MR Thermometry as a Biomarker in Clinical Applications

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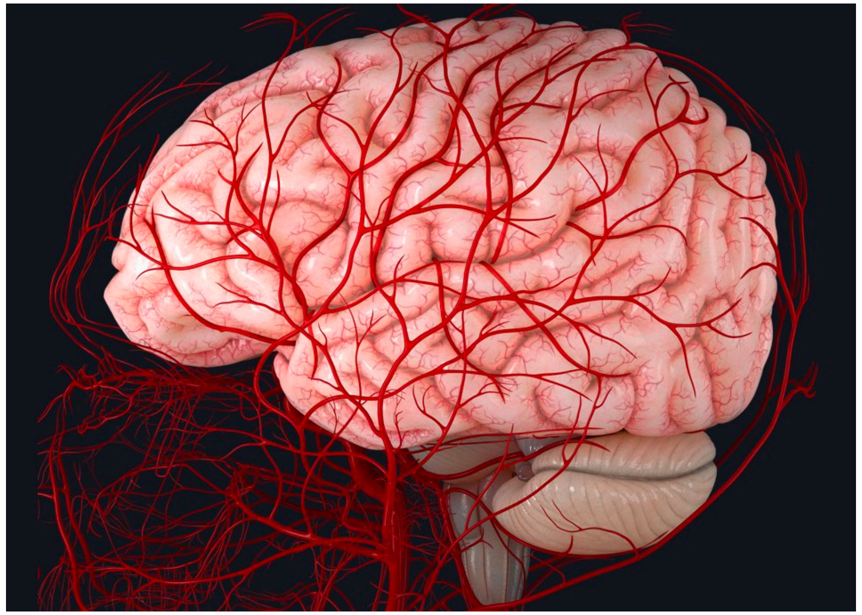
EMORY UNIVERSITY

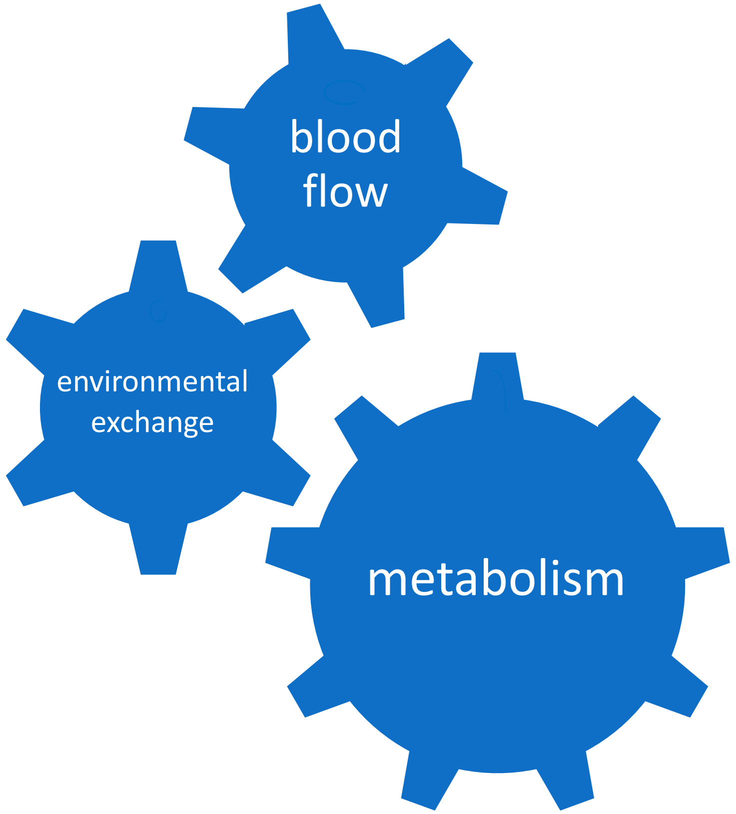
Significance of Brain Temperature

- Temperature affects
  - Affinity of hemoglobin for oxygen
  - Brain functions through protein geometry, assembly and expression
- Temperature affects the outcome of ischemic and traumatic injuries
  - Hypothermia is considered as a therapy
- Higher temperature in brain tumor using intra-op infrared imaging

Burioni, R et al, 2004. Proteins
Busto R et al, 1987. JCBFM
Soukup B, et al, 2002, J Neurotrauma
Kateb B, et al, 2009, Neuroimage

Brain thermal homeostasis



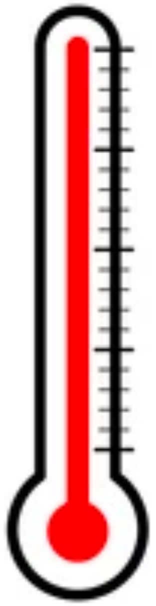


- Metabolism dissipate heat
- Arterial blood cooler than deep brain region
- Cortex might be warmer/cooler depending on environmental exchange
- Brain-body temperature difference ~ -0.3 to 2 ^{o}C

Rumana C, et al, 1998. Critical Care Medicine

Measuring Temperature Using MR

Temperature

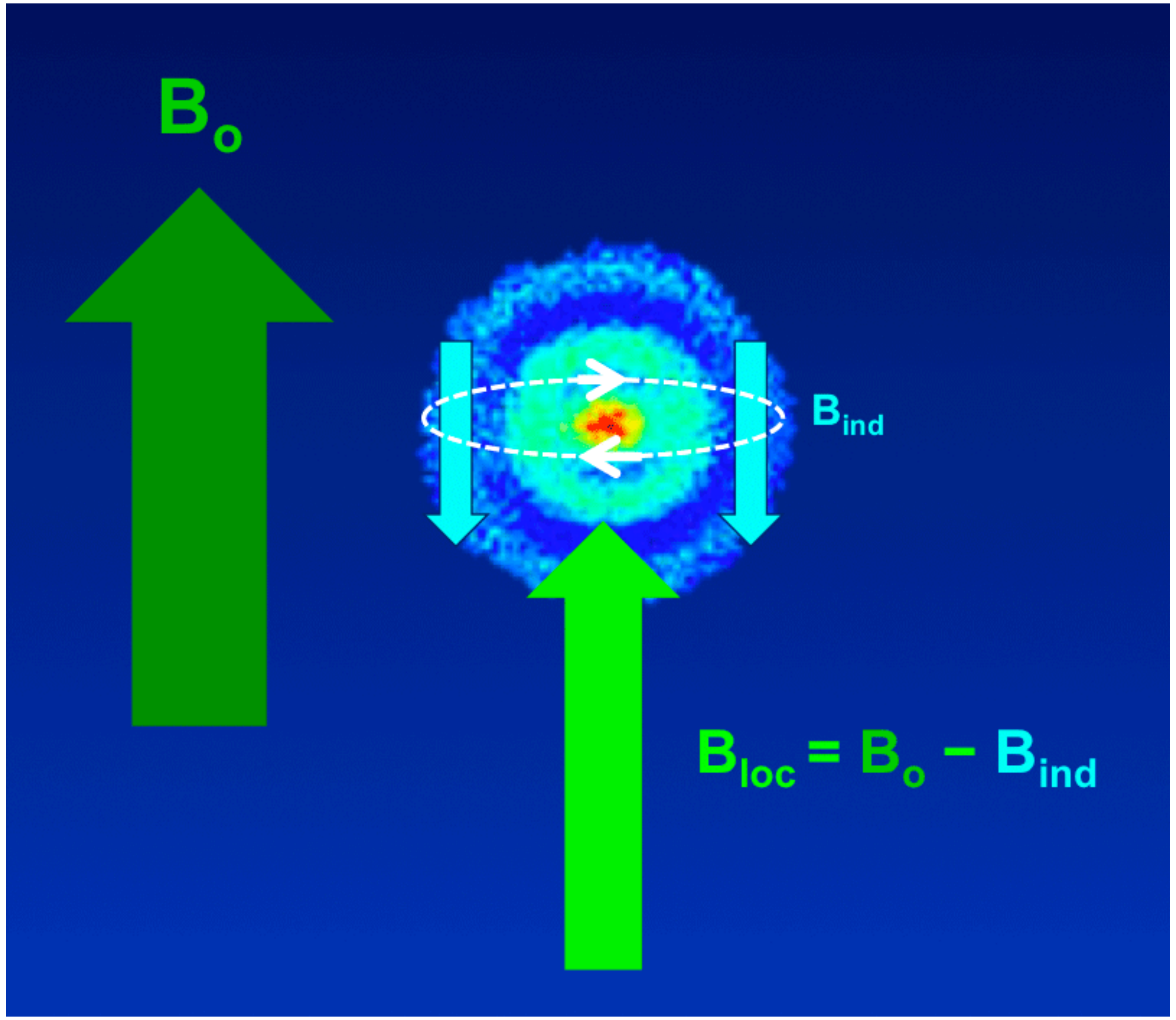


Changes

- Proton Resonance Frequency (PRF)
- Longitudinal Relaxation Rate T1
- Diffusion Coefficient
- …

- Measure MR property
- Use it to estimate temperature by controlling other factors

Temperature-Dependent Proton Resonance Frequency



mriquestions.com

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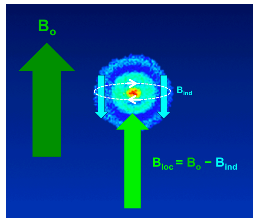
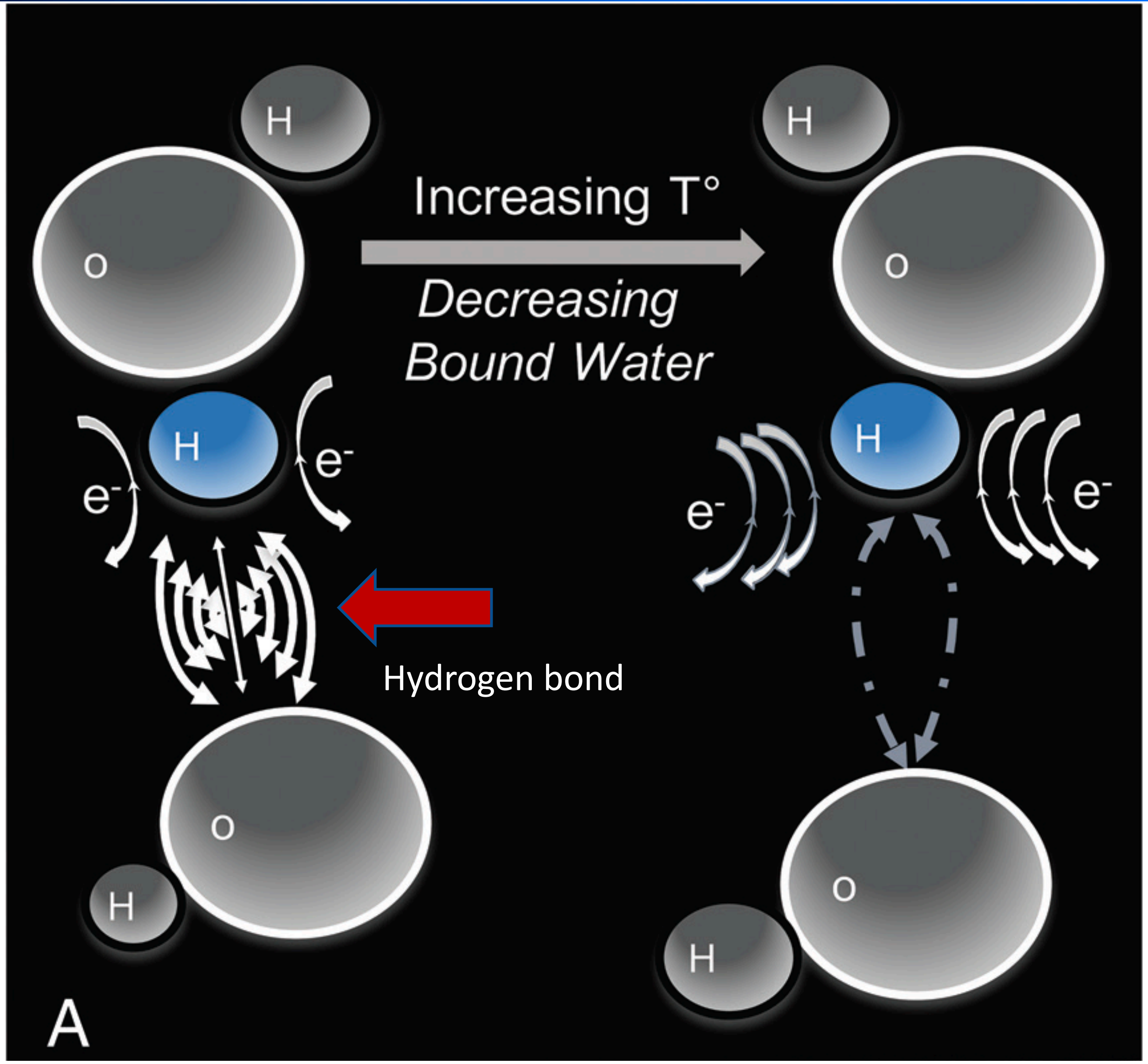
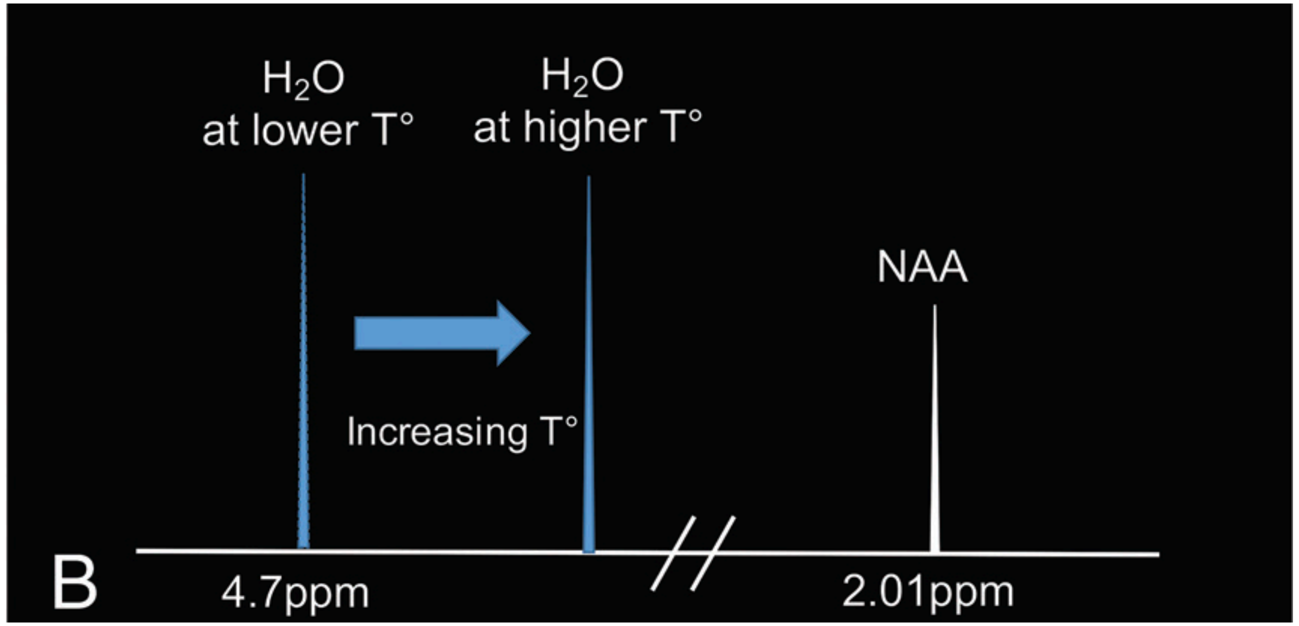
Temperature-Dependent Proton Resonance Frequency

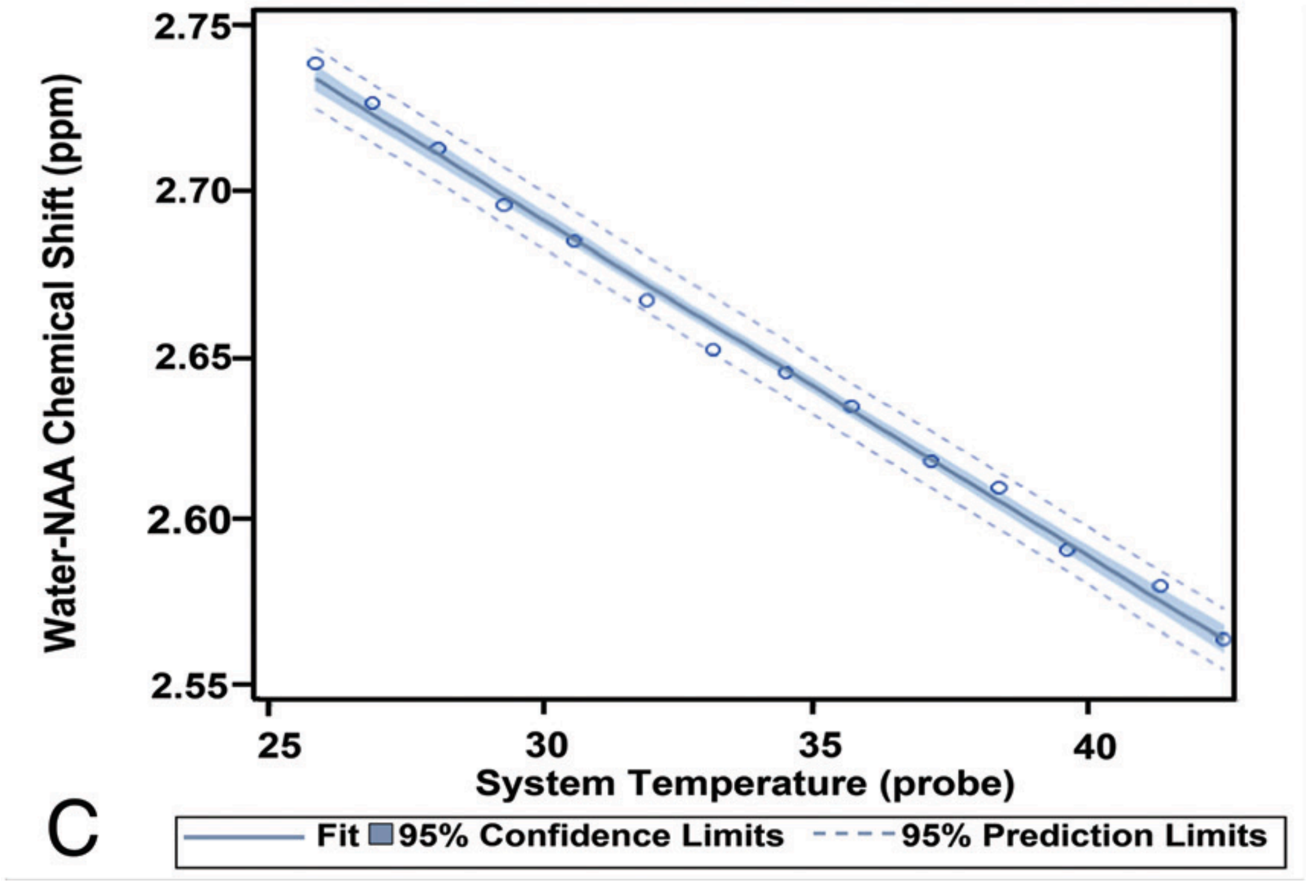






Kuroda K. 2005. Int J Hyperthermia
Dehkharghani S and Qiu D, 2020, AJNR

Temperature-Dependent Proton Resonance Frequency

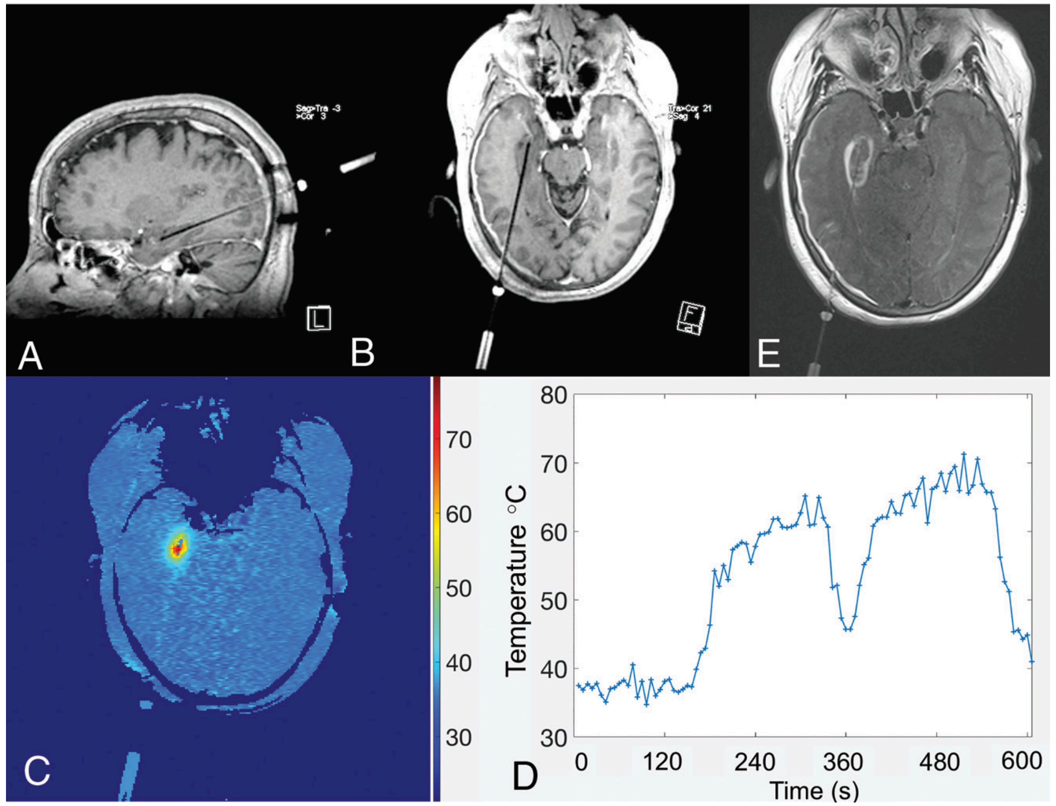


Slope ranges between -0.009 and -0.011 ppm per Celsius degree

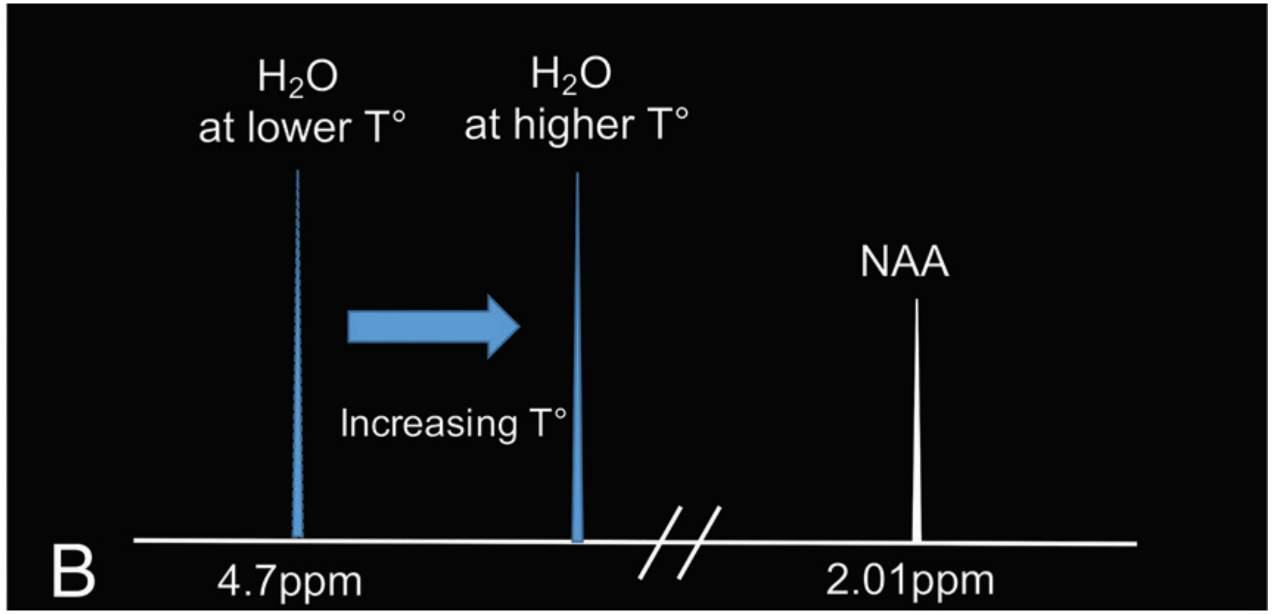
Corbett, RJ et al, 1995. J Neurochem
Coman D et al, 2009. NMR Biomed
Dehkharghani S et al. 2015. AJNR

Relative vs Absolute Temperature Quantification and reference frequency

- Relative Temperature change
  - Baseline water proton frequency
  - Repeated measurement of frequency (typically using GRE phase imaging)



- Absolute Temperature Quantification
  - Metabolites whose temperature dependency is negligible (e.g. NAA, Cr)



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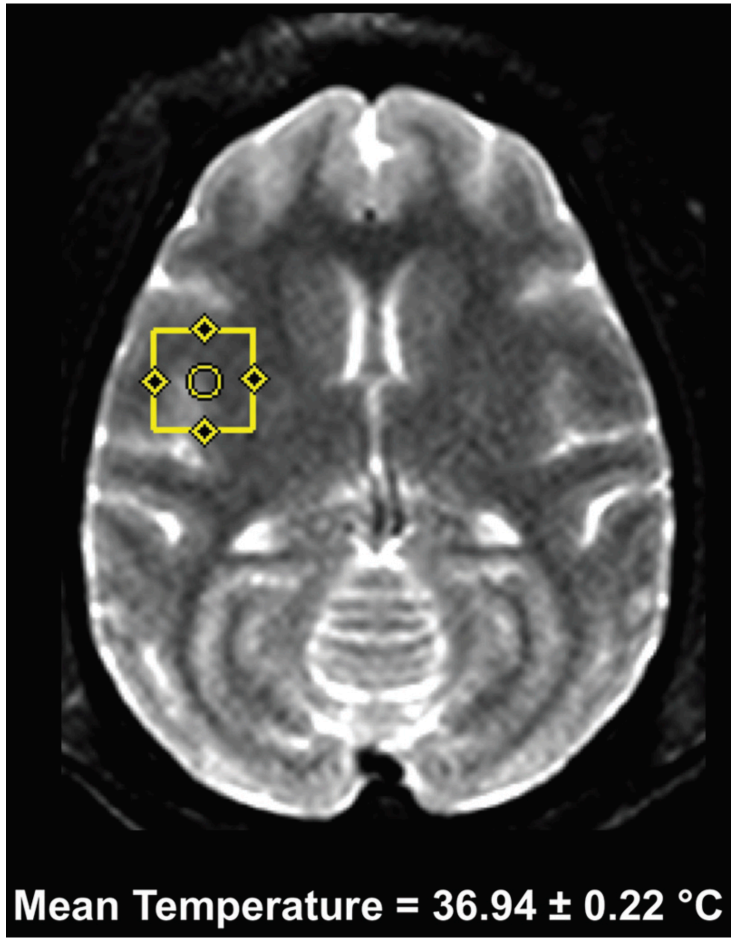
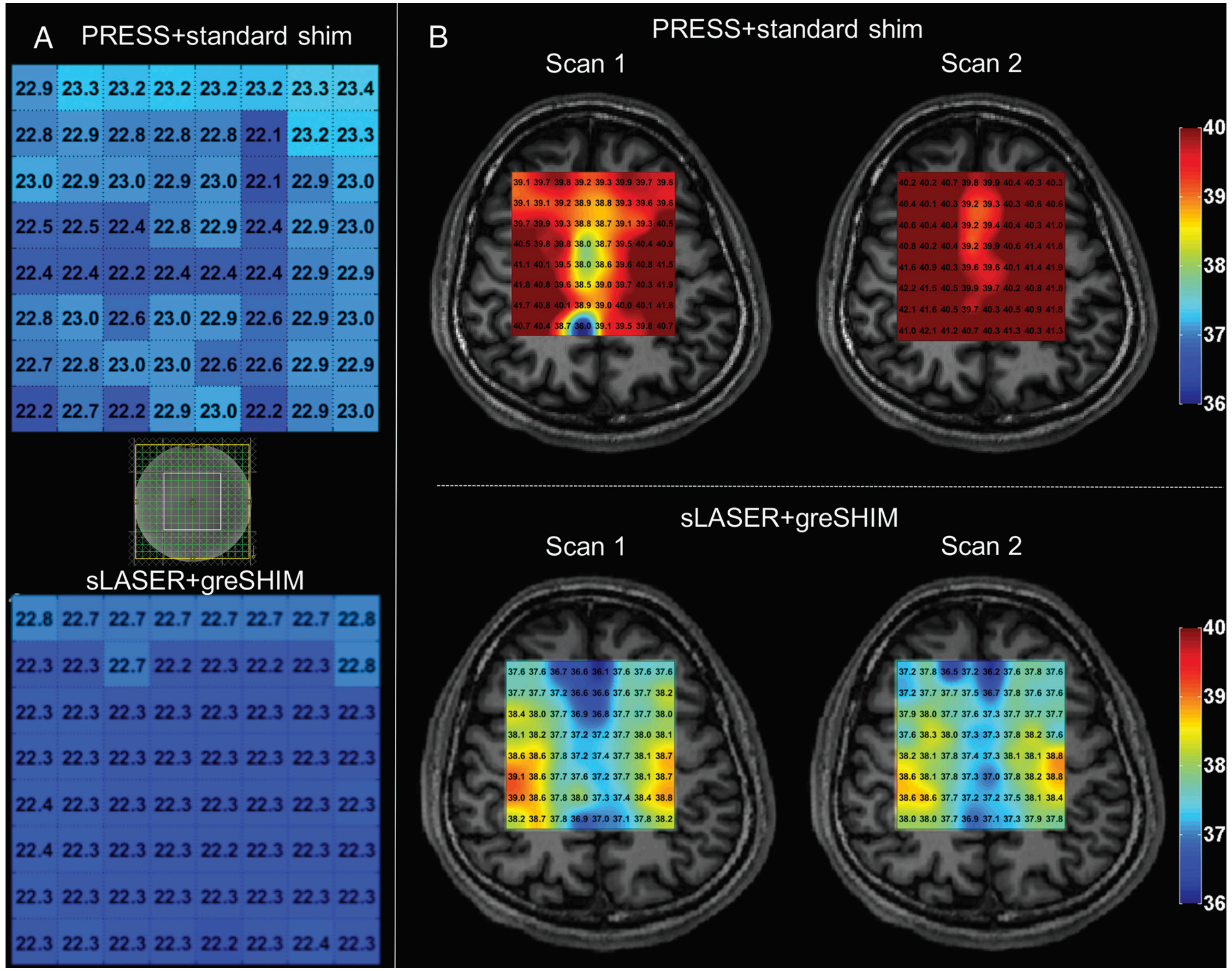
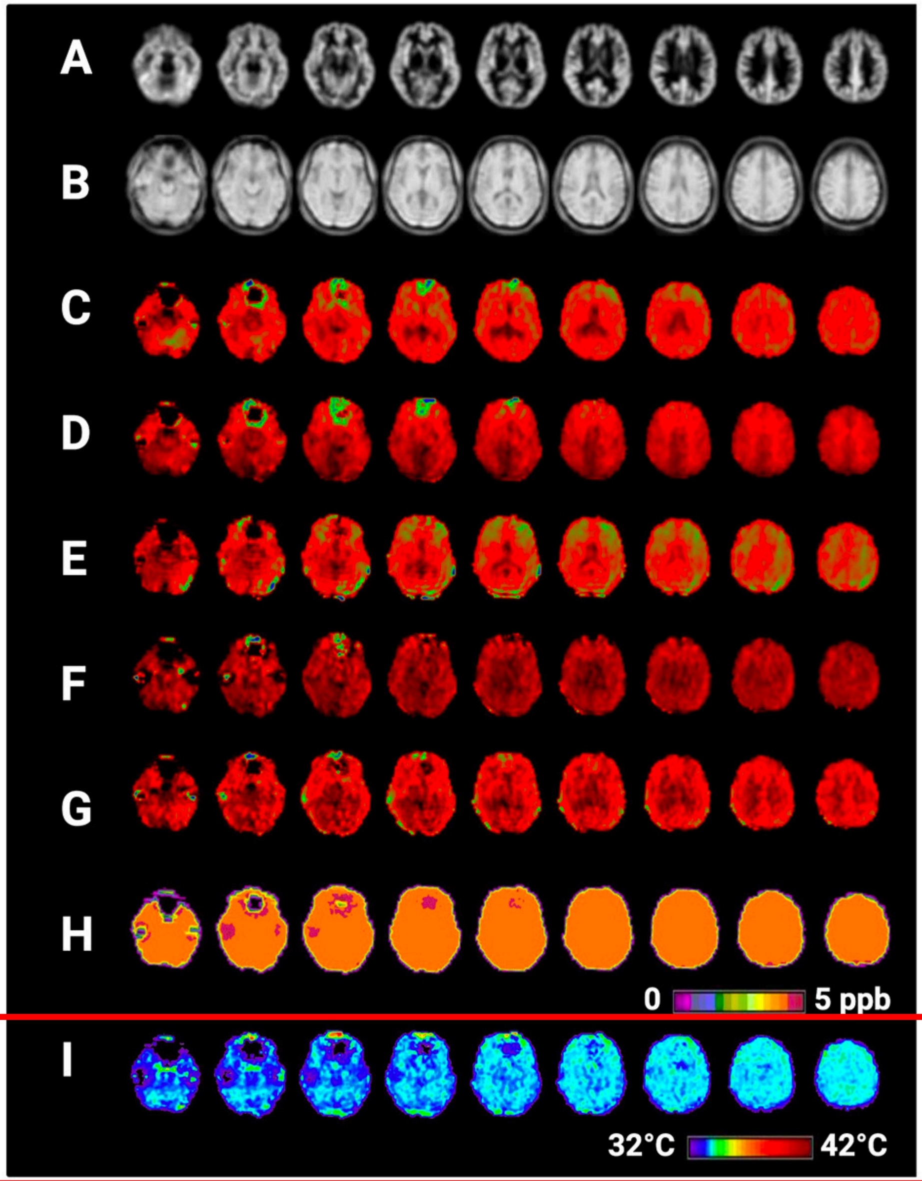
MRS Thermometry Methods





Dehkharghani S, et al. 2015. AJNR
Dehkharghani S and Qiu D, 2020, AJNR

3D MRS Thermometry



(A) gray matter

(B) water

(C) creatine

(D) total choline

(E) NAA

(F) myo-inositol

(G) Glx

(H) frequency difference

(I) temperature

Sharma AA et al. 2020. Front. Hum. Neurosci

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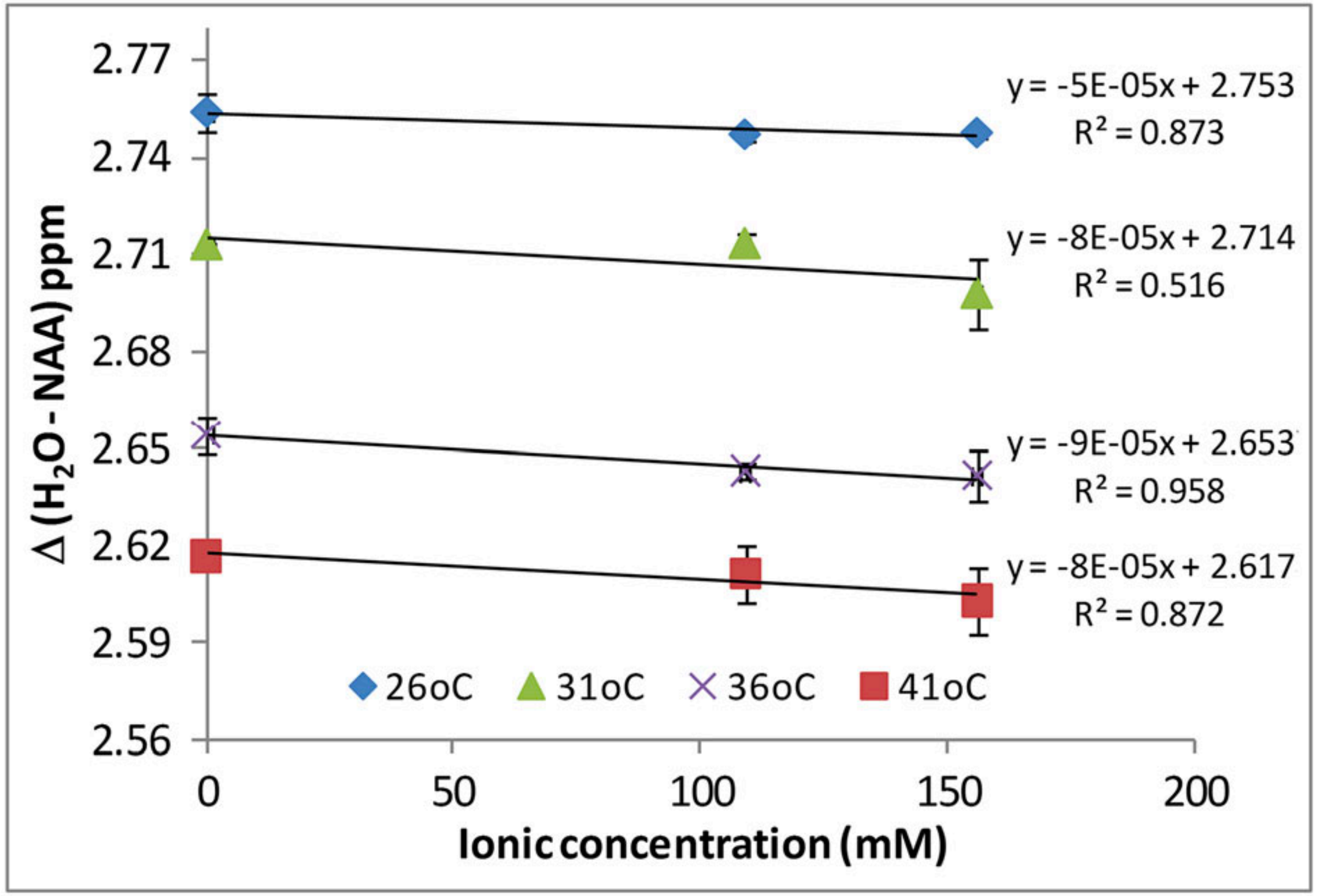
Confounding effects



Babourina-Brooks B, et al. 2014. NMR Biomed

- 100mM increase in ionic concentration ~ 0.5-1 ^{o}C error if unaccounted
- Acute ischemia could result in up to 100mM increase in extracellullar potassium*

*Yi CS, et al, 2003. J. theor. Biol.

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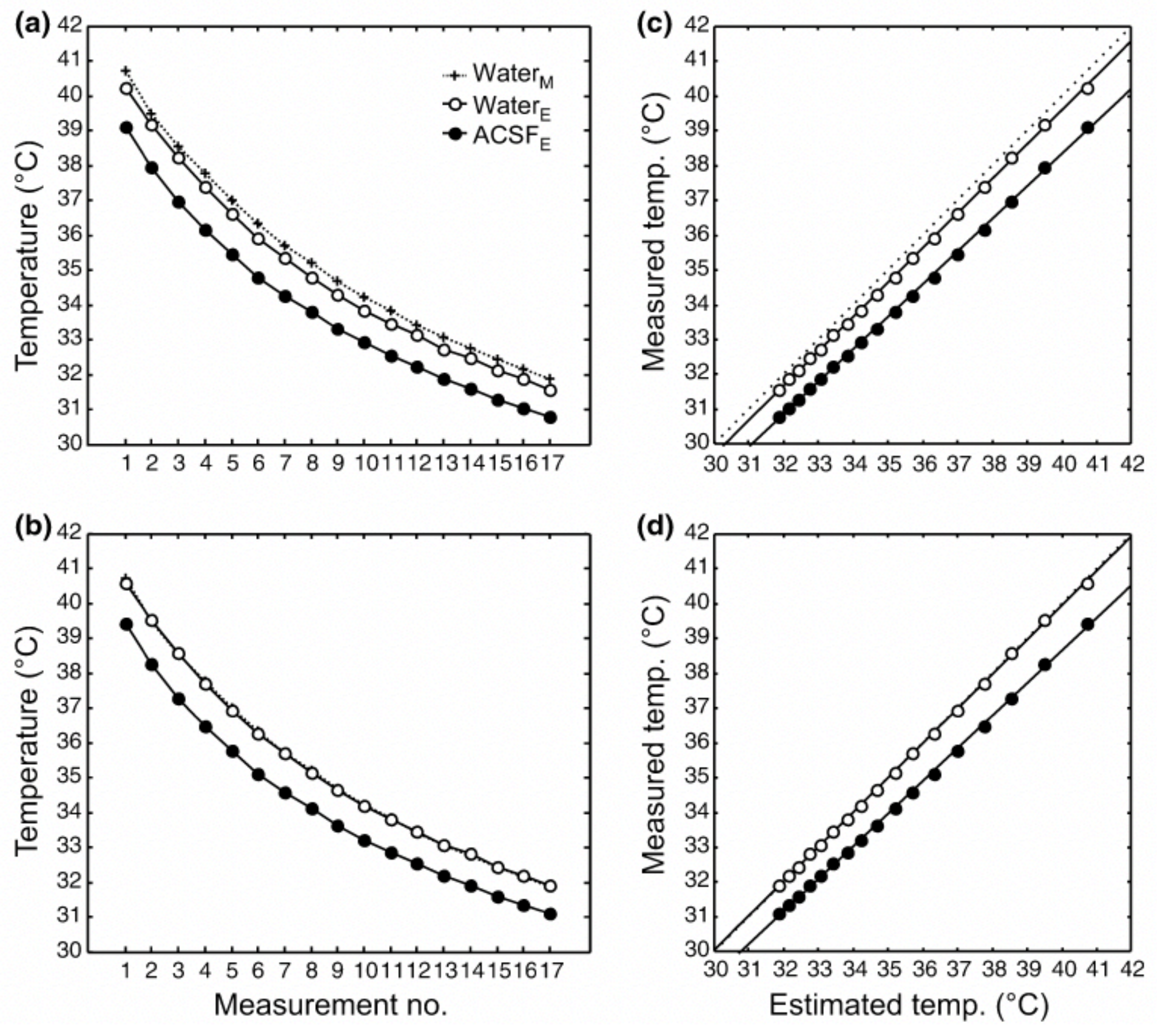
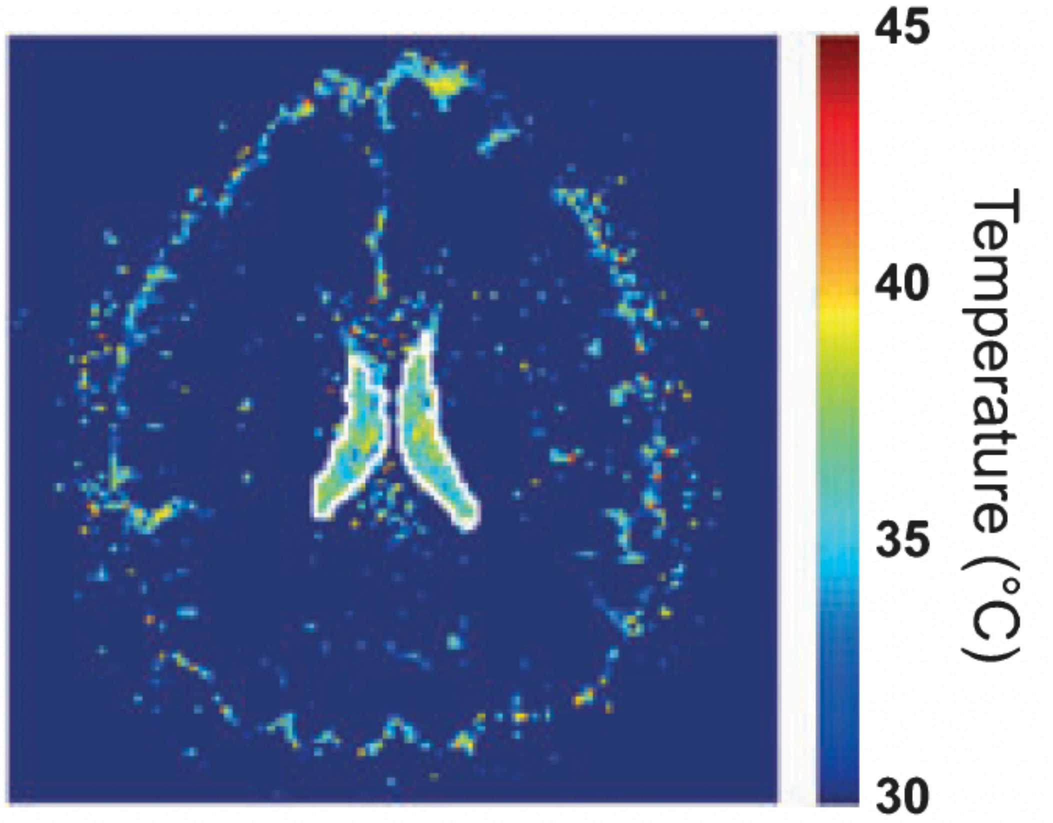
Diffusion coefficient-based thermometry

$$D \sim \exp\left(\frac{-1}{T}\right)$$





Kozak LR, et al, 2010. Acta Paediatrica

Brain-Body Temperature Difference

N=18

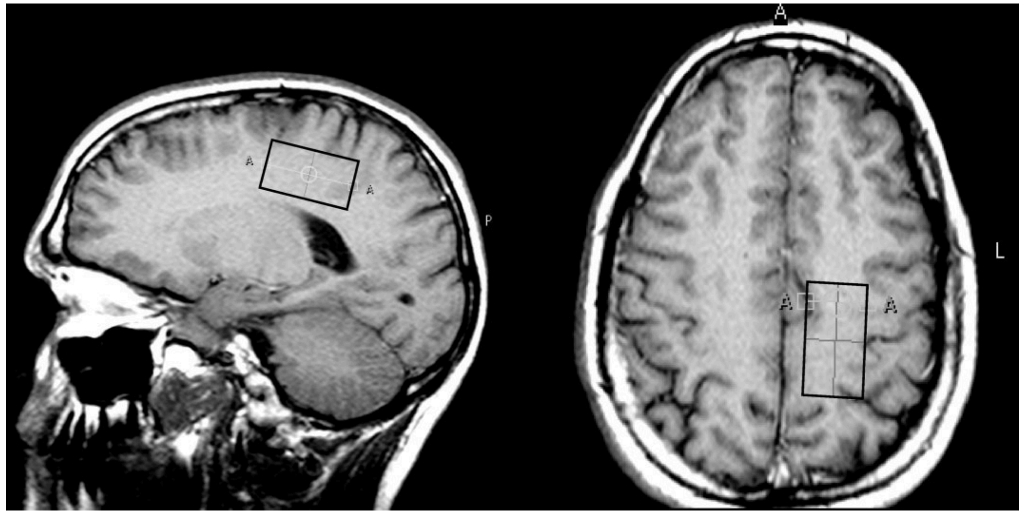


Table 1

Mean Brain, Body Temperature and Brain–Body Temperature Differences (°C) in Healthy Volunteers*

	T_{Cho} n = 72	T_{Cr} n = 72	T_{NAA} n = 72	$T_{Cho,Cr,NAA}$ n = 216	T_{body} N = 18	$\Delta T_{brain\text{–}body}$
Mean	38.1 ± 0.5	38.0 ± 0.5	38.3 ± 0.5	38.1 ± 0.4	36.9 ± 0.2	1.3 ± 0.4
Range	37.1–39.0	37.0–38.9	37.2–39.1	37.4–38.9	36.6–37.3	0.5–1.8

*T_{Cho}, T_{Cr}, T_{NAA} are the mean brain temperatures computed from water-Cho, water-Cr and water-NAA chemical shift differences. $T_{Cho,Cr,NAA}$ is the mean temperature computed from all water-metabolite chemical shift differences. T_{body} is the mean body (rectal) temperature. $\Delta T_{brain\text{-}body} = T_{Cho,Cr,NAA} - T_{body}$ is the mean brain–body temperature difference. n is the number of spectral lines used in the calculations. N is the number of volunteers.

Covaciu L et al, 2010, JMRI

Theoretical model of brain temperature change in functional activity

- Without exchange, brain is 0.36 °C warmer than arterial blood in normal brain
- Predictions:
  - Activation decrease temperature in deep brain
  - Activation might increase/decrease temperature in cortex

Sukstanskii A and Yablonskiy DA. 2006. PNAS

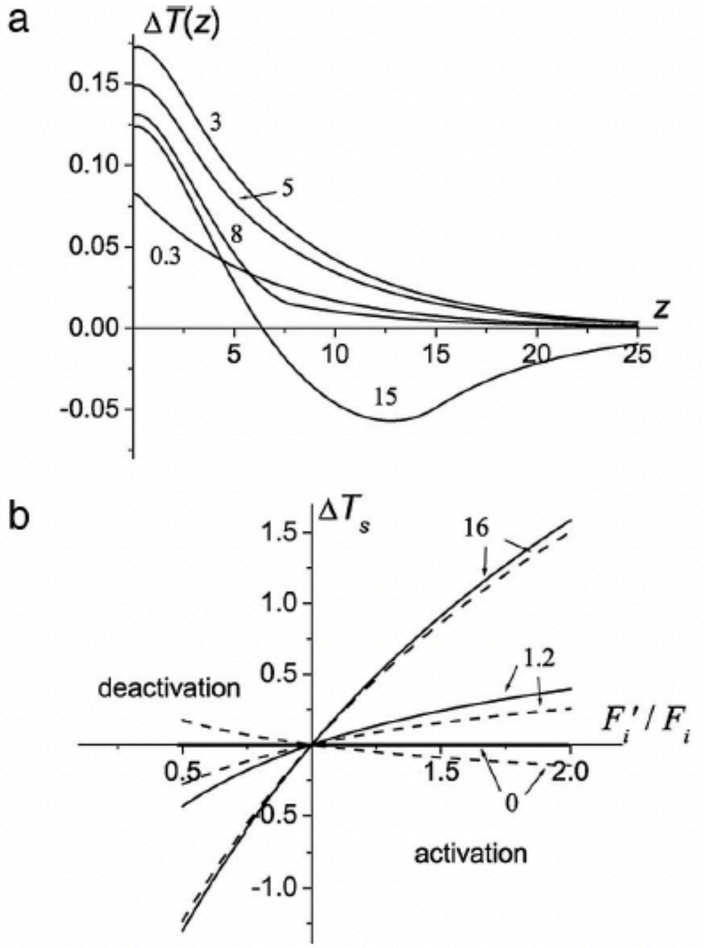


Fig. 2. The temperature change in the cortex-located AFR. (*a*) $\Delta T(z) = T(z) - T_0(z)$ (in °C; *z* in millimeters) for different thicknesses *d* (numbers next to the curves are in millimeters) of the AFR; $F_i' = 1.5 \cdot F_i$, $q_i' = 1.1 \cdot q_i$ and the default values of other parameters (see Table 1). (*b*) ΔT_s (in °C) as a function of the ratio F_i'/F_i for different values of the effective heat transfer coefficient [numbers next to the curves are in 10^{-3} W/(cm^2·°C)] for $OEF_i' = OEF_i$ (solid lines) and $q_i' = q_i$ (dashed lines).

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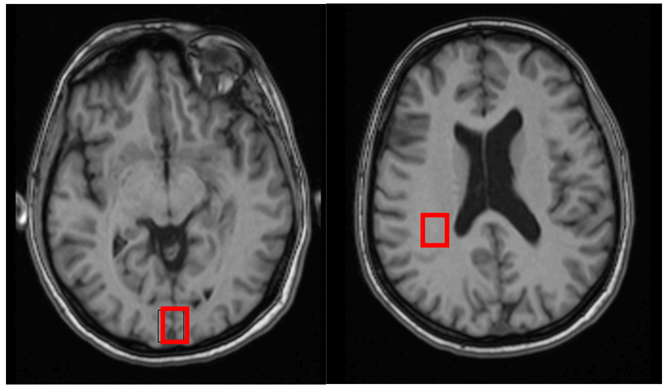
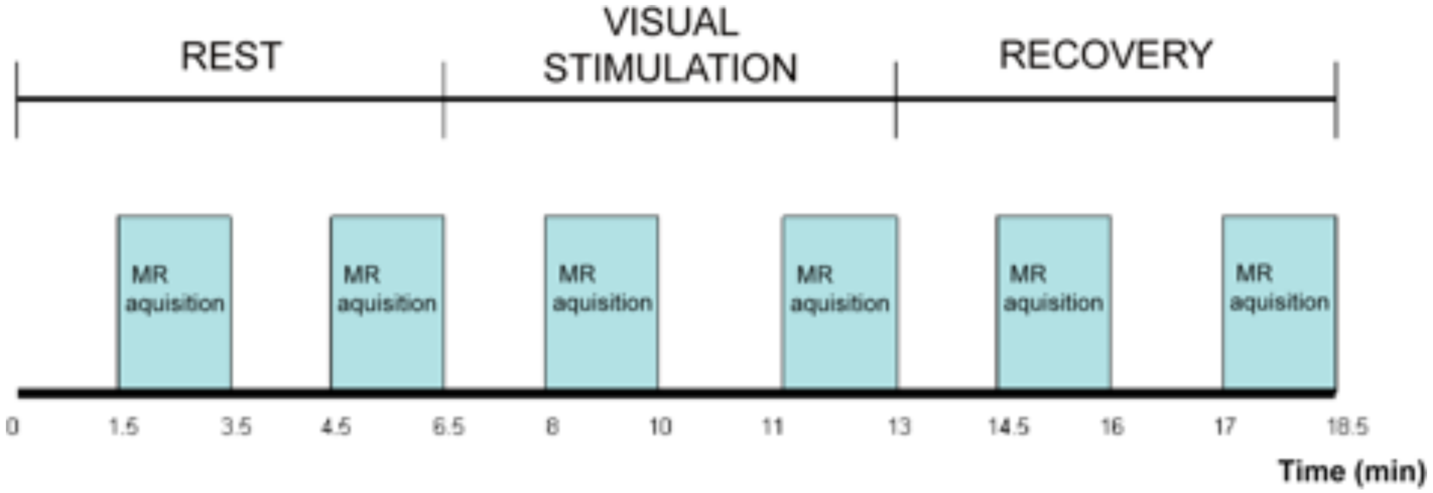
Task fMRI using Thermometry





P<0.002

P<0.001

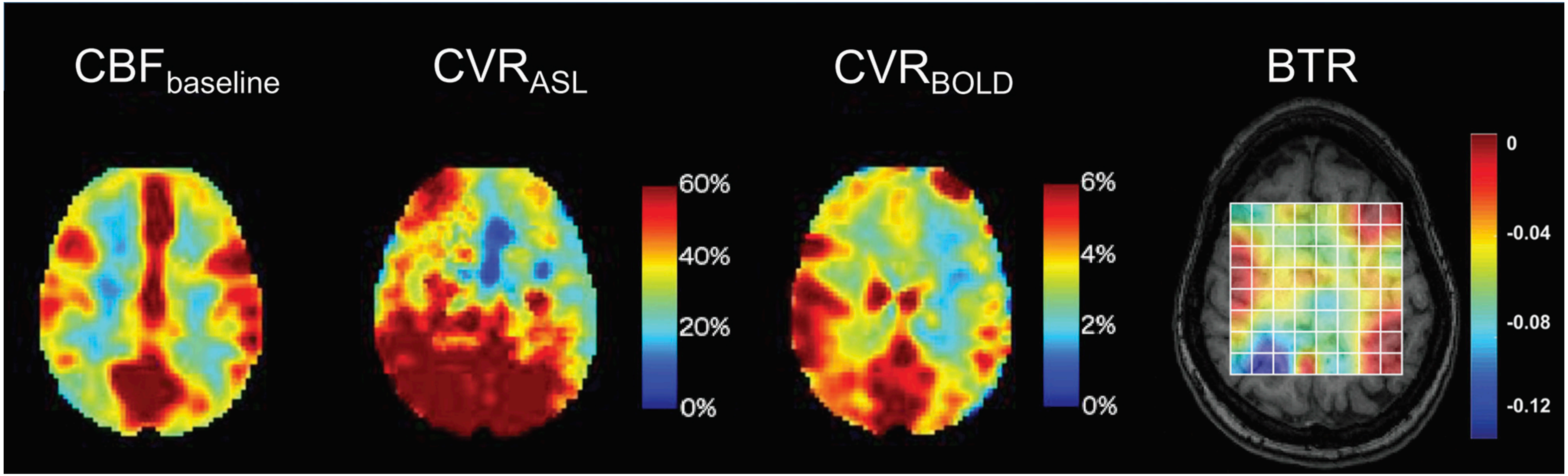
Table 3. Brain temperature mean values

	Rest	Visual stimulation		Recovery	
		First part	Second part	First part	Second part
Visual cortex	37.40 (0.20)	37.40 (0.20)	37.20 (0.20)	37.80 (0.20)	37.40 (0.20)
Centrum semiovale	37.60 (0.20)	37.60 (0.20)	37.60 (0.20)	37.60 (0.20)	37.60 (0.20)

N=20

Rango M. et al 2015. Plos One

Increasing Blood Flow through Acetazolamide Reduce Brain Temperature



Dehkharghani S and Qiu D, 2020, AJNR
Fleischer CC, et al. 2017. AJNR

Brain temperature in ischemia

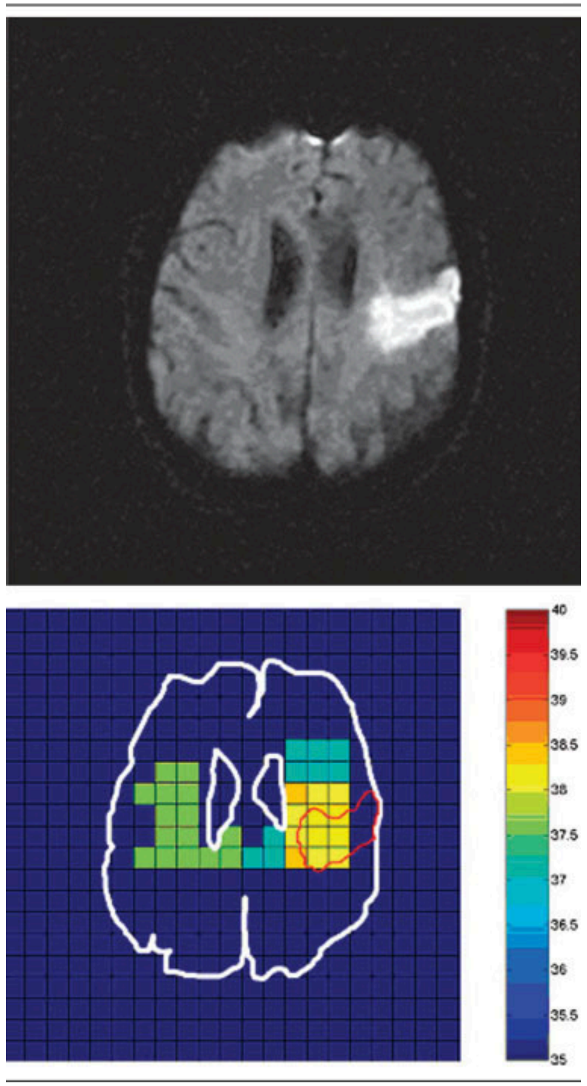


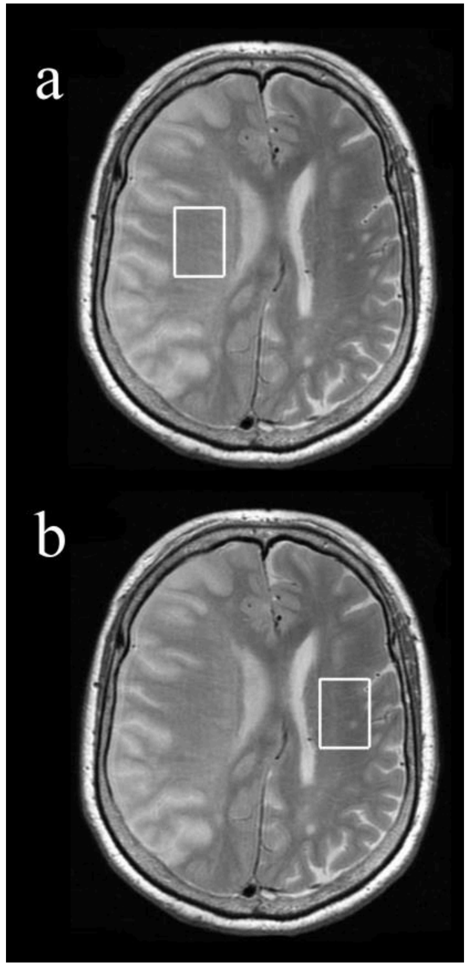
Table 1. Comparison of Temperature Differences and Absolute Mean Temperatures in Acute Ischemic Stroke in Different Brain Tissues as Defined by Diffusion-Weighted Imaging

Comparisons	Weighted Mean Temperature Differences (95% CI), °C	Test for Overall Effect	Maximum Temperature Differences, °C	Mean Patient Temperature, °C*	
DAL vs CNL	0.38 (0.27, 0.49)	$p < 0.00001$	2.91, −2.17	37.30	37.25
DAL vs INL	0.50 (0.34, 0.66)	$p < 0.00001$	1.90, −1.45	37.30	37.16
DAL vs **PAL**	−0.36 (−0.45, −0.26)	$p < 0.00001$	1.28, −2.17	37.30	37.63
DAL vs **PAL+**	−0.17 (−0.30, −0.04)	$p = 0.01$	1.66, −2.23	37.30	37.66
PAL vs INL	0.29 (0.14, −0.44)	$p = 0.0002$	1.92, −0.84	37.63	37.16
PAL vs CNL	0.14 (0.05, 0.23)	$p = 0.004$	2.68, −1.77	37.63	37.25
PAL+ vs INL	0.37 (0.24, 0.51)	$p < 0.00001$	2.43, −1.50	37.66	37.16
PAL vs **PAL+**	−0.15 (−0.26, −0.04)	$p = 0.007$	2.50, −1.66	37.63	37.66
INL vs **CNL**	−0.22 (−0.32, −0.12)	$p < 0.00001$	1.56, −1.08	37.16	37.25
(DAL + PAL) vs (INL + CNL)	0.17 (0.07, 0.27)	$p = 0.0007$	2.45, −2.17	—	—

CI = confidence interval; DAL = definitely abnormal tissue; CNL = contralateral normal brain; INL = ipsilateral normal brain; PAL = possibly abnormal tissue; PAL+ = tissue one voxel in thickness immediately outside the definitely or possibly abnormal tissue. Bold = the hotter of the two tissues in each comparison.
*L column refers to left-hand tissue in 'Comparisons' column; R column refers to right-hand tissue in 'Comparisons'.

Karaszewski B et al, 2006. Ann Neurol

Stroke



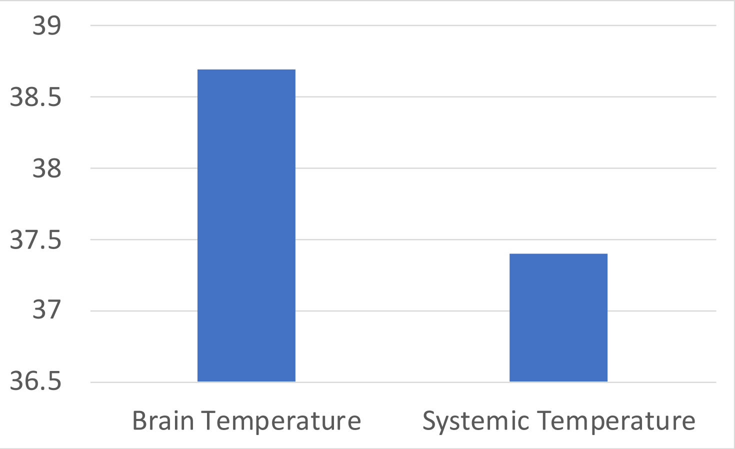


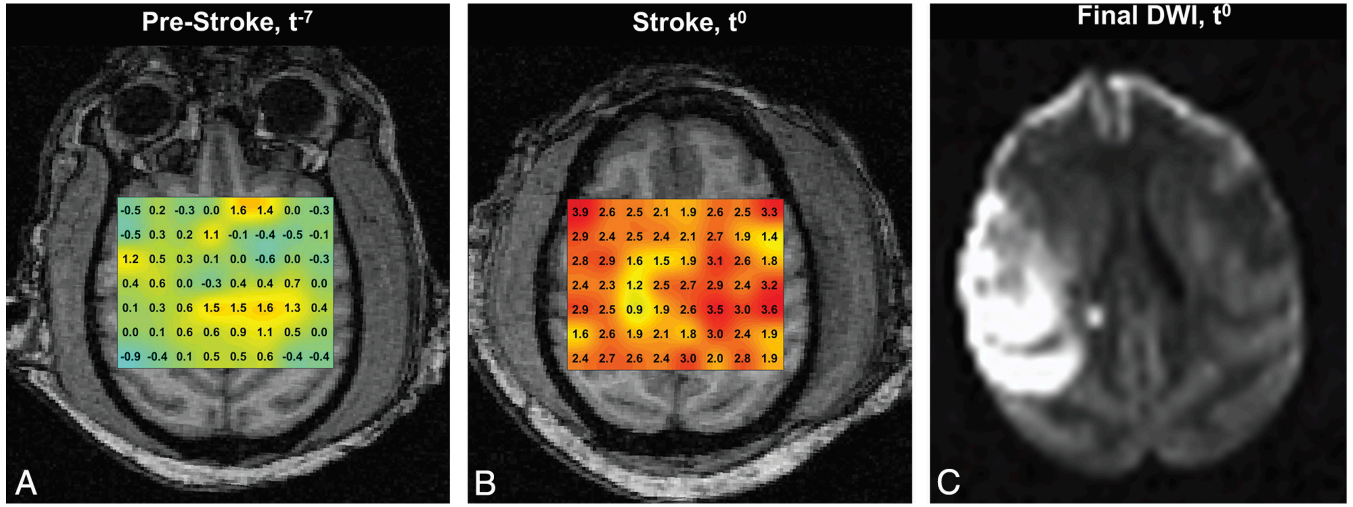
Table 1. Summary of clinical findings in seven patients with internal carotid artery occlusion.

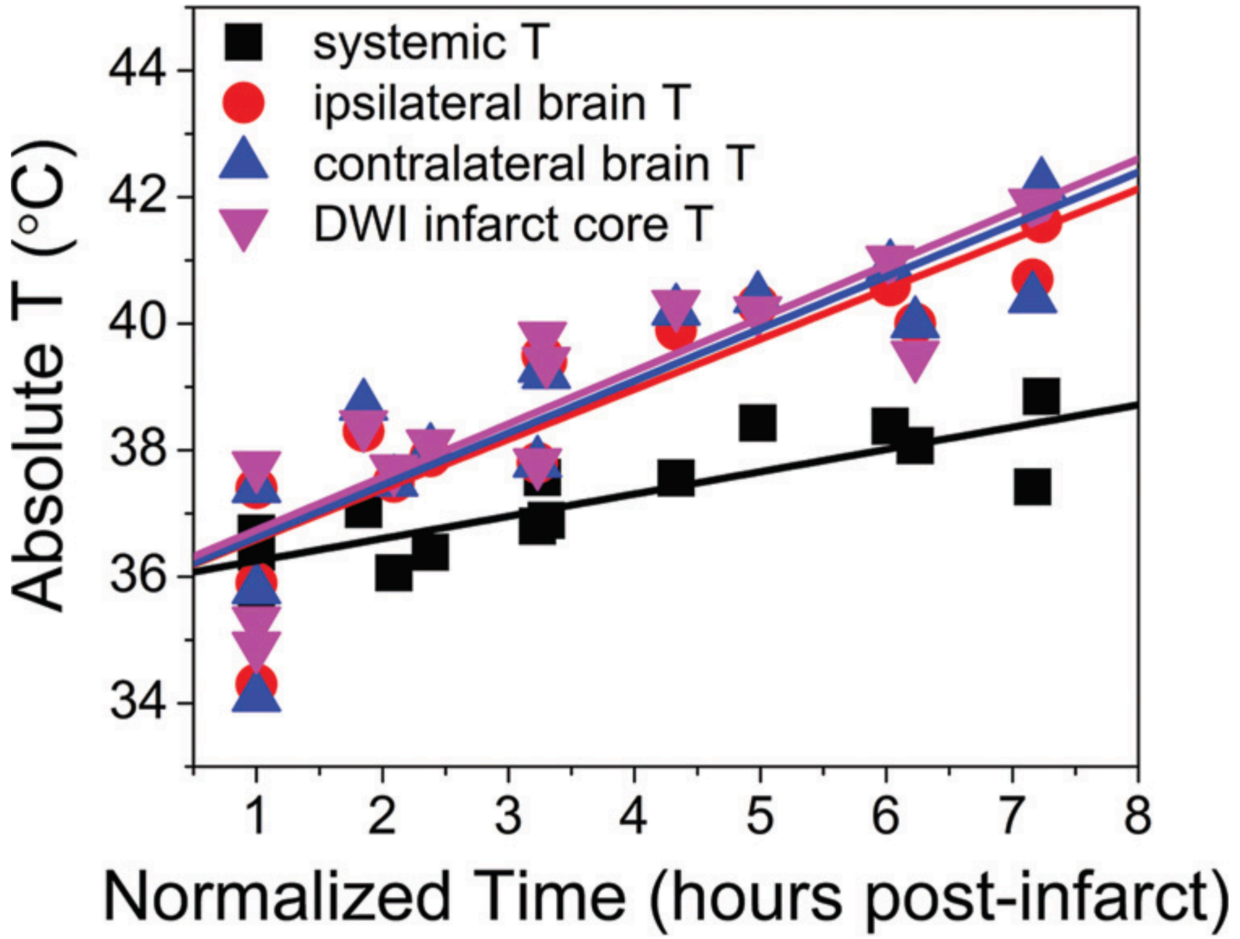
Case No.	Age (Years)	Sex	Side of Occlusion	Brain Temperature Ratio [1]	Time from Onset (h)	Severe Brain Swelling (−/+)	mRS	Systemic Temp. (°C)	NIHSS	Time to Death/ Discharge (Days)
1	72	Male	Rt	1.5	31	−	5	37.8	18	50
2	57	Male	Rt	1.23	28	−	5	37.5	29	27
3	88	Male	Lt	0.91	24	+	6	37.2	37	5
4	69	Male	Lt	0.8	48	−	5	37.6	27	54
5	87	Female	Rt	0.78	24	+	6	37.3	21	4
6	84	Male	Rt	0.71	21	+	6	37.4	30	3
7	70	Male	Rt	0.67	15	−	5	37.1	18	62

[1] Brain temperature ratio: brain temperature in the ischemic lesion/contralateral region. Abbreviations: Lt, left; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; Rt, right; temp., temperature.

Ishida T, et al, 2021. Sensors

Decoupling of body-brain temperature in ischemia in NHP





Dehkharghani S. et al. 2017. AJNR

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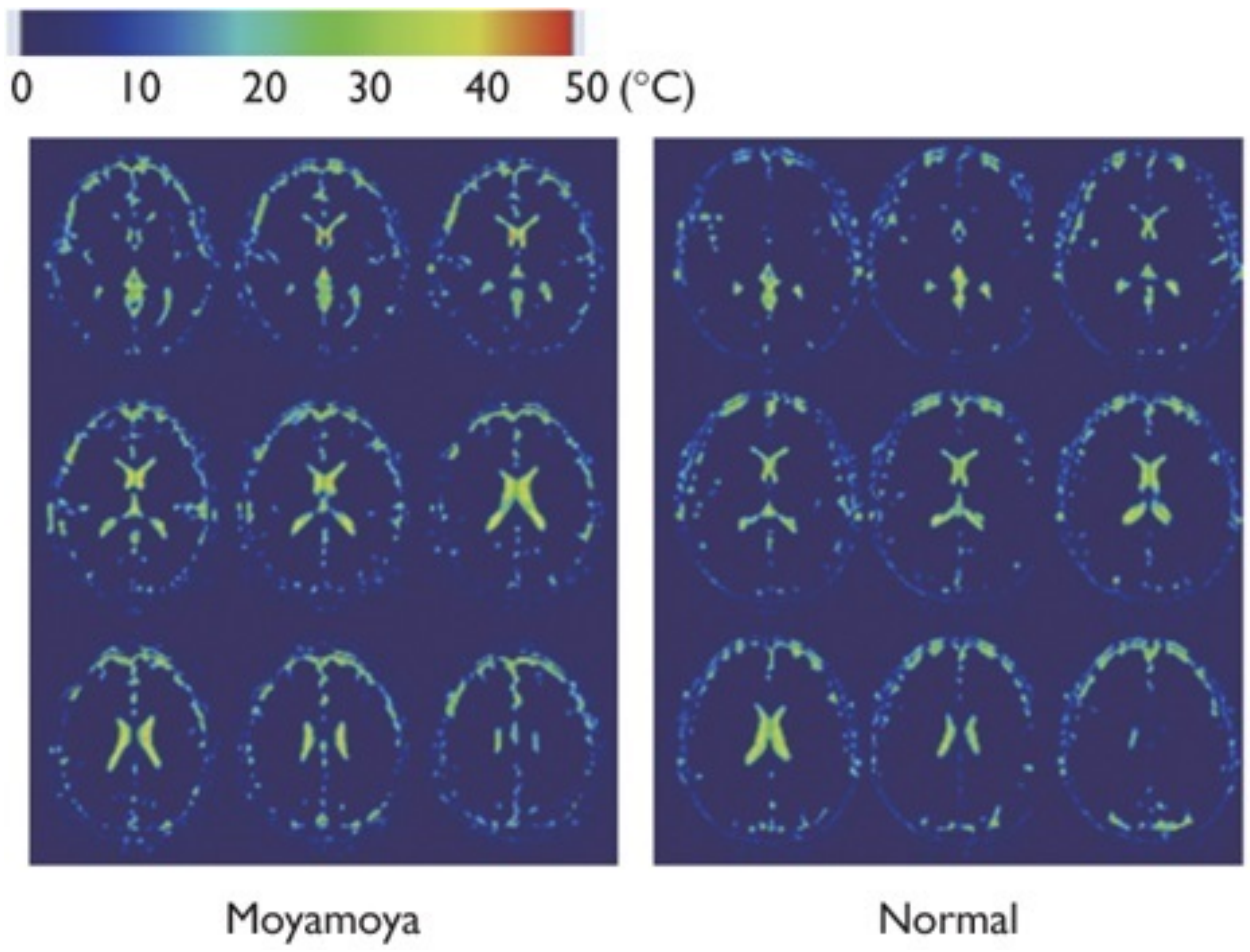
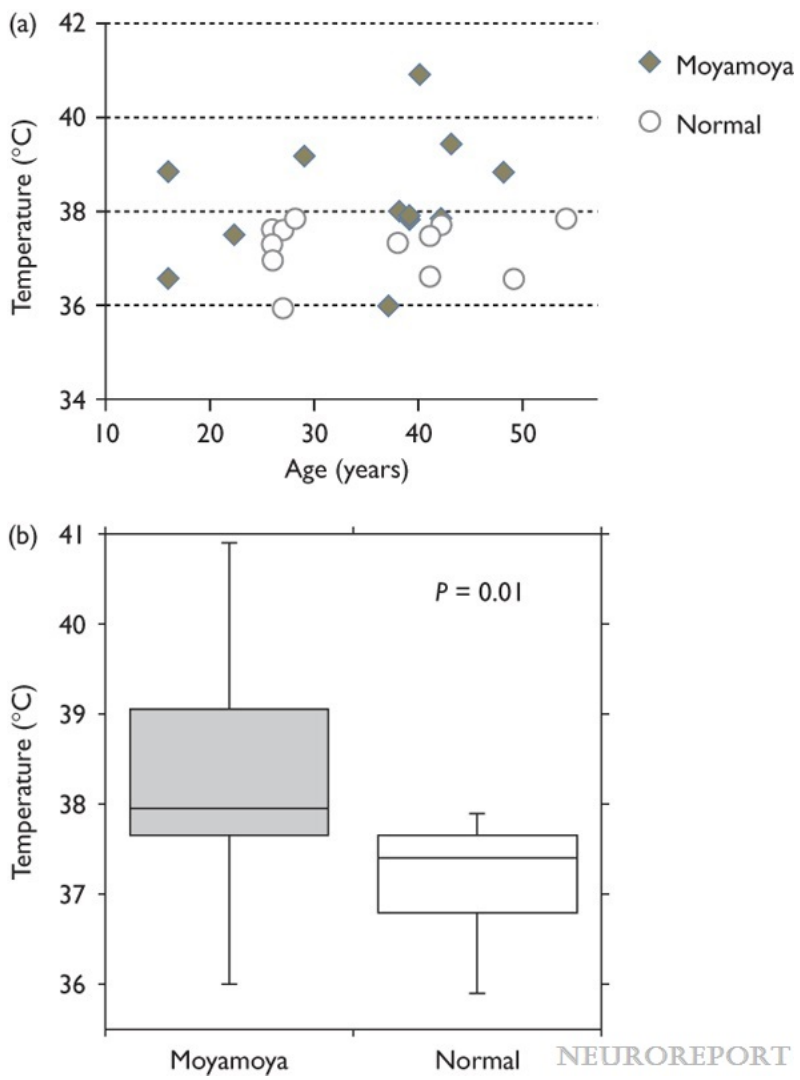
Increased DWI-measured Temperature in Moyamoya Disease





Yamada K, et al, 2010. NeuroReport

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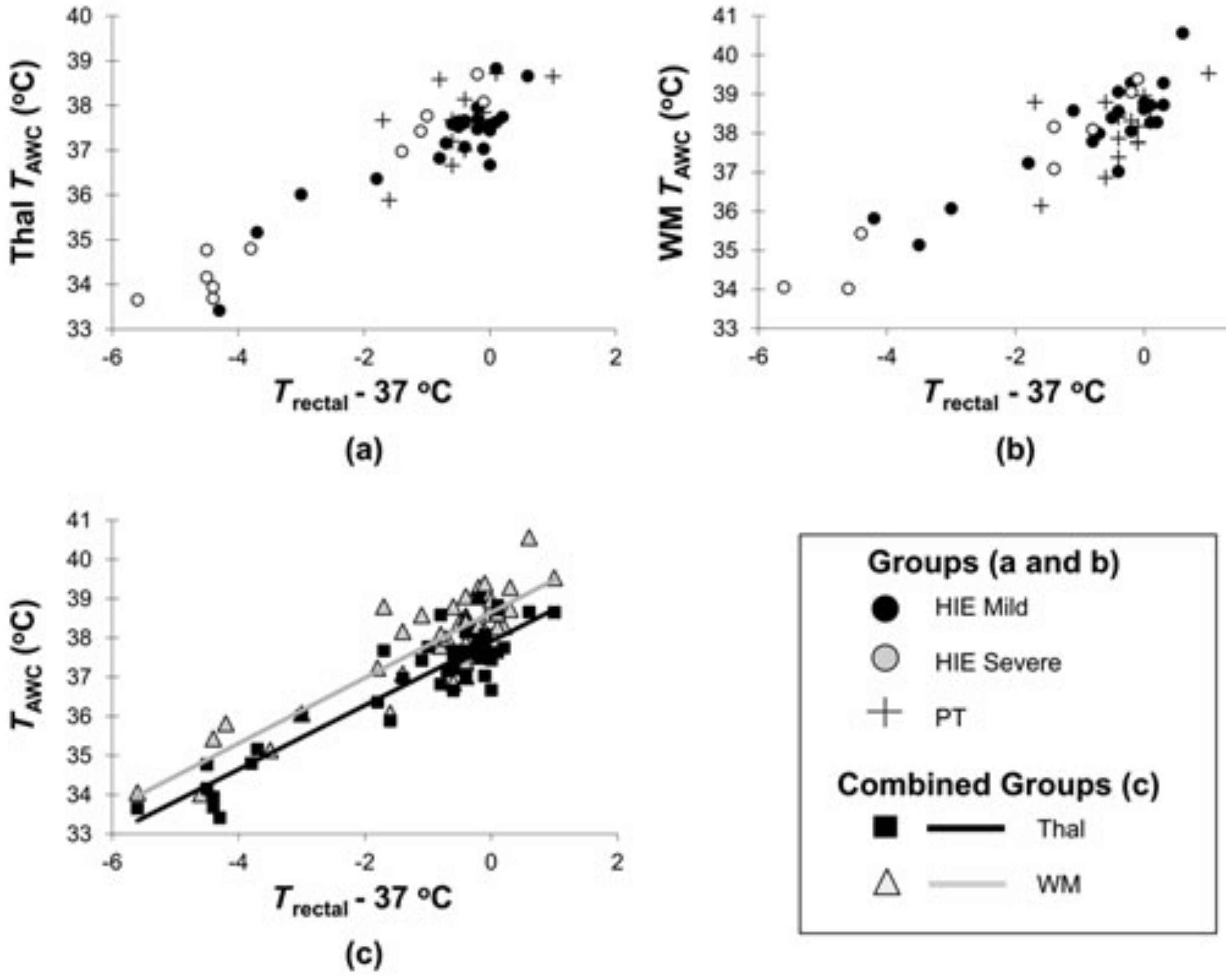
MRS Thermometry in neonates

Thalamus

White matter



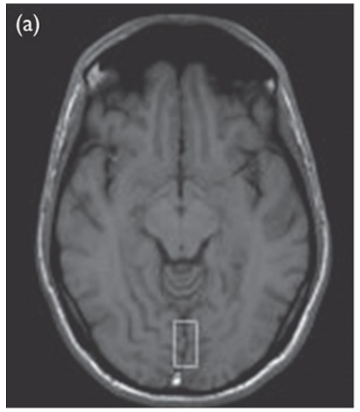
N=38 for HIE (21 cooling therapy)

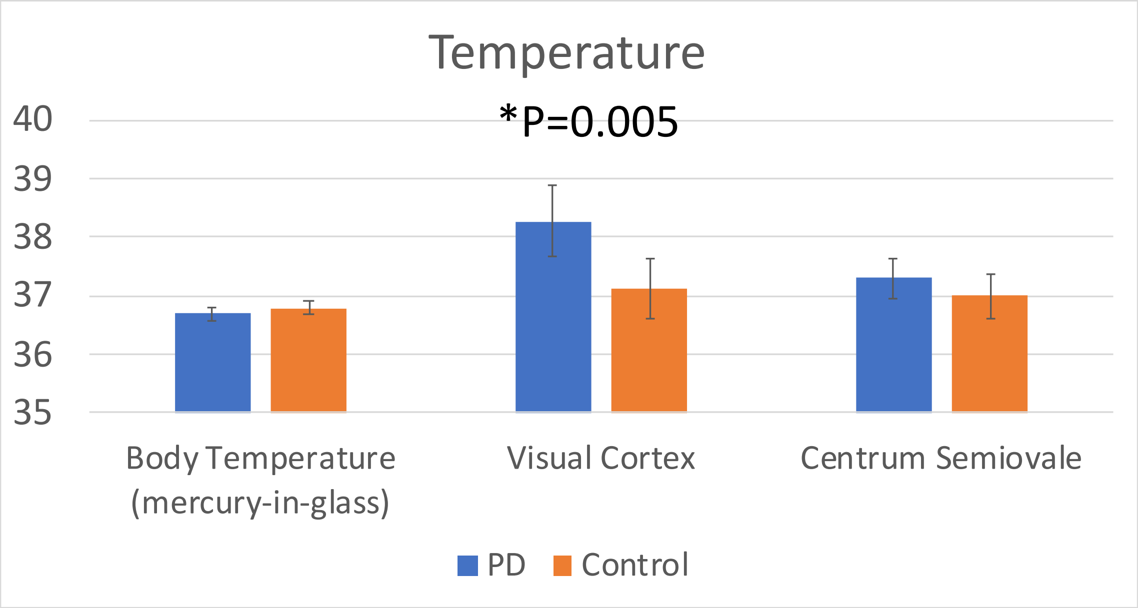
N=18 for PT

Bainbridge A et al, 2012. NMR Biomed

Increased brain temperature in Parkinson's Disease

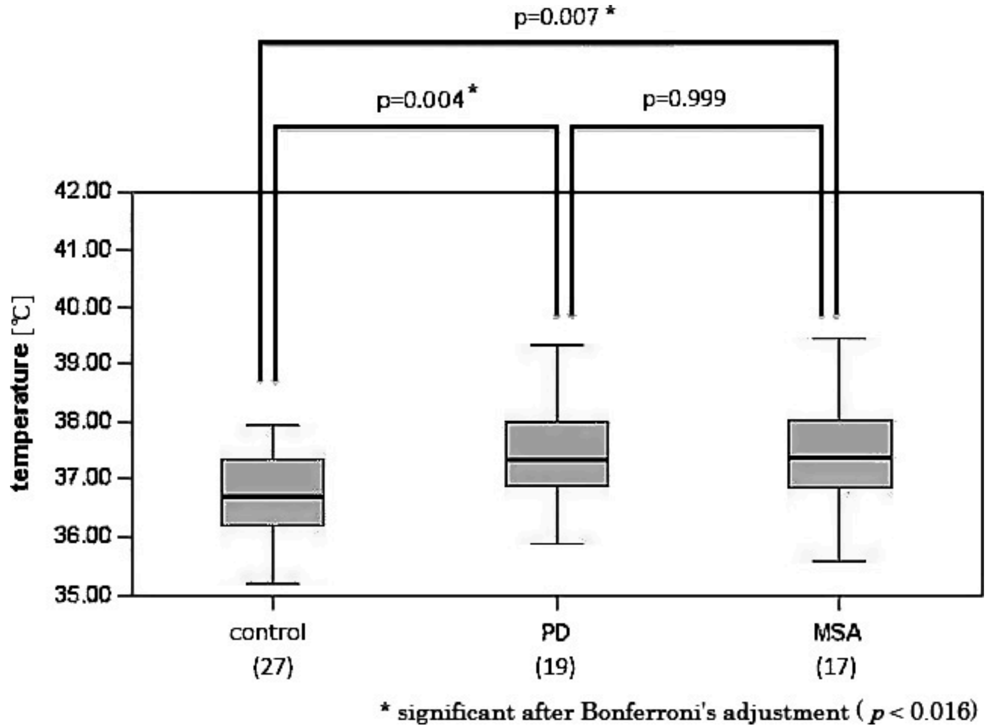
MRS





Mario R et al, 2012. NeuroReport

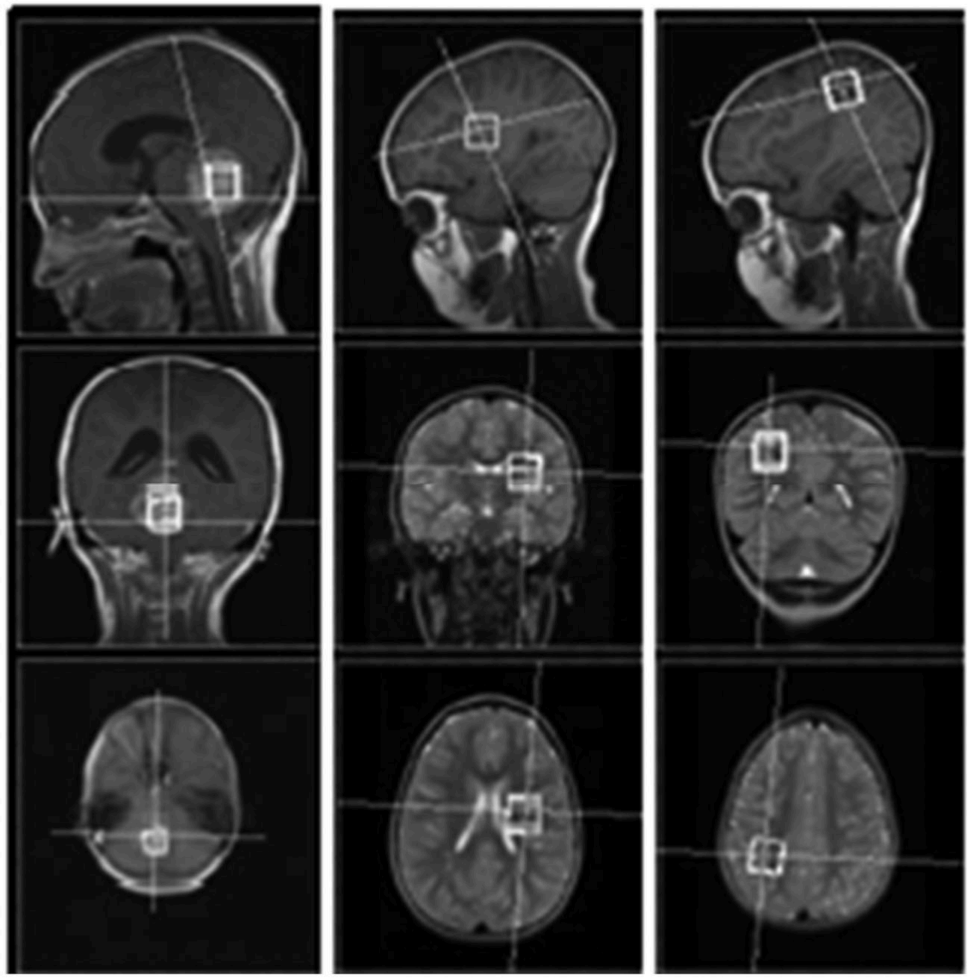
DWI

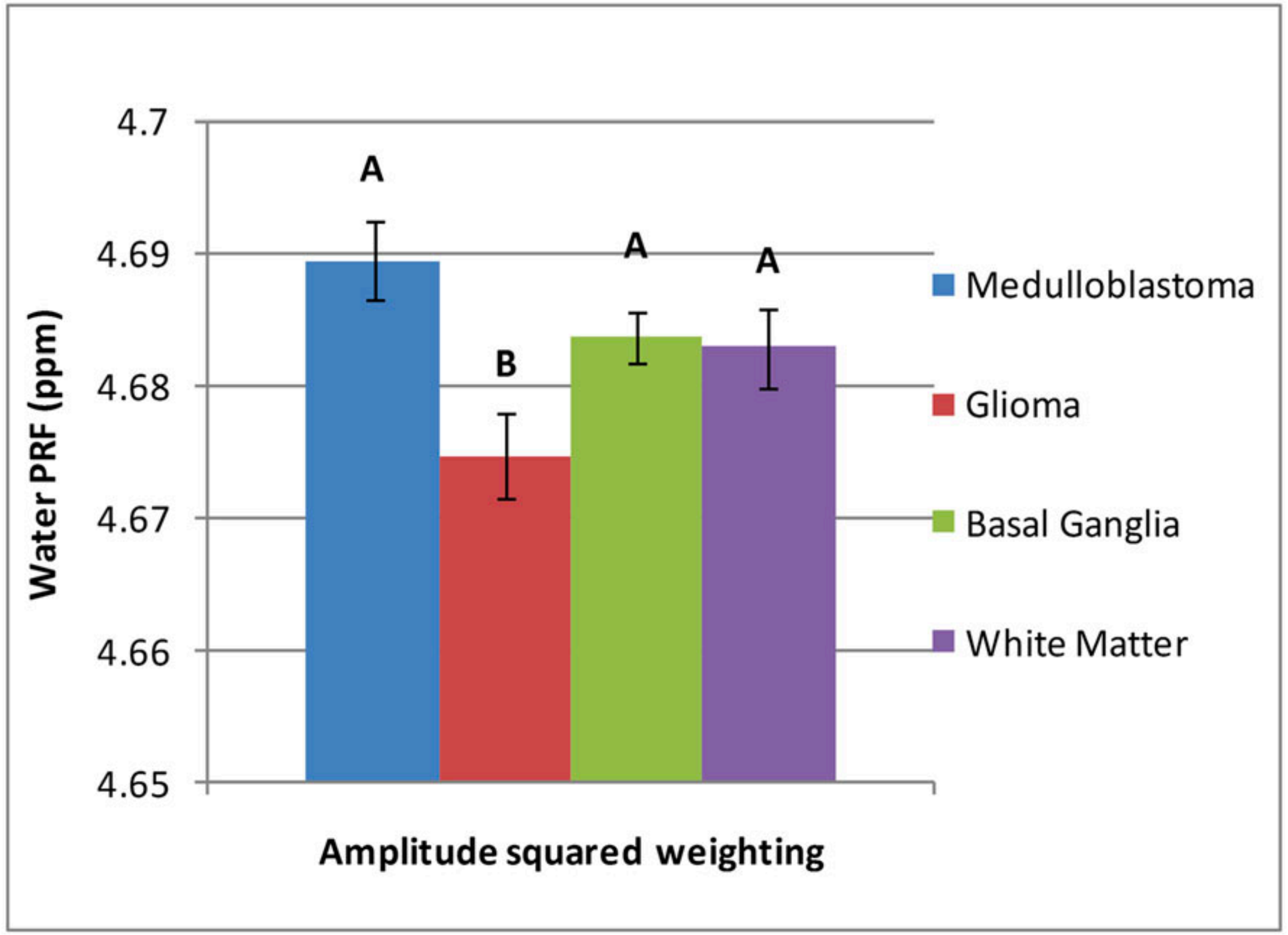


Sumida K et al, 2015. Brain and Behavior

Brain tumor

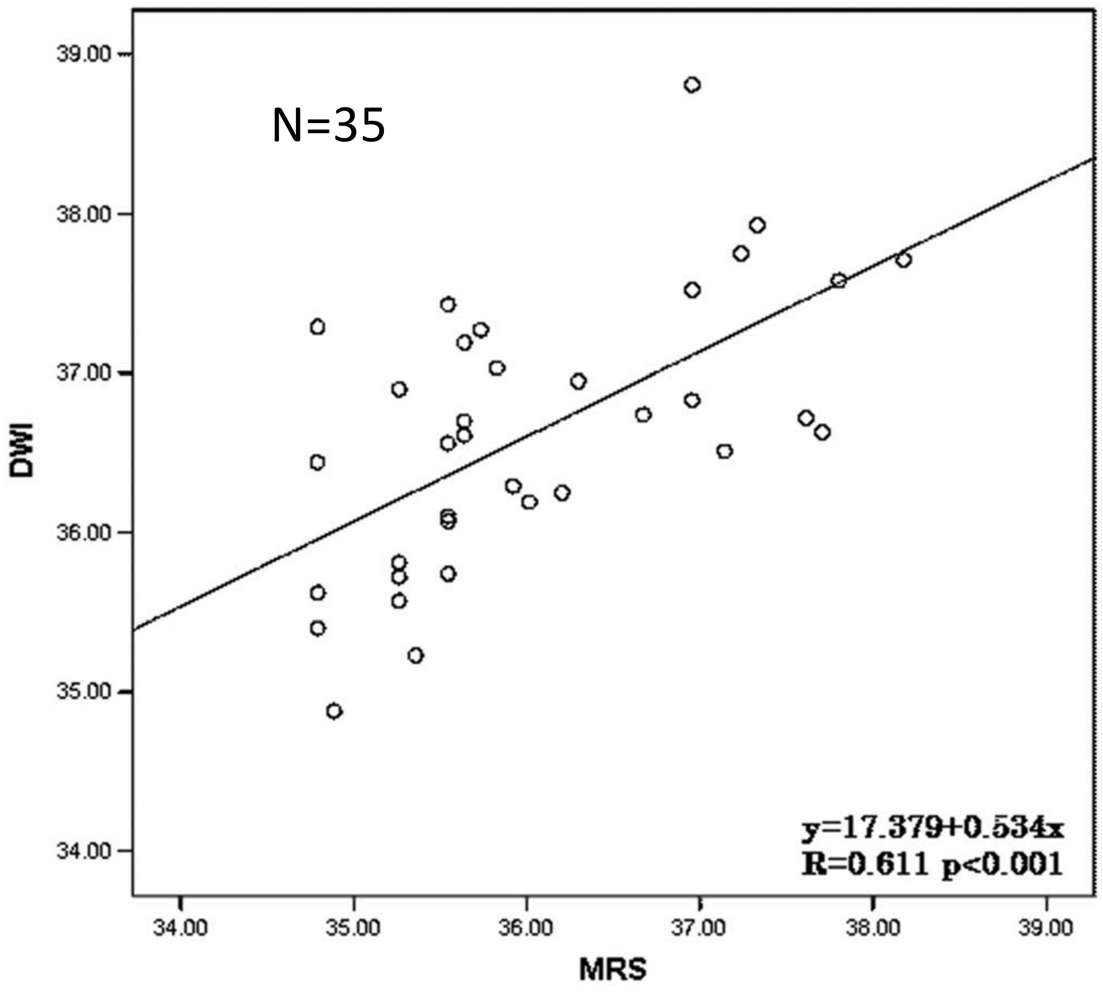
N=19 for Medulloblastoma, N=22 for glioma



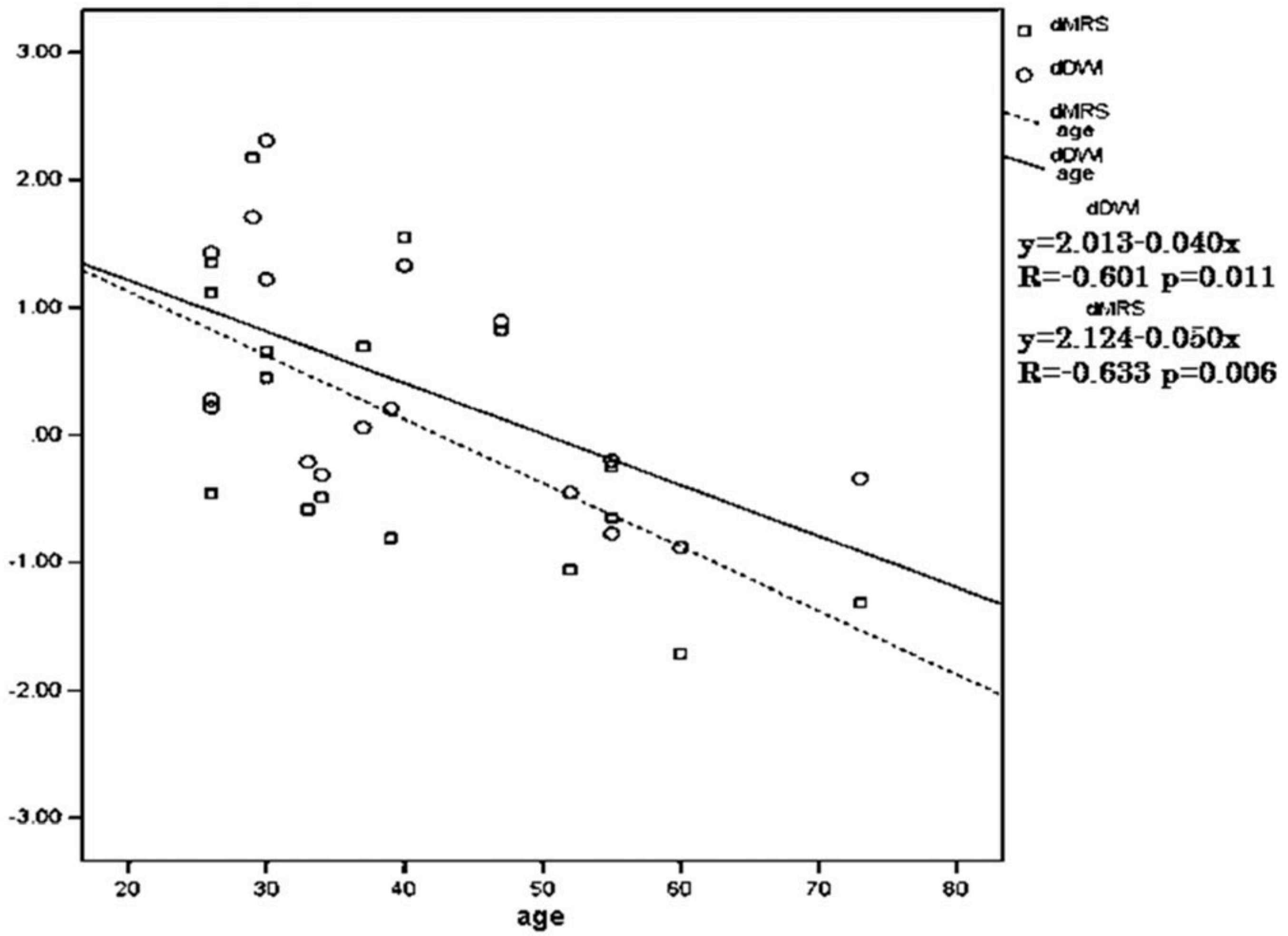


Babourina-Brooks B et al, 2013. NMR Biomed

Thermometry measurements between MRS and DWI in Aging



in right centrum semiovale.



Sumida K et al, 2016. NMR Biomed

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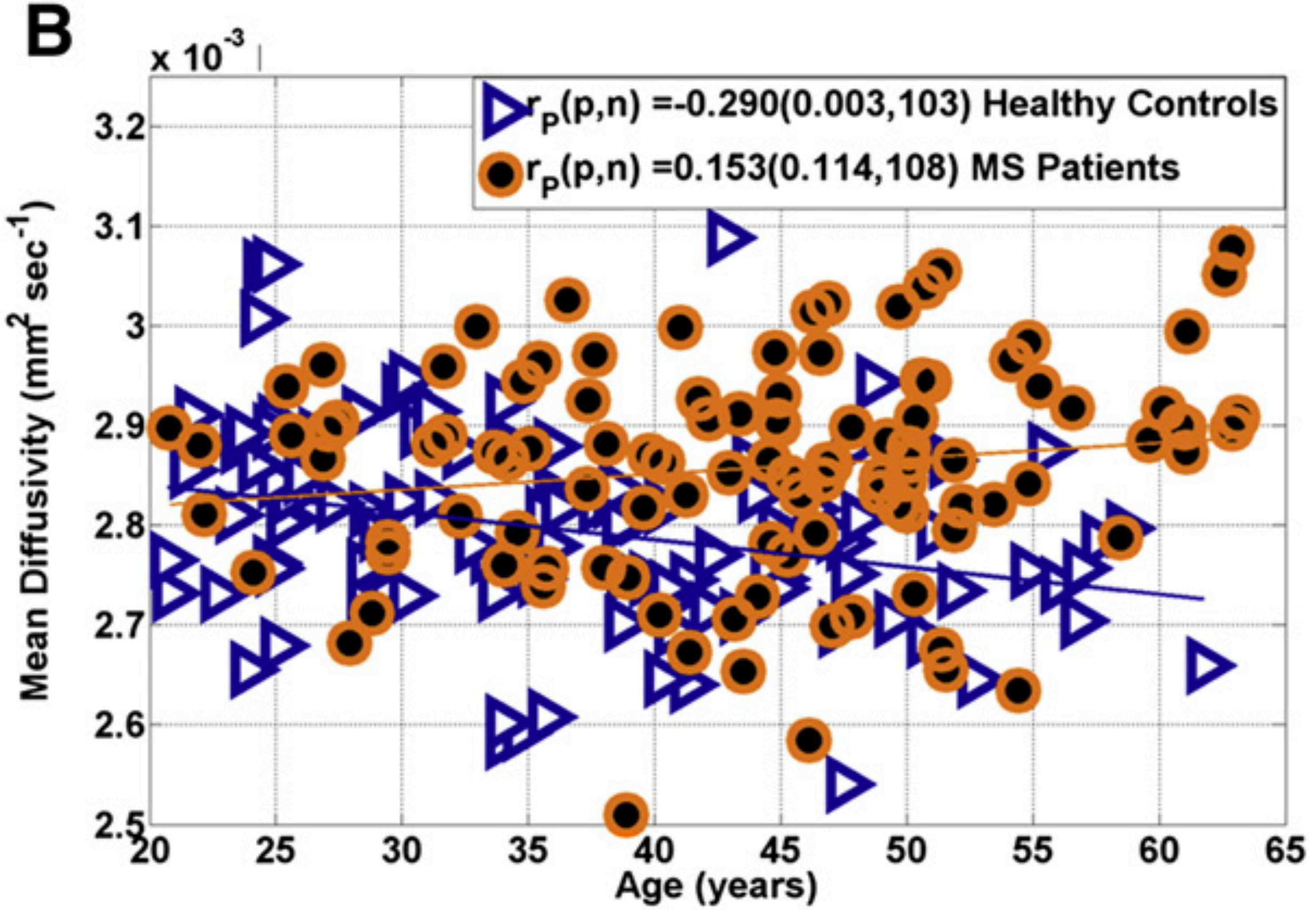
Increased ventricle temperature in MS



Hasan KM et al, 2015. MRI

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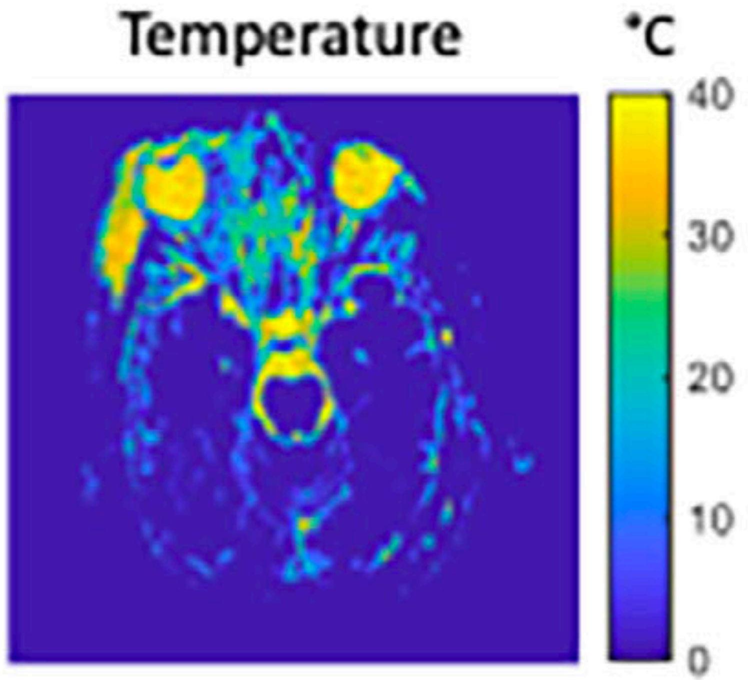
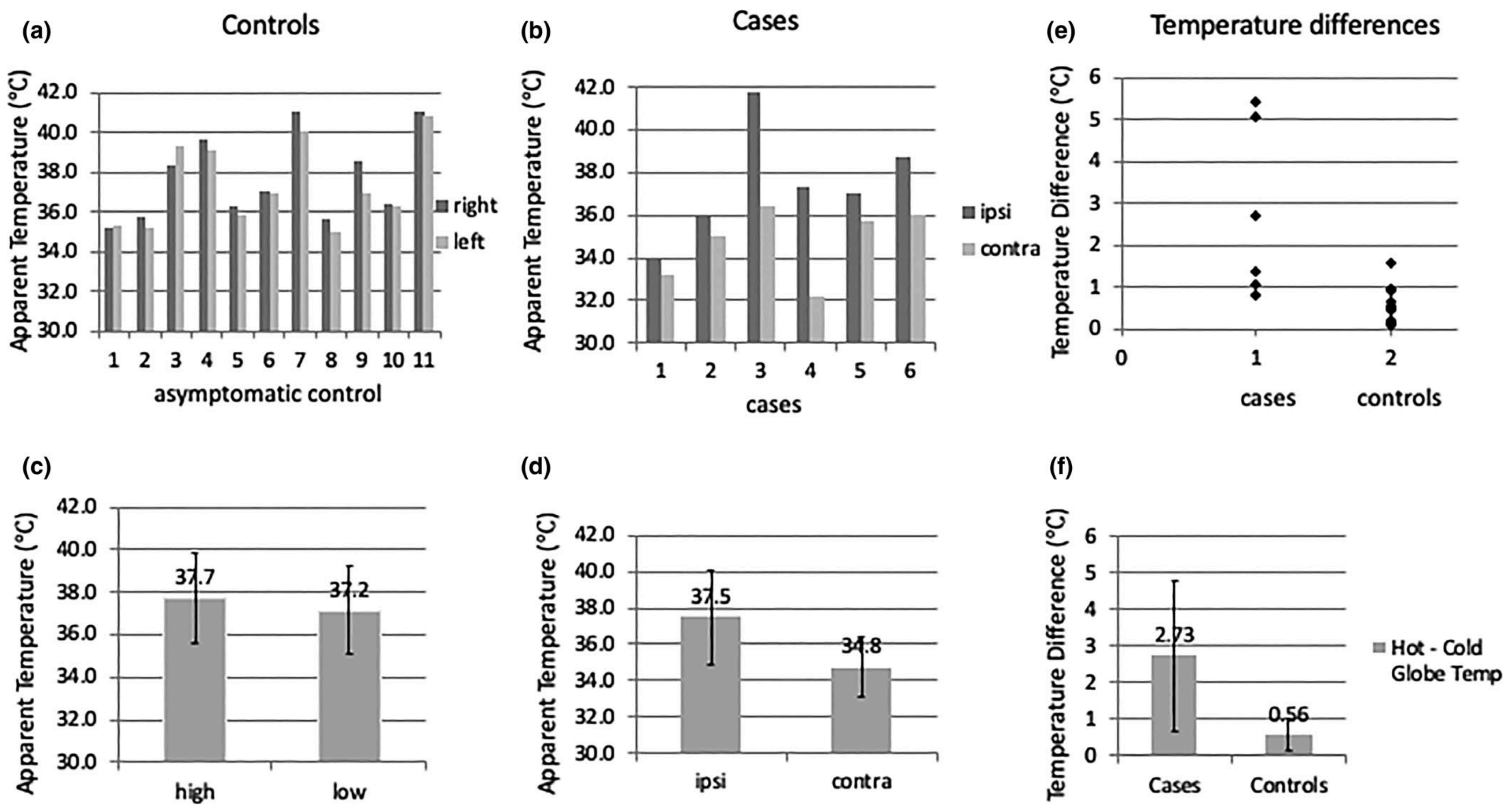
DWI-based measurement of temperature





Derakhshan JJ et al, 2020. Medical Physics

Summary

- Brain temperature is an important but understudied physiological parameter
- Readily accessible MR tools are available to probe brain temperature regulation/dysregulation (technical considerations warranted)
- Apparent brain temperature is altered in many diseases
- More research is needed in this area

References

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