Regional cerebral 2-deoxyglucose uptake during open-field exposure in mice: metabolic patterns of habituation and exploratory activity

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The locomotory pattern of an animal introduced into a novel, open arena, depends on a mixture of motivational drives, from anxiety to exploratory biases, which have proven difficult to disentangle, even by means of pharmacological tools.
We use here a metabolic approach to dissect the variability of responses to the exposure to an open-field, in order to understand the neural circuitry underlying three different components of this form of spontaneous behaviour: ***ambulation, thigmotaxis,*** and ***habituation***

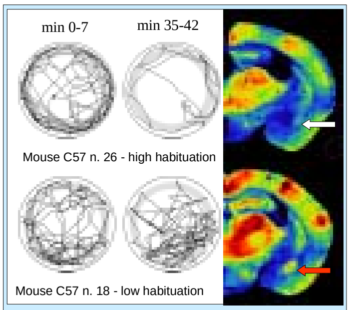
? Are there correlations between these components of open-field behavior, and the **metabolic activation** of any brain region?

In humans, a superiority of the right hemisphere for the decoding of (mostly negative) emotions has been repeatedly reported. In laboratory rodents, neurochemical asymmetries in the neocortex and basal ganglia have been sometimes detected, in association with « emotional » behavioural traits, such as anxiety and impulsivity.

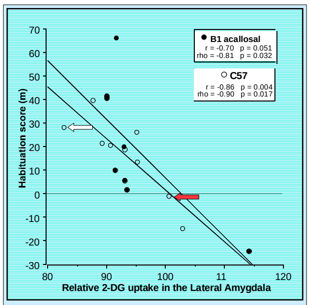
? Does any of these three components of openfield behaviour (ambulation, thigmotaxis, habituation) entail a **lateralised activation** of any brain region?

! YES. **Habituation**, measured as the difference in the amount of locomotion between the first and the last 7 minutes of exposure to the open-field (in a time lapse of 42 minutes) is strongly and negatively correlated to the metabolic activation of the lateral amygdala, measured as relative incorporation of ^{14}C-2-deoxy-D-glucose

Average relative 2-deoxyglucose uptake	Path traveled		Average distance from the walls		Habituation	
	r	*p*	*r*	*p*	*r*	*p*
Superstructures						
whole cortex	0.12	0.633	-0.43	0.066	0.34	0.198
brainstem + diencephalon	-0.26	0.281	-0.32	0.181	0.05	0.843
whole thalamus (dorsal)	0.40	0.089	0.04	0.874	0.38	0.145
Amygdaloid complex	-0.27	0.265	-0.26	0.291	**-0.54**	**0.028**
Lateral amygdala	0.15	0.585	-0.13	0.630	**-0.73**	**<0.001***
Septum	-0.07	0.786	-0.26	0.294	0.10	0.708
Striatum	-0.37	0.116	-0.10	0.700	-0.45	0.080
Accumbens	-0.20	0.407	-0.34	0.161	-0.37	0.158
Cortical regions						
Hippocampus	0.04	0.885	0.19	0.430	0.01	0.987
Retrosplenial cortex	0.30	0.219	-0.10	0.701	0.35	0.184
Cingulate cortex	-0.23	0.340	-0.24	0.317	0.30	0.271
Perirhinal cortex	-0.21	0.405	-0.38	0.109	-0.30	0.273
Infrarhinal cortex	-0.05	0.830	**-0.50**	**0.029**	-0.10	0.726
Occipital cortex	-0.01	0.976	0.16	0.526	0.13	0.628
Temporal cortex	0.02	0.928	0.28	0.257	-0.21	0.450
Somatosensory cortex	0.20	0.410	**-0.52**	**0.021**	0.47	0.067
Medial parietal cortex	0.23	0.356	-0.21	0.385	0.34	0.200
Frontal cortex	0.03	0.903	-0.29	0.225	**0.57**	**0.02**



Tracks of locomotor paths of two C57BL/6 mice showing low (top) and high (bottom) habituation, and their corresponding autoradiograms of brain sections showing the striking difference in metabolic activation of the lateral amygdala (ARROW)

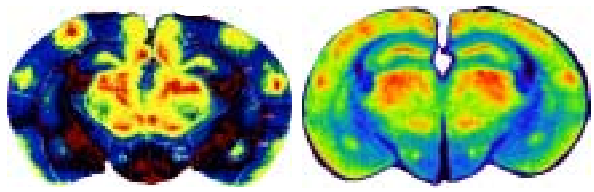


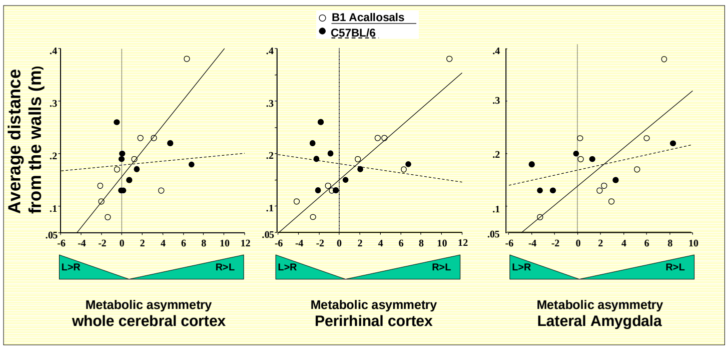
Significance of the correlation is confirmed by the Spearmann's rank procedure, and by its presence in both groups of animals. Arrows indicate the points corresponding to the mice whose tracks are shown at left

! YES. **Thigmotaxis** is correlated with the degree of asymmetry in the activation of limbic cortex and amygdala: the higher the frequentation of the central part of the arena, the higher the activation of the right hemisphere.
CAVEAT! The scatterplots show that these correlations are mostly contributed by the mice with callosal agenesis

Asymmetry indices of 2-deoxyglucose uptake	Path traveled		Average distance from the walls		Habituation	
	r	*p*	*r*	*p*	*r*	*p*
Superstructures						
whole cortex	-0.02	0.924	**0.55**	**0.012***	-0.08	0.785
brainstem + diencephalon	0.18	0.450	0.22	0.376	-0.30	0.291
whole thalamus (dorsal)	0.45	0.050	0.24	0.333	-0.08	0.778
Amygdaloid complex	0.06	0.816	0.03	0.909	0.39	0.156
Lateral amygdala	-0.27	0.305	**0.56**	**0.012**	0.34	0.246
Septum	0.03	0.903	0.38	0.109	-0.32	0.257
Striatum	**0.48**	**0.037***	0.40	0.089	-0.07	0.806
Accumbens	0.15	0.554	-0.05	0.848	-0.22	0.443
Cortical regions						
Hippocampus	-0.18	0.469	0.00	0.990	0.11	0.710
Retrosplenial cortex	-0.10	0.673	0.05	0.885	-0.20	0.486
Cingulate cortex	0.06	0.810	**0.57**	**0.009***	-0.07	0.820
Perirhinal cortex	-0.12	0.621	**0.63**	**0.003***	0.06	0.839
Infrarhinal cortex	0.11	0.656	**0.51**	**0.023***	-0.09	0.742
Occipital cortex	-0.15	0.556	0.14	0.570	0.04	0.881
Temporal cortex	0.03	0.904	0.05	0.856	0.02	0.951
Somatosensory cortex	-0.01	0.965	**0.54**	**0.015***	-0.01	0.983
Medial parietal cortex	-0.23	0.357	0.38	0.113	-0.06	0.839
Frontal cortex	-0.34	0.158	**0.52**	**0.022**	-0.10	0.741

Acallosal, high asymmetry — C57BL/6, low asymmetry





CONCLUSIONS

❶ The amount of locomotion is not clearly associated to bilateral or asymmetrical activation of any brain region. Thus, it remains a behavioural measure of difficult interpretation

❷ The negative correlation between metabolic activation of the amygdala and habituation suggests that an intrasession increase in locomotion does NOT imply a decline in anxiety!

❸ Correlations between *asymmetries* in 2-deoxyglucose uptake in (mostly limbic) cortical fields and distance from the walls suggest opposite contributions of the two hemispheres in the generation of a behavioral response, and indicate measures of thigmotaxis/agoraphobia as meaningful behavioural markers of neurobiologically different coping strategies