



# HIGHER CENTRES MAY ENCODE CARDIORESPIRATORY RESPONSES TO EXERCISE WITHOUT MOVEMENT FEEDBACK IN HUMANS

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## INTRODUCTION

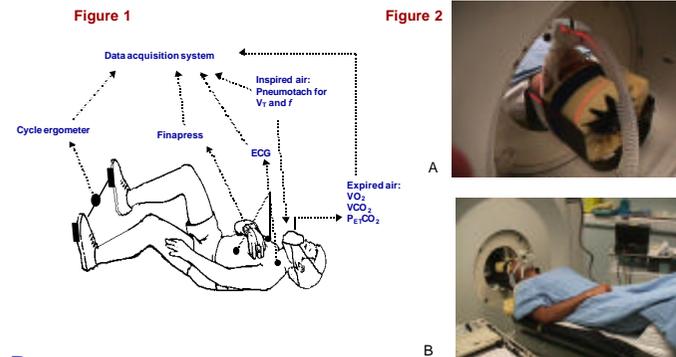
How humans can match the cardiorespiratory responses to the increase in metabolic rate of exercise has proved difficult to unravel. We have used Positron Emission Tomography (PET) to identify the neuroanatomical correlates underlying 'central command' during imagination of exercise under hypnosis whilst at rest, in order to uncouple 'central command' from peripheral feedback.

## METHODS

Experimentally naive and athletically untrained subjects were familiarised with leg exercise cycle ergometry in the semi-reclined position (Figure 1). On another day subjects were hypnotised on the scanning table, after which the head was positioned to minimise movement under laser beam alignment (Figure 2A-B). The positron emitting  $^{15}\text{O}$  in the form of  $5\text{mCi}$  of  $\text{H}_2^{15}\text{O}$  was given iv and breathing and HR were recorded.

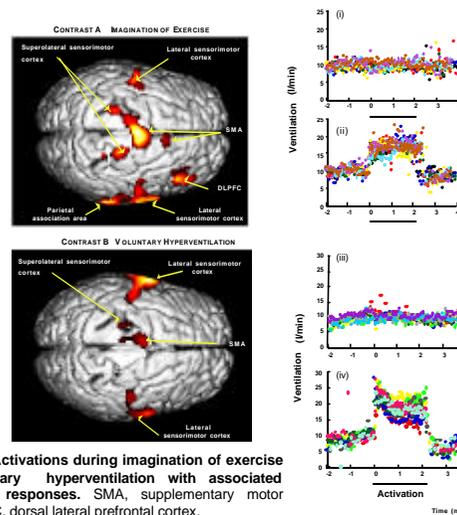
## Positron emission tomography

Three cognitive conditions were used: I, 'imagination of cycle freewheeling downhill' (no change in heart rate, HR, or ventilation,  $V_E$ ); II, 'imagination of exercise' cycling uphill (increased HR by 12% and  $V_E$  by 30% of the actual exercise response); III, voluntarily-driven hyperventilation to match that achieved in II (no change in HR). We employed cognitive subtraction methodology to create two contrasts (A and B) in two separate studies with different subjects ( $n=4$  for both; eight scans per subject). *Contrast A* (II minus I) highlighting cerebral areas involved in the imagination of exercise and *Contrast B* (III minus I) highlighting areas activated in the direct volitional control of breathing. End-tidal  $\text{PCO}_2$  was held constant throughout PET scanning. ( $n=4$  for both; eight scans per subject).

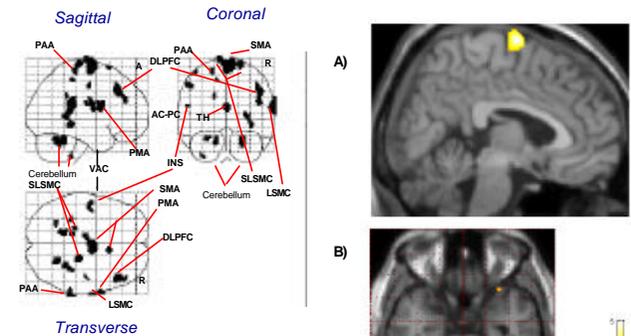


## RESULTS

The supplementary motor area (SMA), superolateral sensorimotor areas, the lateral sensorimotor areas and the cerebellum had activations in both Contrasts, whereas the right dorso-lateral prefrontal cortex, premotor area (PMA), left insula cortex, parietal association areas and the thalamus were activated in *Contrast A* alone. The SMA/PMA, cerebellum and the dorso-lateral prefrontal cortex are concerned with volitional/motor control, including that of the respiratory muscles, whereas the left insula cortex is concerned with vagal modulation of HR.

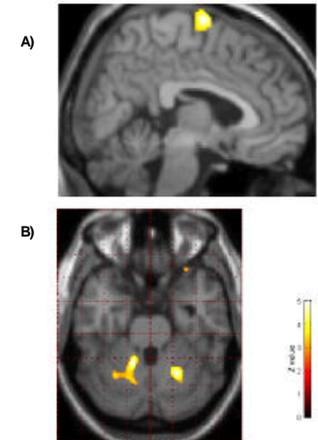


**Figure 3.** Activations during imagination of exercise and voluntary hyperventilation with associated respiratory responses. SMA, supplementary motor area, DLPFC, dorsal lateral prefrontal cortex.



**Figure 4.** Activations in three views during imagination of exercise at rest.

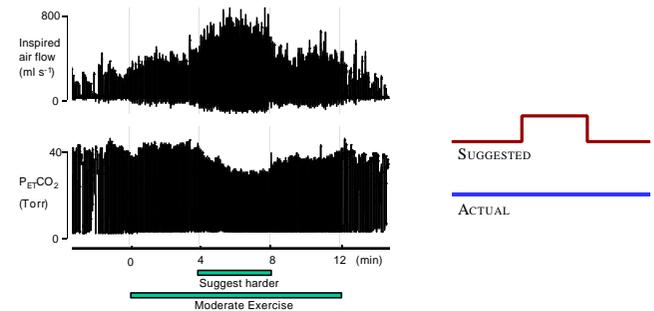
A - Anterior; AC-PC Commissural plane; VAC - vertical plane through anterior commissure; SMA - Supplementary motor area; PMA - Premotor Area; DLPFC - Dorso-lateral prefrontal cortex; PAA - parietal association area; INS - Insula; TH - Thalamus; SLSMC - Superolateral sensorimotor cortex; LSMC - Lateral sensorimotor cortex.



**Figure 5.** Areas of activation during imagination of exercise (compared to imagination of 'freewheeling downhill') overlaid on a 'typical' MRI.

CONTRAST A (Imagined Exercise)		LEFT					RIGHT				
		x	y	z	Z	p	x	y	z	Z	p
Dorso-lateral prefrontal area)		43	24	36	4.8	<0.001*					
Supplementary motor area (SMA)		4	-9	64	5	<0.001*					
Premotor area (PMA)		8	12	62	3.6	<0.001*					
Supero-lateral sensorimotor		59	3	19	4.4	<0.001*					
Lateral sensorimotor		18	-29	63	4	<0.001*					
Insula		43	-9	52	3.3	0.001					
Parietal lobe											
Precuneus		-10	-36	45	3.4	<0.001*					
Medial parietal		-13	-46	26	3.6	<0.001*					
Temporo-parietal junction							62	-40	19	4.6	<0.001*
Cerebellum											
Antero-lateral		-24	-60	-24	3.5	<0.001*	22	-60	-26	4.2	<0.001*
Antero-medial		-12	-50	-27	4.2	<0.001*					
Postero-lateral		-29	-38	-44	3.2	0.001*					
Thalamus							1	-9	15	4.1	<0.001*
CONTRAST B (Voluntary hyperventilation)											
SMA		-4	-11	54	4.7	<0.001*					
Supero-lateral sensorimotor		-4	-25	57	2.6	0.005					
Posterior temp/parietal		-45	-34	-12	4.7	<0.001*					
Lateral sensorimotor (a)		-48	-5	19	7	<0.001*	43	-19	36	3.9	<0.001*
Lateral sensorimotor (b)		-56	-15	15	4.8	<0.001*	55	-5	21		
Insula										5.1	<0.001*
Cerebellum (a)		-38	-63	-41	3.9	<0.001*	47	-7	21	3.2	0.001
Cerebellum (b)		-8	-63	-28	3.4	<0.001*	11	-69	-48	3.2	0.001

**Table 1.** Stereotactic coordinates (mm) in Talairach space of voxels maximally activated within sites; voxels are unit cubes of 2 mm side length. significant after correction for multiple comparisons (a) from SPM (b) correlation between voxel activation and  $V_E$ ,  $Z>4.8$ . x, lateral to midline, -ve to right; y, anterior/posterior to anterior/commissure +ve anterior; z, superior/ inferior to anterior/posterior commissural plane, +ve superior.



**Figure 6.** Altered perception of exercise load during actual exercise

## CONCLUSIONS

A significant component of the respiratory response to 'exercise', in the absence of both movement feedback and an increase in  $\text{CO}_2$  production, can be generated by what appears to be a behavioural response, given the identified neuroanatomical areas activated.

## ACKNOWLEDGEMENTS

We are grateful to the McDonnell-Pew Centre for Cognitive Neuroscience, Oxford, UK for financial support.