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correlates with subsequent learned helpless behavior**

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Medial thalamic 18-FDG uptake following inescapable shock correlates with subsequent learned helpless behavior

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Background: The learned helplessness paradigm has been repeatedly shown to correlate with neurobiological aspects of depression in humans. In this model, rodents are exposed inescapable foot-shock in order to reveal susceptibility to escape deficit, defined as 'learned helplessness' (LH). Few methods are available to probe the neurobiological aspects underlying the differences in susceptibility in the living animal, thus far being limited to studies examining regional neurochemical changes with microdialysis. With the widespread implementation of small animal neuroimaging methods, including positron emission tomography (PET), it is now possible to explore the living brain on a systems level to define regional changes that may correlate with vulnerability to stress.

Methods: In this study, 12 wild type Sprague-Dawley rats were exposed to 40 minutes of inescapable foot-shock followed by metabolic imaging using 2-deoxy-2-[¹⁸F]fluoro-D-glucose (18-FDG) 1 hour later. The escape test was performed on these rats 48 hours later (to accommodate radiotracer decay), where they were given the opportunity to press a lever to shut off the shock. A region of interest (ROI) analysis was used to investigate potential correlations (Pearson Regression Coefficients) between regional 18-FDG uptake following inescapable shock and subsequent learned helpless behavior (time to finish the test; number of successful lever presses within 20 seconds of shock onset).

Results: ROI analysis revealed a significant positive correlation between time to finish and 18-FDG uptake, and a negative correlation between lever presses and uptake, in the medial thalamic area ($p=0.033$, $p=0.036$). This ROI included the paraventricular thalamus, mediodorsal thalamus, and the habenula. In an effort to account for possible spillover artifact, the posterior thalamic area (including ventral medial and lateral portions) was also evaluated but did not reveal significant correlations ($p=0.870$, $p=0.897$). No other significant correlations were found in additional regions analyzed including the nucleus accumbens, caudate putamen, substantia nigra, and amygdala.

Discussion: These data suggest that medial thalamic 18-FDG uptake during inescapable shock may contribute to subsequent escape deficits, and are not confounded by shock effects per se, since all animals received the same treatment prior to scanning. We have previously explored 18-FDG differences following the escape test session which also showed hyperactivity in the medial thalamus of learned helpless animals compared to non-learned helpless, and included additional cortical-limbic changes. Given the neuroanatomical connections between the medial thalamus (and habenula) with the prefrontal cortex and monoaminergic brain stem, one possible speculation is that abnormal neuronal activity in these areas during stress may set in motion circuitry changes that correlate with learned helpless behavior.