OFC LESIONS AFFECT MONKEYS' NEURAL RESPONSES TO A HUMAN INTRUDER

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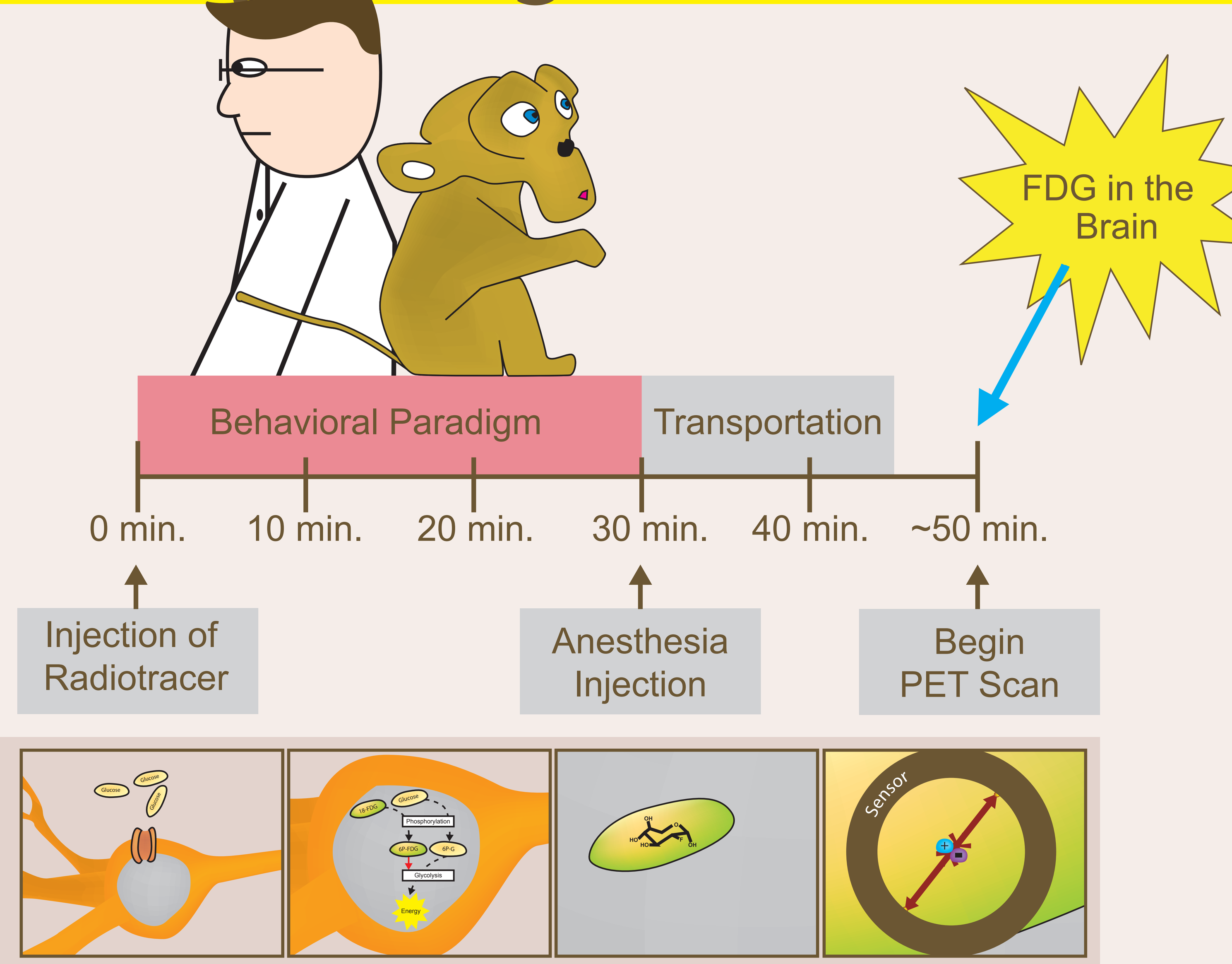
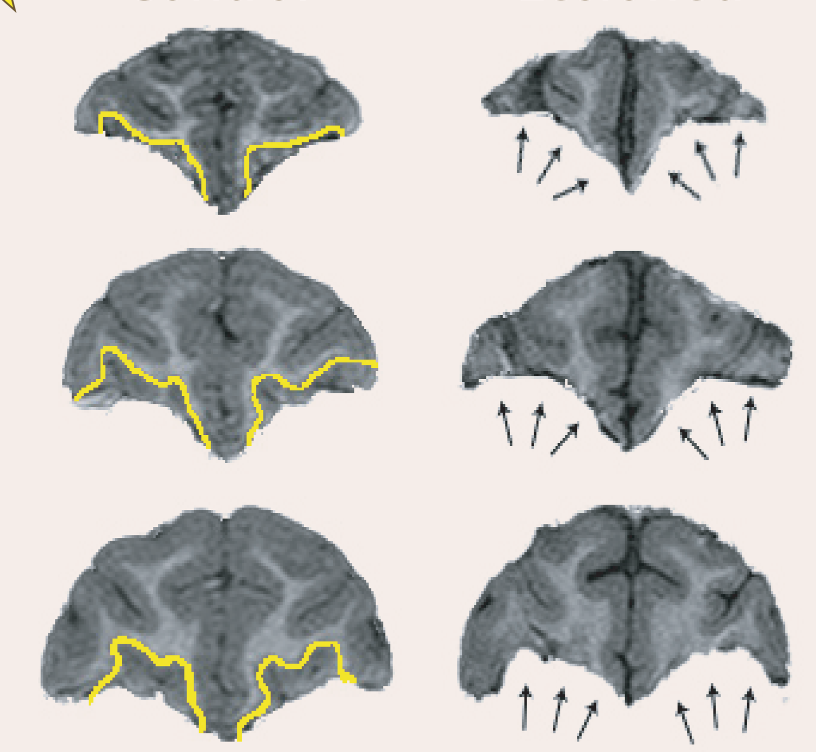
Study Design

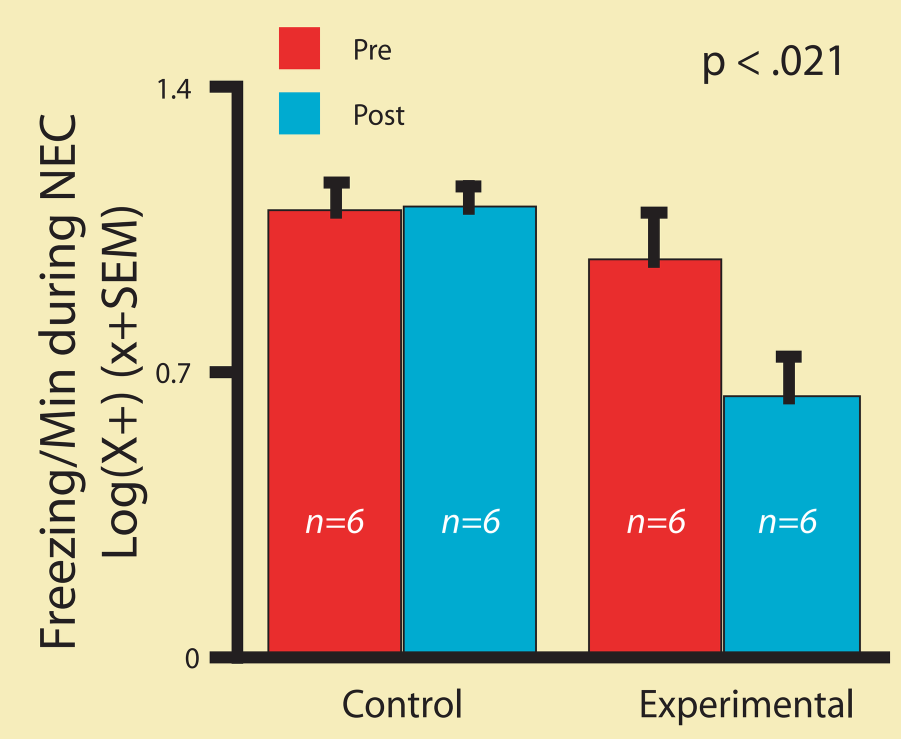
Kalin et al., Submitted



Three anterior to posterior (top to bottom) coronal OFC sections from a control animal with the intended lesion outlined in yellow. In the lesioned animal, the lesion incorporates areas 11, 12, 13, 14 and is indicated by the arrows.



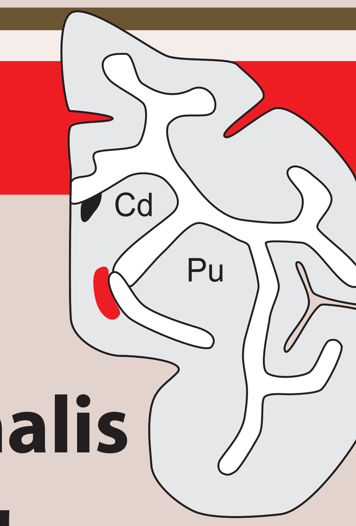
Lesions to the Orbital Frontal Cortex Decrease Freezing



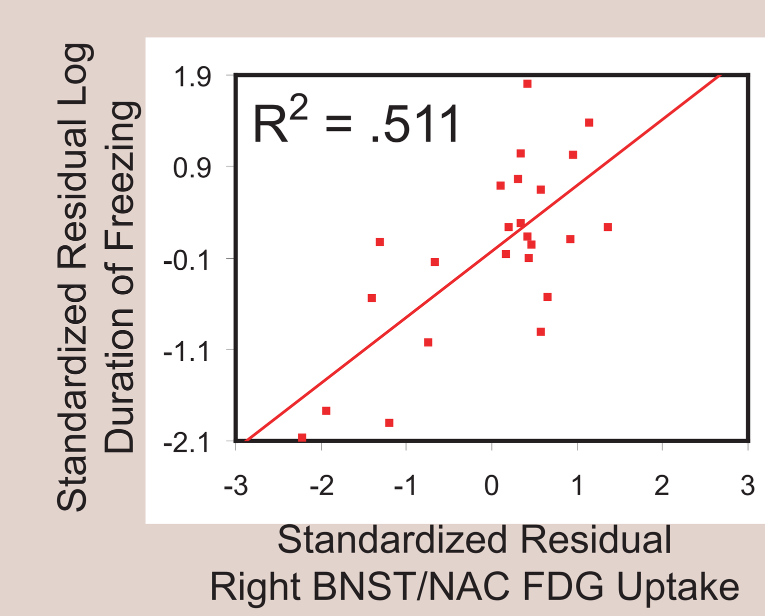
Kalin et al., (2005). Biological Psychiatry. 58:796-804

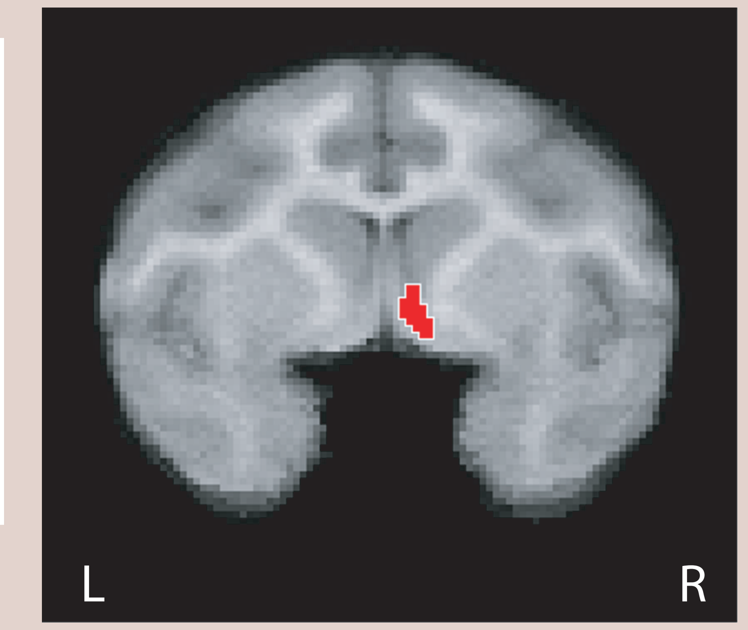
.9 mm anterior to the center of the AC

Bed Nucleus of the Stria Terminalis



Bed Nucleus of The Stria Terminalis (BNST) Correlates with Freezing

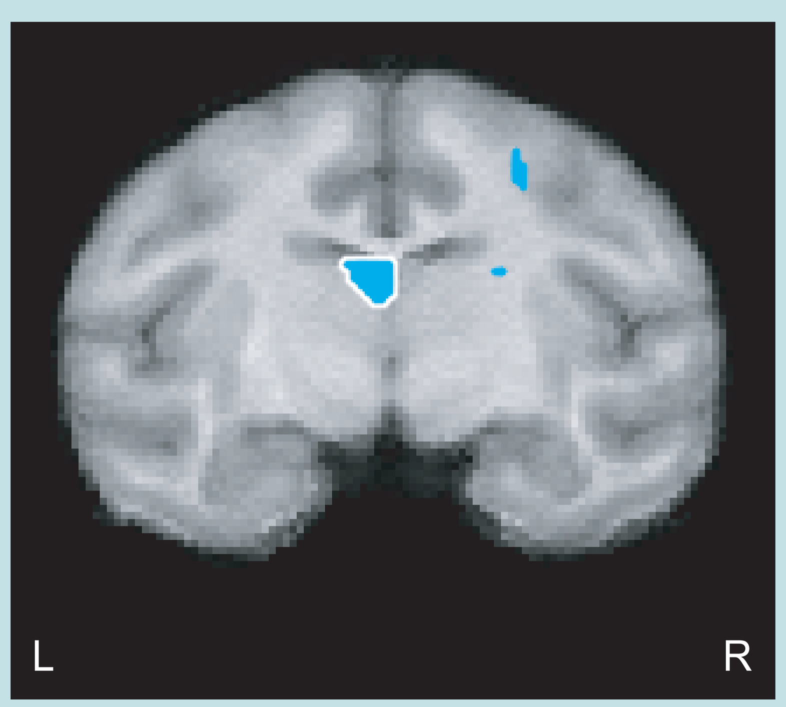


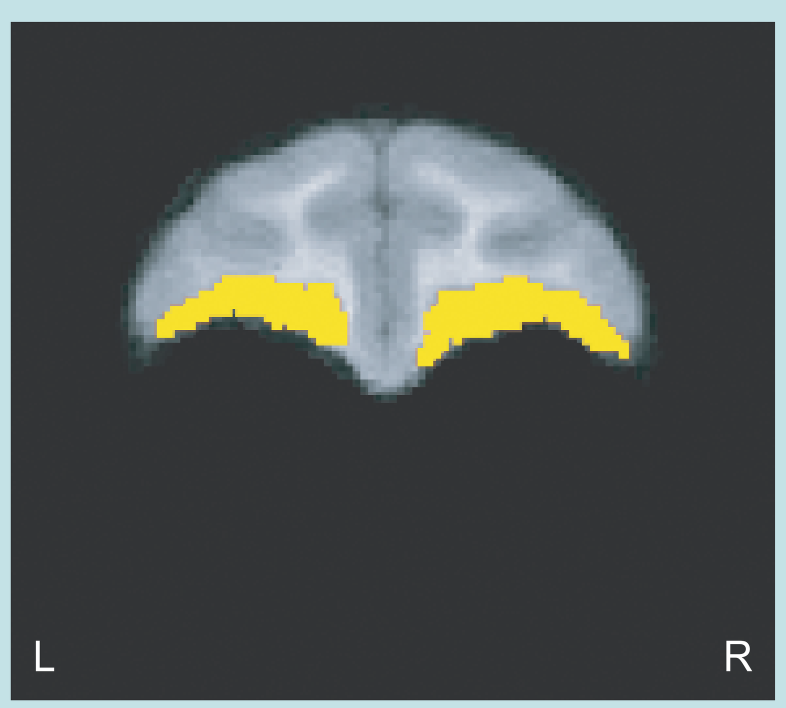


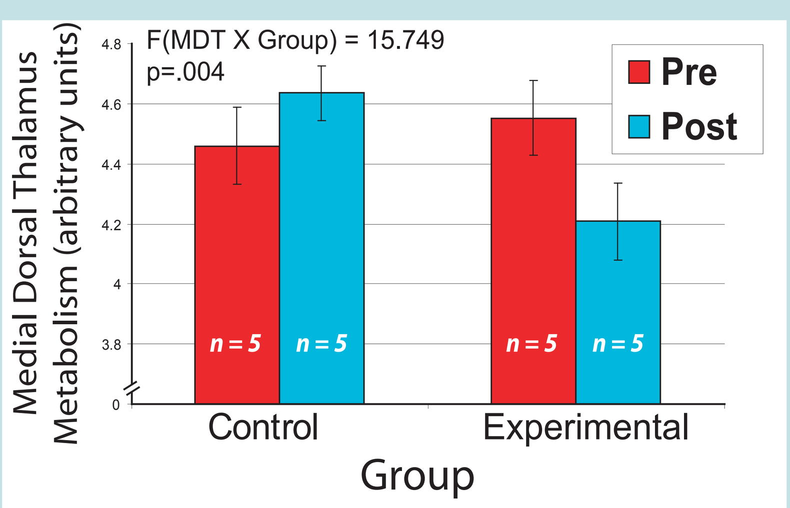
Note: This findng holds for the n=10 used in post-lesion analysis.

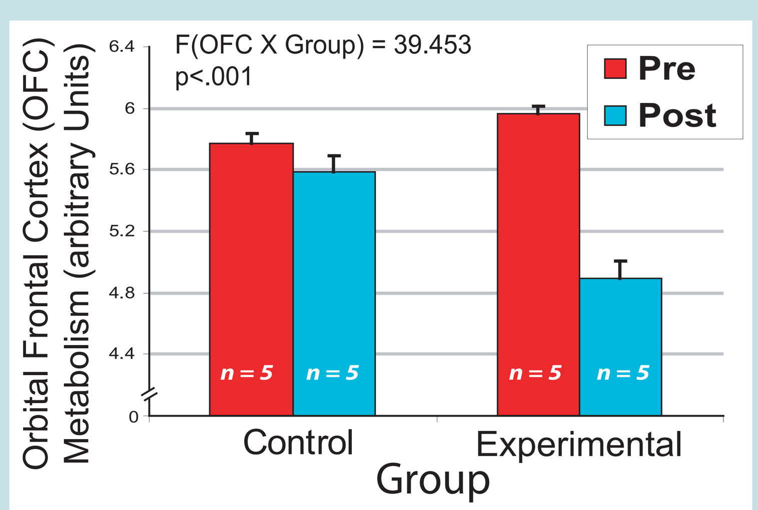
OFC Lesions Decrease BNST Metabolism

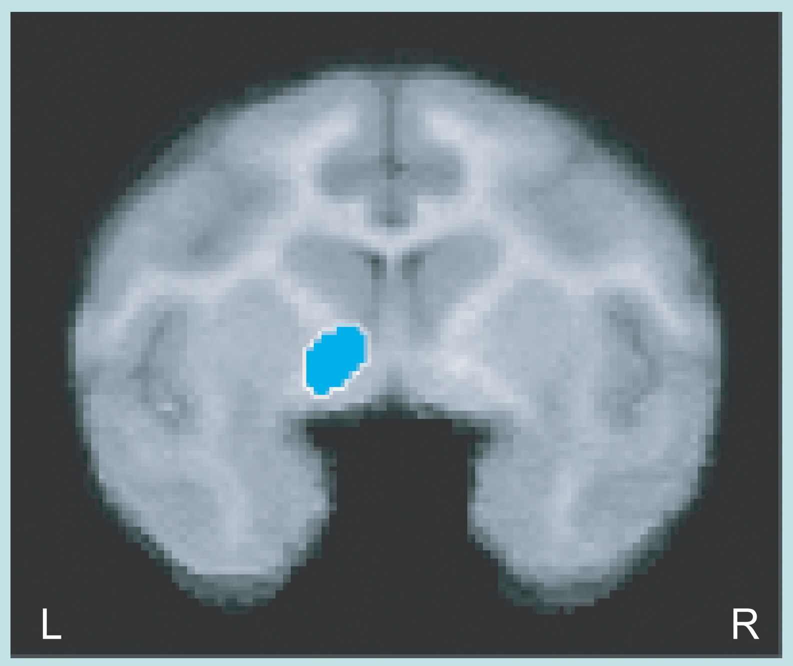
OFC Lesions Decrease Medial Dorsal Thalamus and OFC Metabolism



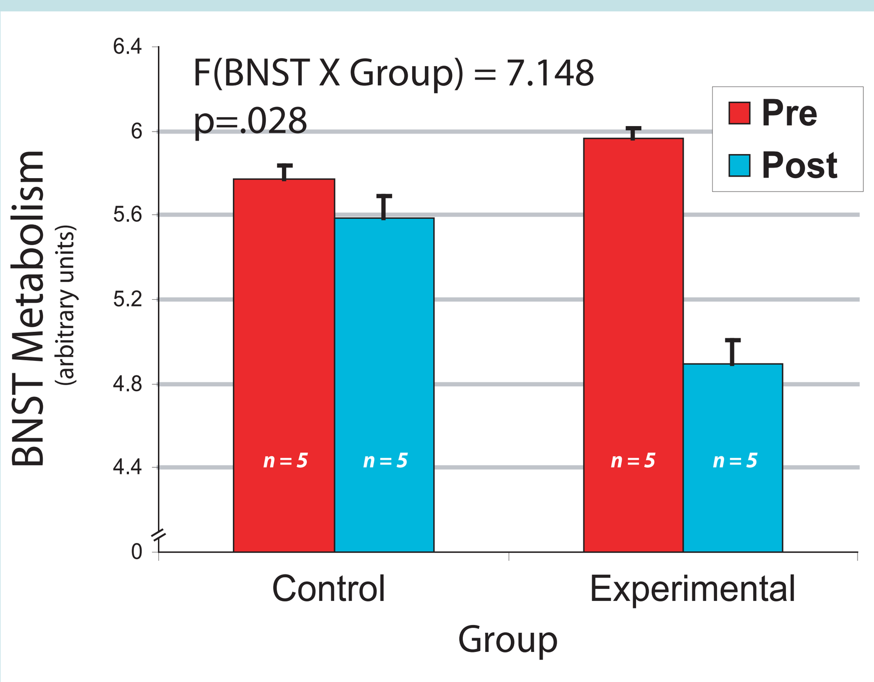






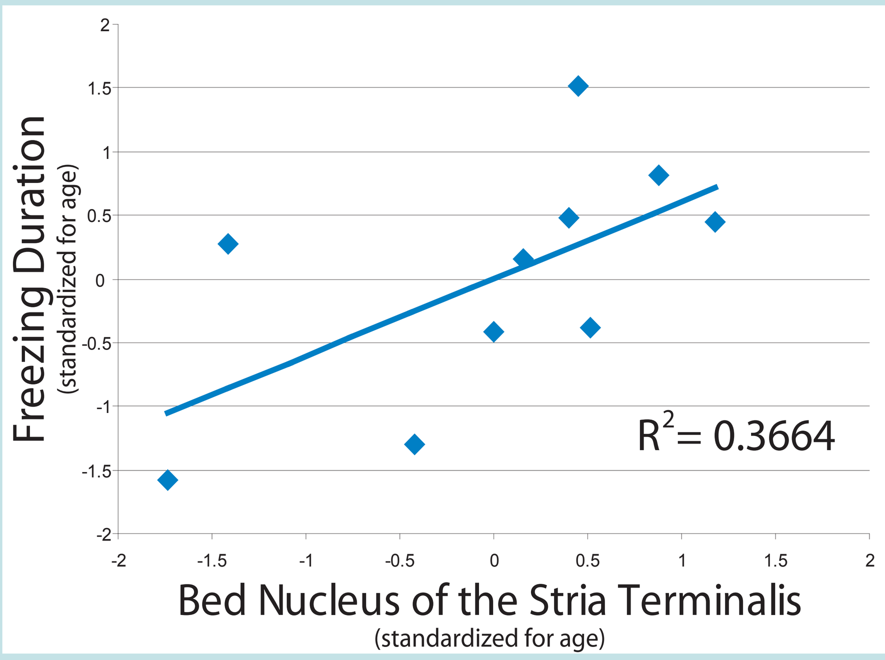


BNST: p<.005 two-tailed uncorrected



BNST Correlates with Freezing

We examined regions that showed a significant Group(Lesion vs. Control) by Time(Pre- vs. Post-Surgery) interaction (p<.05) and a significant post-lesion main effect of Group (p<.005). Further analyses revealed a significant correlation between between the BNST and freezing behavior.



Total Pre n=25

Twenty-five male rhesus monkeys (Macacca mulatta) (age: mean=3.1 years) originally underwent FDG-PET scans to assess brain metabolism while a human intruder entered the room and presented their profile to the monkey while making No-Eye-Contact (NEC). Data from this portion of the experiment was previously published in Kalin et al., 2005.

Total Lesion n=6

Six animals received bilateral OFC aspiration lesions, which included Areas 11, 12, 13 and 14 as defined by Paxinos, Huang, and Toga (1999) (Kalin, Shelton & Davidson, Submitted). Lesion extent was determined based on post-surgical MRIs. Post-surgery MRI images were compared to pre-surgery MRI images for animals that received them (n=2) and to age-matched male monkeys for animals that did not receive a pre-surgery MRI scan (n=4). Six males underwent lesioning procedures at an average age of 35.6 months of age.

Total Post n=5

Ten animals (age: mean=2.86 years) from the lesion portion of the study underwent an additional FDG-PET scan; five OFC lesioned animals and five unoperated matched cage-mate control animals. The animals were housed as pairs with one experimental animal living with a control animal.

FDG microPET scans were performed to assess brain metabolism during the NEC condition prior to and after the lesioning procedure. In order to classify the extent of functional differences in the post-surgical animals, we used a standard-space analysis approach. A multi-stage process described in Kalin et al. (2005) was used to transform the pre-lesion images into a standard space defined by Paxinos, Huang and Toga (2000). Post-surgical PET scans were masked to exclude prefrontal regions where anatomy may have changed, and posterior brain regions which were misplaced outside of the PET scanner field of view in some of the pre-surgery images (e.g. Kalin et al., 2005). Each animal's masked images were transformed using a 6-parameter rigid-body transformation to match the mean of their three pre-lesion PET scans. Transformations were applied to the unmasked PET scans and manually inspected to assure each subject's post-surgery PET scans were accurately aligned to the pre-surgery mean PET image. Non-linear transformations determined based on the pre-surgery images were applied to the post-surgical images, resulting in post-surgery images in standard space. To facilitate inter-scan comparisons, images were globally scaled by adjusting the mean, based on a partial brain ROI created by intersecting the masked images used for alignment (Carmargo et al., 1992; Kalin et al., 2005). Statistical analyses were performed using voxelwise and region of interest (ROI) based techniques. To verify lesion efficacy in decreasing OFC metabolism, a region of interest based on the target lesion area was drawn on an MRI template, and relative glucose metabolism within this region was extracted for each subject. An ANOVA was performed to assess the group (lesion vs control) x test (pre surgery vs. post surgery) interaction. In order to assess brain differences in non-OFC regions, analyses were performed using a voxelwise search within regions where data were accurately aligned to standard space. Posterior visual regions were excluded from the analyses, since this region was outside of the scanner FOV in some of the pre-lesion PET scans (see Kalin et al., 2005), and anterior regions were excluded because we could not accurately account for lesion-induced deformation in brain structure within these regions. Within trusted regions, we identified regions that showed a significant Group(Lesion vs. Control) by Time(Pre- vs. Post-Surgery) interaction (p<.05, two-tailed uncorrected) and a significant post-lesion main effect of Group (p<.005, two-tailed uncorrected).

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