Hypoxia alters posterior cingulate cortex metabolism during a memory task: a 1H fMRS study

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Supplementary Materials:
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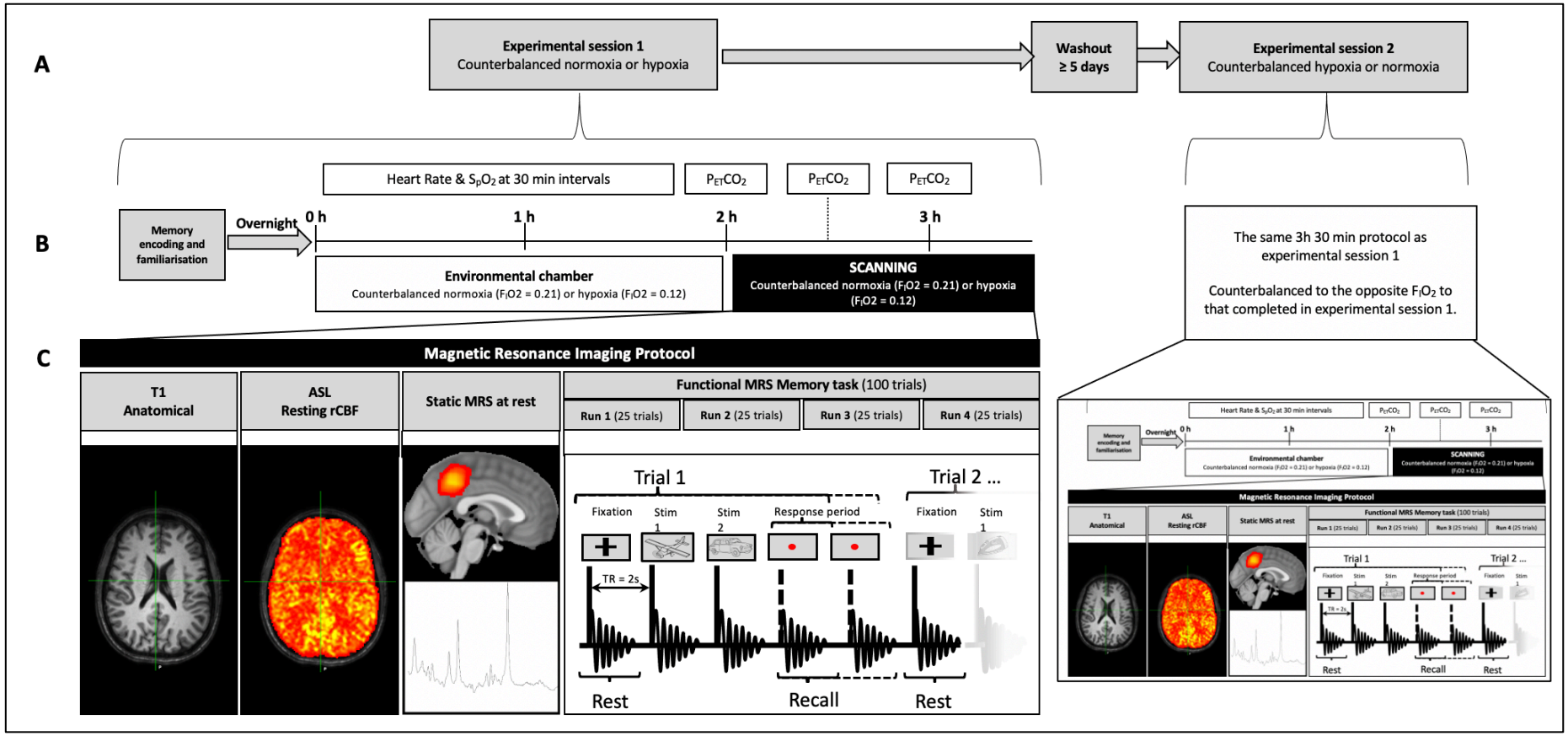


Supplementary figure S1. Study design and procedure schematic. Section A displays the counterbalancing of the experimental sessions. Section B displays the within session timeline of events, duration of hypoxic stimulus and the occurrence of data acquisition, both physiological monitoring and MRI scanning. Section C displays the MRI protocol with an example of how spectra acquisition was locked to individual FID acquisition in the functional MRS task.

Supplementary table S1. Physiologic data for each condition

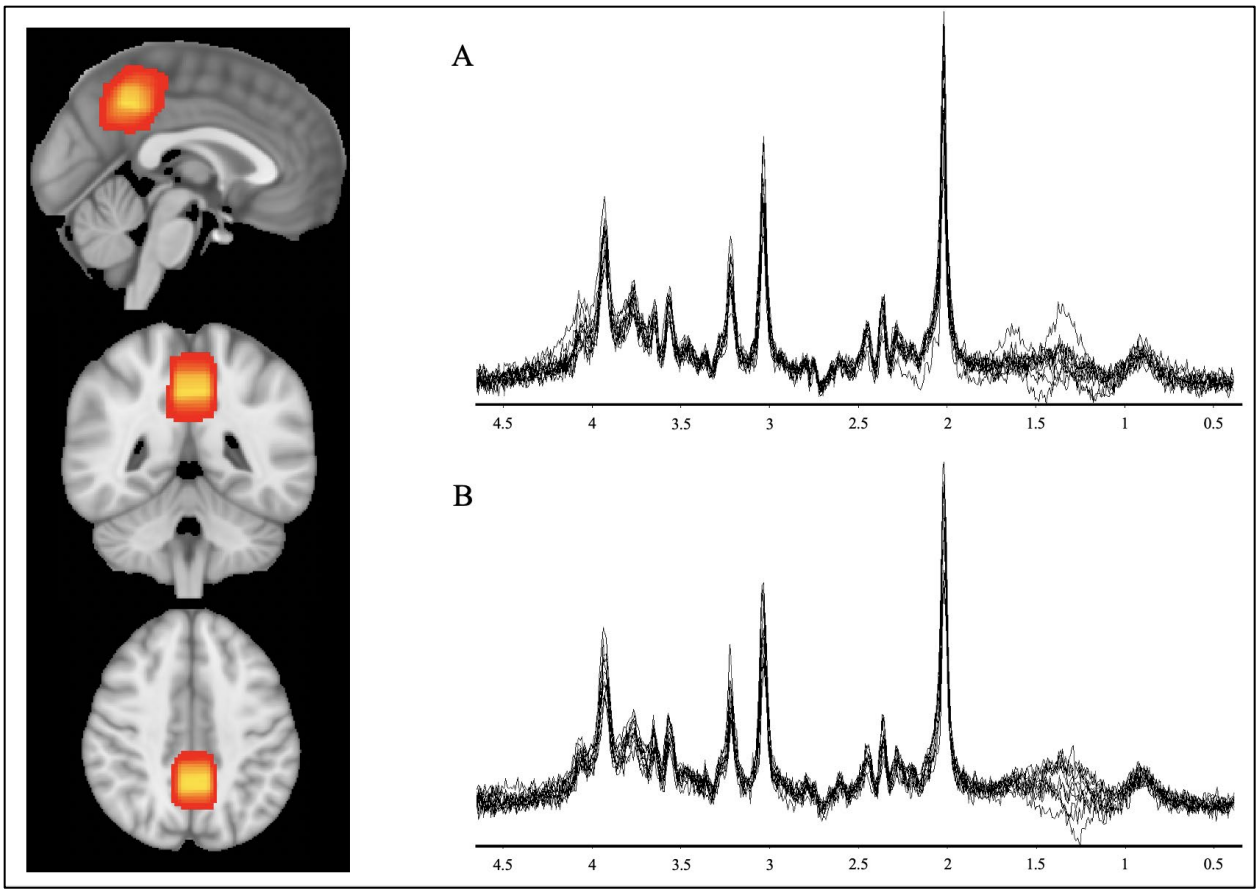
	2 h		2.15 h		2.30 h		3 h	
	Normoxia	Hypoxia	Normoxia	Hypoxia	Normoxia	Hypoxia	Normoxia	Hypoxia
SpO_2	99 (1)	84 (7)	-	-	-	-	-	-
HR	68 (8)	74 (9)	-	-	-	-	-	-
$P_{ET}CO_2$	-	-	35 (5)	33 (6)	36 (8)	31 (7)	35 (7)	30 (3)

Note. Condition comparison of physiology data. Peripheral arterial oxygen saturation (SpO_2), Heart Rate (HR) and Partial pressure of end tidal carbon dioxide ($P_{ET}CO_2$). Values in () represent the standard deviation of the above mean value.

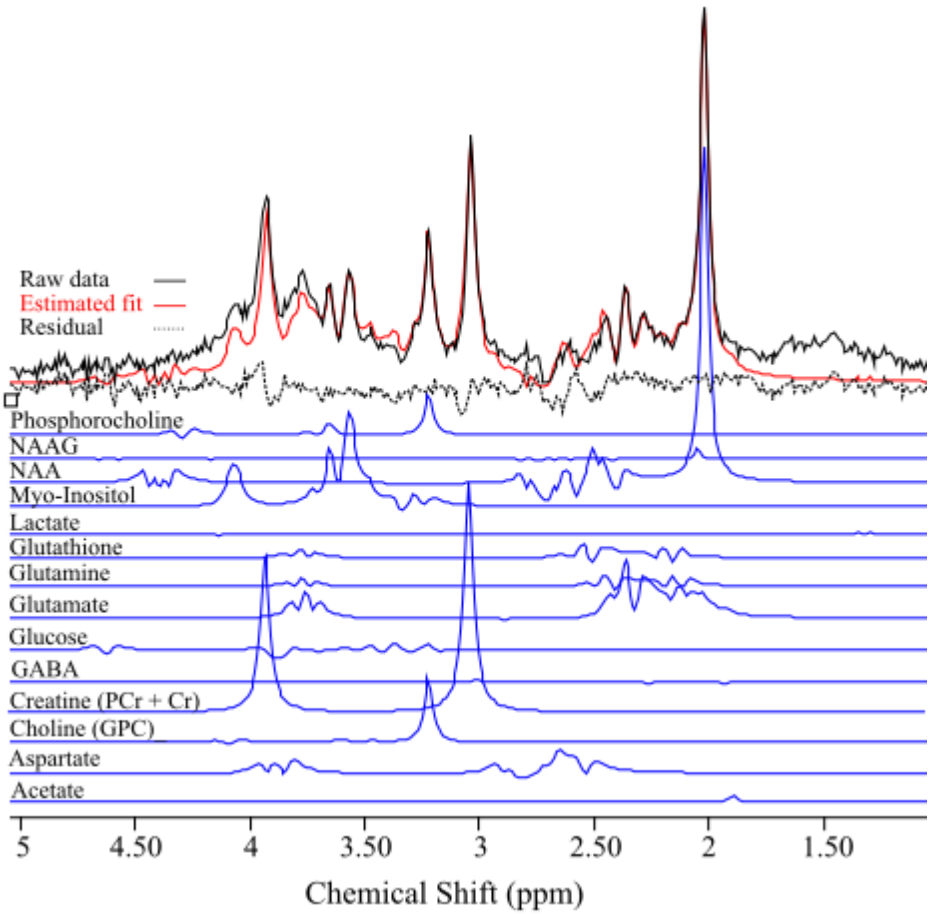
Supplementary table S2. Physiologic data and calculated blood T1 values for ASL analysis

Participant Number	Normoxia			Hypoxia		
	SpO_2	Haematocrit	T1 Blood	SpO_2	Haematocrit	T1 Blood
1	100	47.7	1.70	85	43.0	1.64
2	98	44.3	1.73	87	47.7	1.58
3	100	37.3	1.83	87	36.0	1.76
4	99	43.0	1.75	96	40.3	1.73
5	100	37.7	1.83	76	40.3	1.65
6	98	48.3	1.68	91	46.7	1.62
7	100	38.7	1.81	89	37.7	1.74
8	97	46.3	1.70	88	42.3	1.67
9	100	46.7	1.71	78	46.7	1.56
10	100	40.3	1.79	92	40	1.72
11	100	48.0	1.70	92	48.7	1.60
12	99	47.0	1.70	83	44.0	1.62
13	100	43.3	1.75	79	44.0	1.60

Note. SpO_2 is peripheral arterial oxygen saturations measured using pulse oximetry at the 2 h time point in each condition. Haematocrit was estimated using a capillary finger-tip blood sample taken at the start of each session. Both of these values were then used in the model suggested by Hales et al., 2016 to estimated individual T1 values for each participant.



Supplementary figure 2. The average location of the MRS acquisition voxel is shown on the left. Yellow reflects greater overlap in positioning across participants and conditions. Acquired spectra across all participants in each condition are shown for visual assessment of quality.



Supplementary Figure S3. Estimated fit (in red) residual (Black dashed line) and estimated components of fit (in Blue) from one participant during the "rest" period of the fMRS task in normoxia.

Supplmentary Table S3: MRSinMRS checklist

Site (Name or Number) Bangor University 1. Hardware	
a. Field strength [T]	3T
b. Manufacturer	Philips
c. Model (software version if available)	Acheiva
d. RF coils: nuclei (transmit/ receive), number of channels, type, body part	Body coil transmit, 32 channel head coil recieve
e. Additional hardware	
2. Acquisition	
a. Pulse sequence	PRESS (using a patch which allows a TTL pulse)
b. Volume of Interest (VOI) locations	Posterior Cingulate Cortex
c. Nominal VOI size [cm^3, mm^3]	20 x 20 x 20 mm^3
d. Repetition Time (TR), Echo Time (TE) [ms, s]	Tr = 2000 ms TE = 40 ms
e. Total number of Excitations or acquisitions per spectrum In time series for kinetic studies i. Number of Averaged spectra (NA) per time-point ii. Averaging method (e.g. block-wise or moving average) iii. Total number of spectra (acquired / in time-series)	Static MRS acquisition was collected as a single average of 64 single shots. fMRS acquisition was collected as a single shot per timepoint/event, across 4 runs of 128 shots. Shots were then "binned" and averaged according to condition (across runs), producing a single FID for each condition of interest.
f. Additional sequence parameters (spectral width in Hz, number of spectral points, frequency offsets) If STEAM:, Mixing Time (TM) If MRSI: 2D or 3D, FOV in all directions, matrix size, acceleration factors, sampling method	Spectral Width = 2000 Hz, 2048 spectral points. Planned using a voxel depicting the NAA voxel.
g. Water Suppression Method	CHESS
h. Shimming Method, reference peak, and thresholds for "acceptance of shim" chosen	Shimmed using the unsuppressed water peak. Threshold for acceptable shim set at 12 Hz as reported by the system.
i. Triggering or motion correction method (respiratory, peripheral, cardiac triggering, incl. device used and delays)	No triggering used for acquisition
3. Data analysis methods and outputs	
a. Analysis software	jMRUI
b. Processing steps deviating from quoted reference or product	

c. Output measure (e.g. absolute concentration, institutional units, ratio)Processing steps deviating from quoted reference or product	Reported as absolute concentration (in millimolar units)
d. Quantification references and assumptions, fitting model assumptions	Using the QUEST algorithm in jMRUI
4. Data Quality	
a. Reported variables (SNR, Linewidth (with reference peaks))	*The full width at half maximum (FWHM) for the NAA peak (Hz) in normoxia for rest (mean ± SD; 4.74±2.33) and response (4.60±2.64) did not significantly differ (P=0.464) nor did it for rest (5.67±2.71) and response (5.74±2.63) in hypoxia (P=0.609).* *The slightly larger linewidth in Hypoxia is expected due to the effect of increased de-oxyhemoglobin in this condition.*
b. Data exclusion criteria	*None applied, but strength of result was weighted by level of SD, with those results for metabolites with SD > 10% considered tentative only.*
c. Quality measures of postprocessing Model fitting (e.g. CRLB, goodness of fit, SD of residual)	*Across all participants, metabolite estimation for Glutamate, Myo-Inositol, Creatine, N-Acetyl Aspartate, and Choline, had a standard deviation lower than 10%. Glutamine, Glucose and Glutathione had a SD lower than 40%. Lactate and Gamma-Aminobutyric Acid had a SD greater than 40%.*
d. Sample Spectrum	Included in paper (figure 1) and supplementary material (supplementary figure S3)