56, 1.77)	0.47	84	-0.65 (-2.50, 1.21)	-1.23	(-2.78, 0.32)	0.62
Premotor/somatosensory cortex (12)	93	-0.34 (-3.42, 2.75)	-1.24	(-3.91, 1.43)	0.65	94	-1.04 (-2.95, 0.86)	0.59	(-1.03, 2.21)	0.19
Posterior superior/middle temporal sulcus (13)	94	0.54 (-2.65, 3.72)	-0.68	(-3.44, 2.09)	0.56	94	0.06 (-1.82, 1.94)	-0.11	(-1.71, 1.49)	0.89
Inferior parietal lobule (14)	93	-1.88 (-5.00, 1.24)	-1.11	(-3.82, 1.60)	0.70	94	-1.53 (-3.31, 0.25)	-0.63	(-2.15, 0.88)	0.43
Superior parietal lobule (15)	85	0.44 (-2.45, 3.32)	0.03	(-2.60, 2.66)	0.83	87	-2.23 (-3.80, -0.66)*	-0.95	(-2.31, 0.42)	0.21

Abbreviations: BA=Brodmann Areas, PFC=prefrontal cortex

[a]Adjusted for age of child at assessment (continuous variable), child's sex, maternal age at delivery (continuous), maternal education at delivery (<6th grade, 7-12th grade, completed high school), and quality of the home environment at the 10½-year visit (continuous HOME z-score)

[b]Wald p-value for interaction by sex

*non-FDR corrected p<0.05 †FDR-corrected p<0.05

Figure S1. Visual representation of the association between OP exposure and fNIRS activation during the Wisconsin Card Sort task, stratified by test performance [dichotomized at the median for total errors (median = 24)], by region of interest. A. High performers categorized by total errors. B. Low performers categorized by total errors. C. High performers categorized by perseverative errors. D. Low performers categorized by perseverative errors.

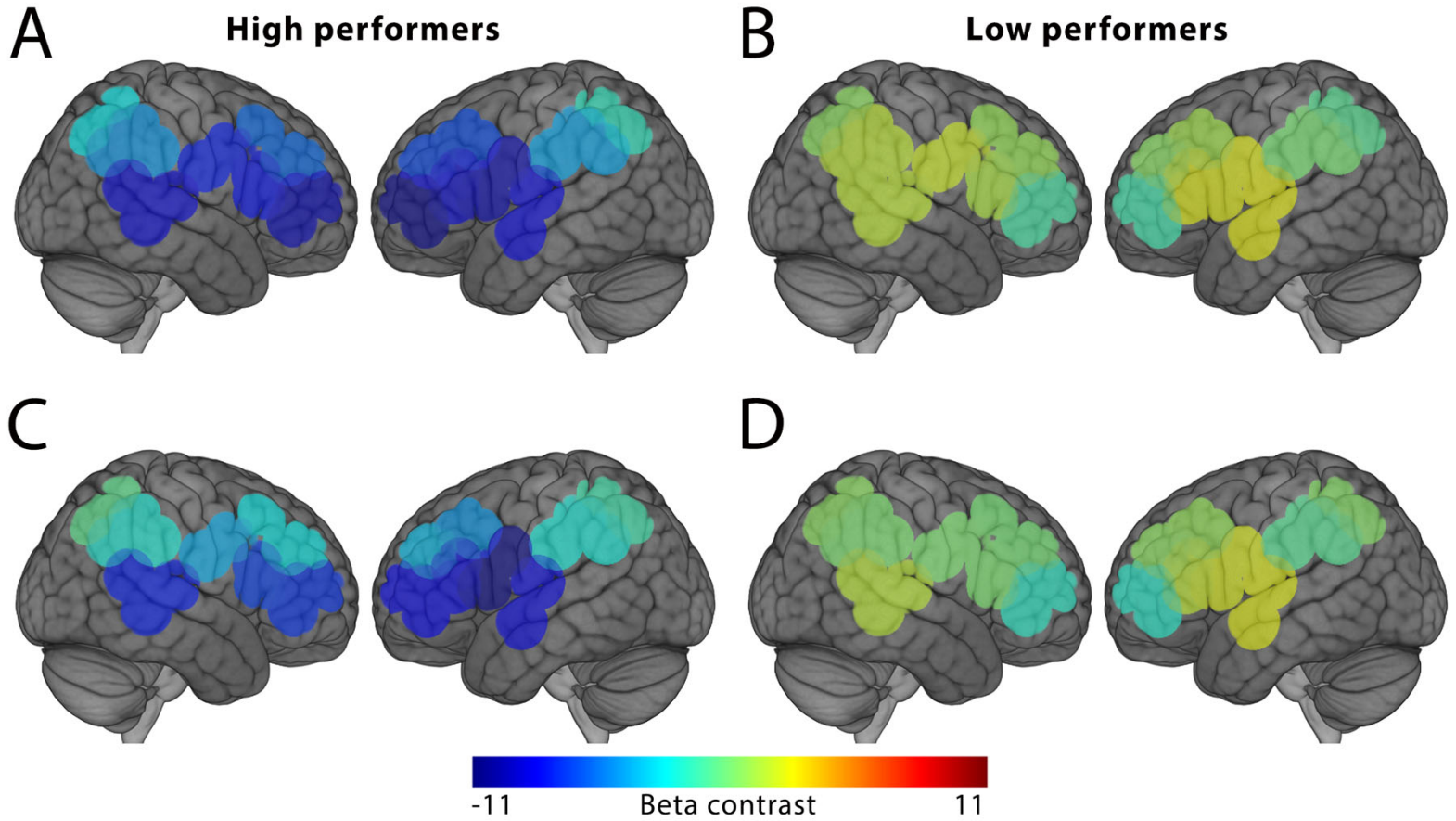


Figure S2: Directed acyclic graph (DAG) for the association of prenatal organophosphate exposure and brain activation in the CHAMACOS study, Salinas Valley, California. Figure generating using DAGitty (11).

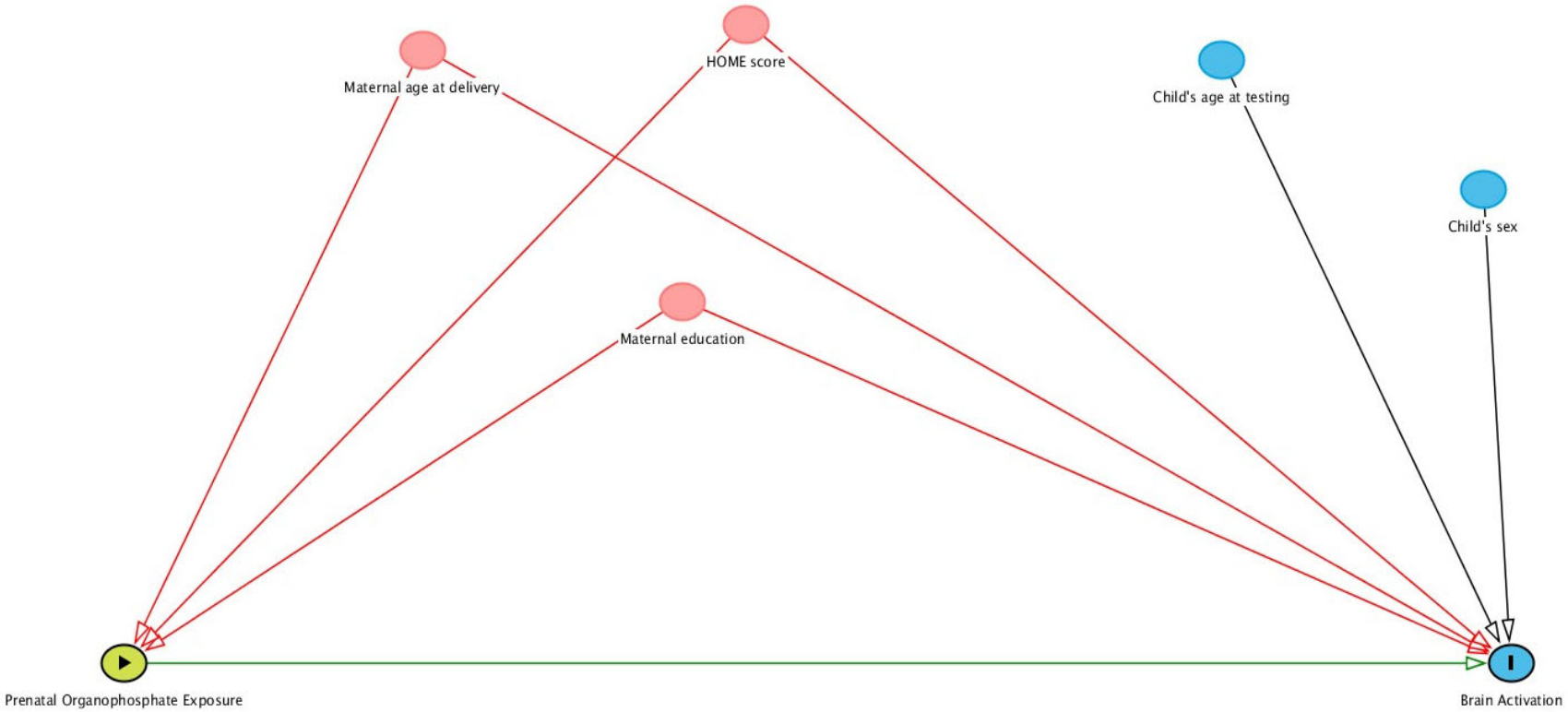


Figure S3. Pre and post-filtering example of fNIRS HbO and HbR data from the Sternberg Working Memory task. A. 150 second section of unfiltered HbO and HbR data streams. High-frequency noise from physiological processes including heartbeat and respiration are visibly present in both data streams. Similarly, low-frequency drift is apparent in both signals B. Decomposition of the unfiltered HbO signal via wavelet transform highlights high relative power at or near the 1Hz frequency, which corresponds with the heartbeat signal. This high-frequency band is outlined in these data by a red box. C. Bandpass filtering removes physiological artifacts in the fNIRS signal, which is apparent by the smoother data traces, as well as a flattening of the signals along the y-axis. D. Removal of psychological artifacts are also apparent in wavelet decomposition plots, wherein all power about the 1Hz frequency has been removed.

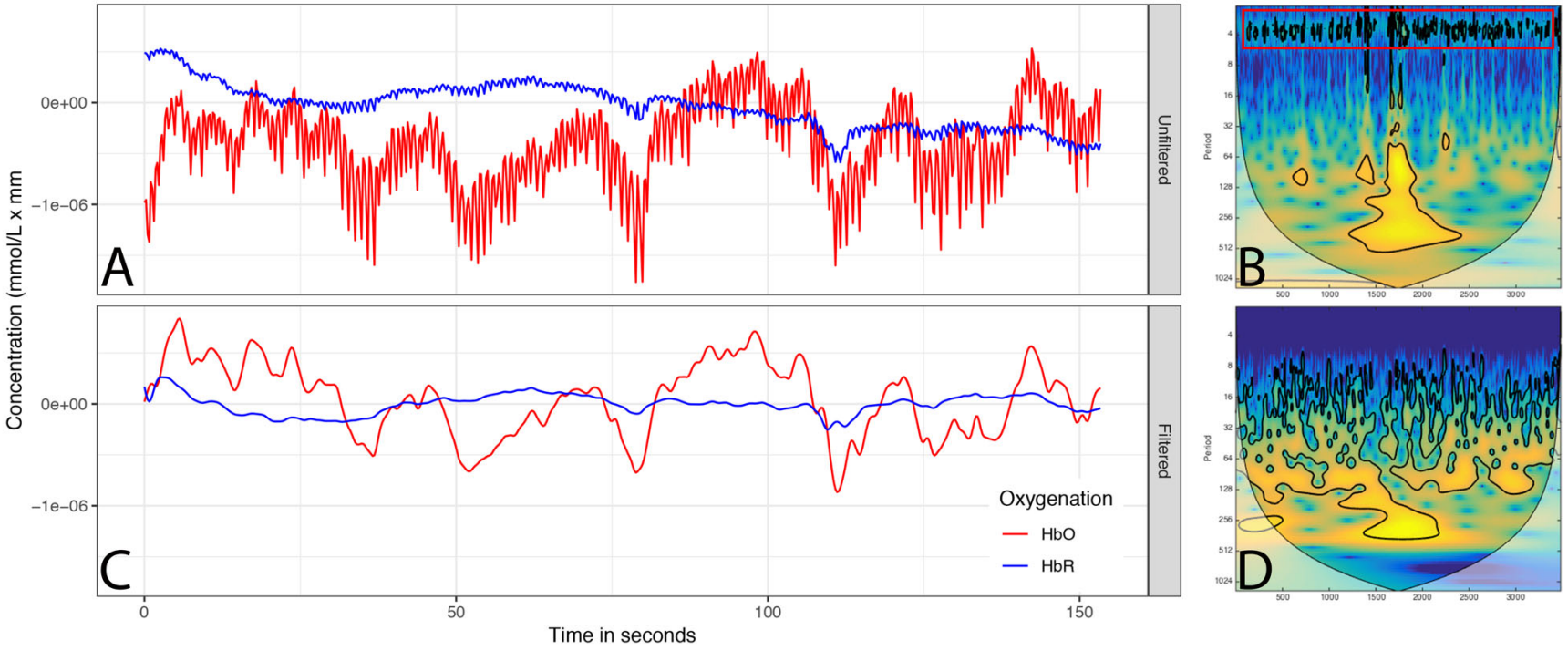
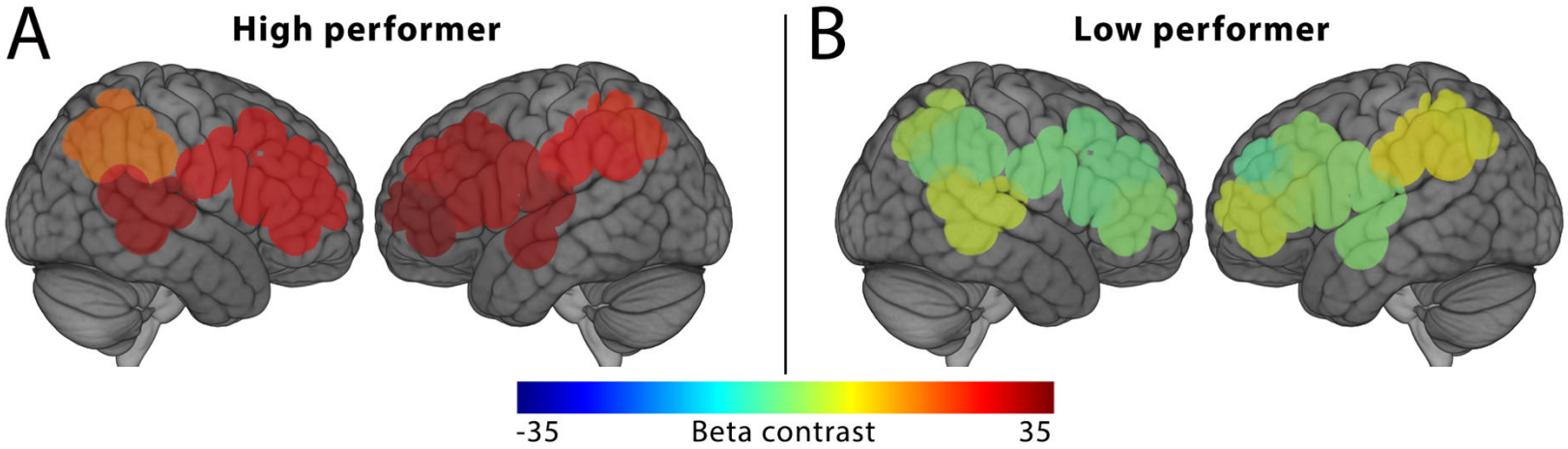


Figure S4. Exemplar cortical activation in relation to Wisconsin Card Sort task performance. A. This participant was randomly selected from all participants with behavioral performance in the first quartile (n match errors = 15, mean match response time = 1.98s). This participant exhibited significant cortical activations throughout the bilateral prefrontal and parietal cortices during match compared to control task conditions. B. Another participant was randomly selected from all participants with behavioral performance in the 3rd quartile (n match errors = 32%, mean response time = 2.42s). This participant exhibited lower levels of cortical activation during the same conditions.



References

1. Lie C-H, Specht K, Marshall JC, & Fink GR (2006) Using fMRI to decompose the neural processes underlying the Wisconsin Card Sorting Test. *Neuroimage* 30(3):1038-1049.
2. Thompson DG*, et al.* (2015) FMRI activation during executive function predicts response to cognitive behavioral therapy in older, depressed adults. *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry* 23(1):13-22.
3. Roman-Urrestarazu A*, et al.* (2016) Brain structural deficits and working memory fMRI dysfunction in young adults who were diagnosed with ADHD in adolescence. *European child & adolescent psychiatry* 25(5):529-538.
4. McGeown WJ, Shanks MF, Forbes-McKay KE, & Venneri A (2009) Patterns of brain activity during a semantic task differentiate normal aging from early Alzheimer's disease. *Psychiatry Res* 173(3):218-227.
5. Plichta MM, Heinzel S, Ehlis AC, Pauli P, & Fallgatter AJ (2007) Model-based analysis of rapid event-related functional near-infrared spectroscopy (NIRS) data: a parametric validation study. *Neuroimage* 35(2):625-634.
6. Baker JM, Bruno JL, Gundran A, Hosseini SMH, & Reiss AL (2018) fNIRS measurement of cortical activation and functional connectivity during a visuospatial working memory task. *PLoS One* 13(8):e0201486.
7. Brigadoi S, Aljabar P, Kuklisova-Murgasova M, Arridge SR, & Cooper RJ (2014) A 4D neonatal head model for diffuse optical imaging of pre-term to term infants. *Neuroimage* 100:385-394.
8. Cui X, Bray S, & Reiss AL (2010) Functional near infrared spectroscopy (NIRS) signal improvement based on negative correlation between oxygenated and deoxygenated hemoglobin dynamics. *Neuroimage* 49(4):3039-3046.
9. Hosseini SMH*, et al.* (2017) Neural, physiological, and behavioral correlates of visuomotor cognitive load. *Sci Rep* 7(1):8866.
10. Bruno JL*, et al.* (2018) Mind over motor mapping: Driver response to changing vehicle dynamics. *Hum Brain Mapp* 39(10):3915-3927.
11. Textor J, van der Zander B, Gilthorpe MS, Liskiewicz M, & Ellison GT (2016) Robust causal inference using directed acyclic graphs: the R package 'dagitty'. *Int J Epidemiol* 45(6):1887-1894.