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Functional MRI of Conscious Dogs: Relationship Between Brain Activity and Measures of Working Dog Performance

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Interdisciplinary Canine fMRI Team

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Canine Performance Sciences

Applying Science to the Working Dog

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Support for this Work

- DARPA *FIDOS* (Functional Imaging to Develop Outstanding Service Dogs) STTR Program
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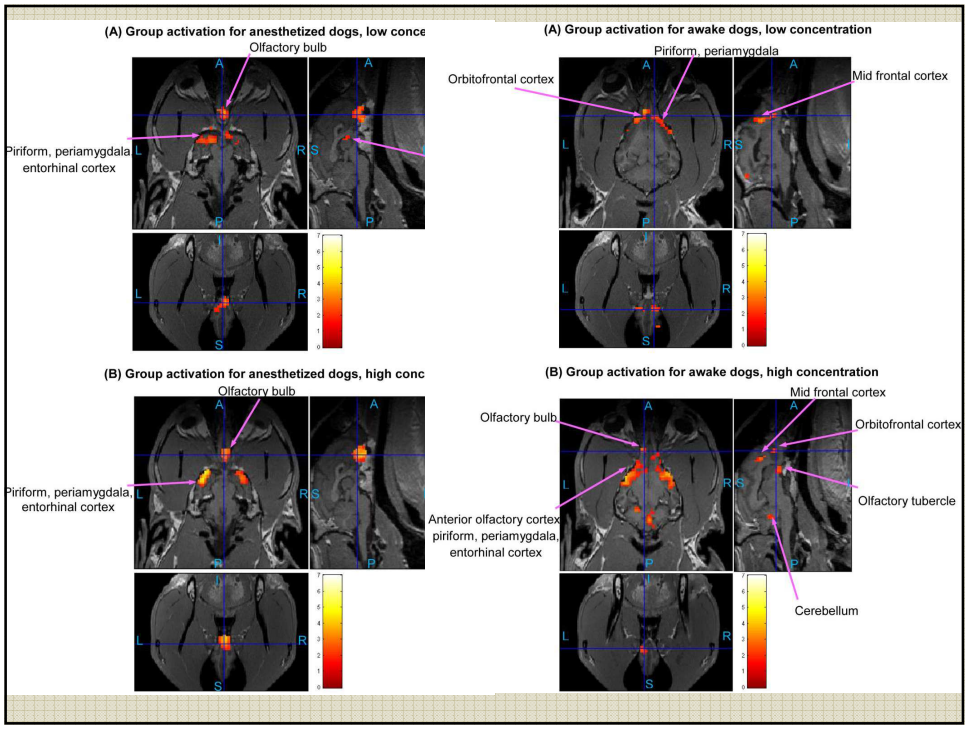
- Auburn University Intermural Competitive Research Grant Program, Office of the VP for Research

Prior Auburn Canine fMRI Work

- Demonstrated difference in magnitude of neural activation in response to high vs. low concentration odorant
  - Procedural validity
- Demonstrated difference in magnitude and location of neural activation in awake vs. lightly anesthetized dogs
  - Awake dog activity focused and in higher cognitive function areas
  - Procedural validity

H. Jia, O. Pustovyy, P. Waggoner, R. Beyers, J. Schumacher, C. Wildey, J. Barret, E. Morrison, N. Salibi, T. Denney, V. Vodyanoy and G. Deshpande, "Functional MRI of the Olfactory System in Conscious Dogs.," *PLoS One,* vol. 9, no. 1, p. e86362, 2014.



Cluster-level statistics of activations for anesthetized dogs

Number of activated clusters: 6, total number of activated voxels: 171			
Properties Clusters	Anatomical areas included	Number of activated voxels	Peak F value
Cluster 1	Olfactory bulb	34	6.19
Cluster 2	Anterior cingulate cortex	25	5.85
Cluster 3	Left piriform cortex, left periamygdaloid cortex	42	5.68
Cluster 4	Brainstem	16	4.73
Cluster 5	Left periamygdaloid cortex, left entorhinal cortex	35	4.70
Cluster 6	Right periamygdaloid cortex, right entorhinal cortex	19	4.44

Cluster-level statistics of activations for awake dogs

Number of activated clusters: 2, total number of activated voxels: 205			
Properties Clusters	Anatomical areas included	Number of activated voxels	Peak F value
Cluster 1	Mid cingulate cortex, superior frontal cortex, left caudate	171	14.84
Cluster 2	Olfactory bulb	34	8.42

Prior Auburn Canine fMRI Work

- Demonstrated increased magnitude of neural activation in response to odorant in presence of zinc nanoparticles.
  - Confirmed increased olfactory response in presence of zinc seen at level of receptors in electrophysiology study is seen upstream in higher brain area.
- Demonstrated local association but disassociation of the anterior and posterior regions of the *default mode network* (DMN) in resting state anesthetized and awake dogs
  - DMN implicated in self-referential processing, emotional and social processing.
  - In humans, functional connectivity in DMN important in working memory efficiency and higher level cognition
  - Dogs DMN localized connectivity similar to that of human child
  - DMN in dogs may have potential as predictor of behavioral performance and individual traits, such as empathetic response useful in emotional support dogs

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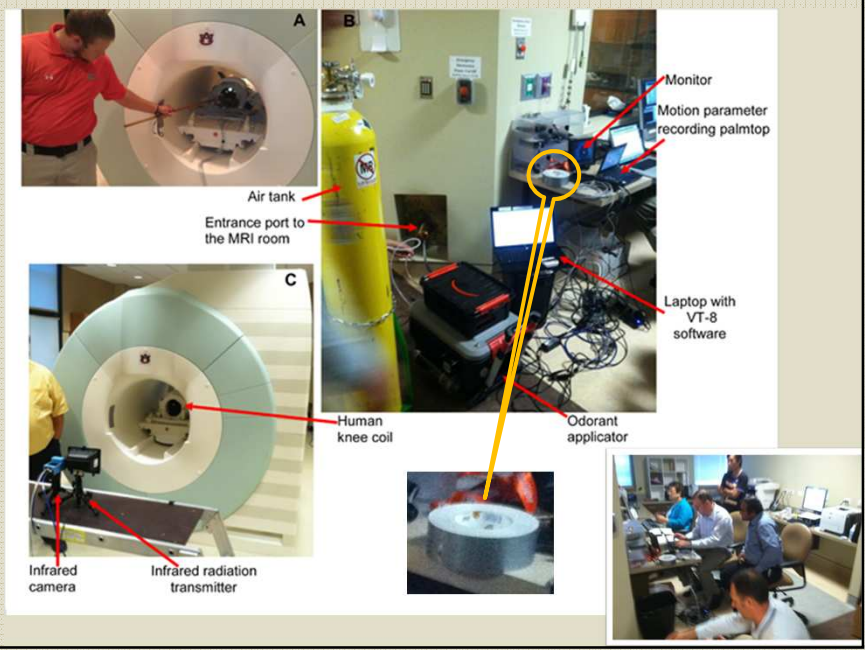
Preparation of Dogs for Awake & Unrestrained fMRI

Instrumentation and General Experimental Setup

- Siemens Verio Open-Bore 3 Tesla Clinical Scanner
- Six Channel Odorant delivery device (Vodyanoy & Pustovvy)
- Optical head motion tracking (MRRA, Inc. HT-1000)

Interlinked Trigger System

General Experimental Setup



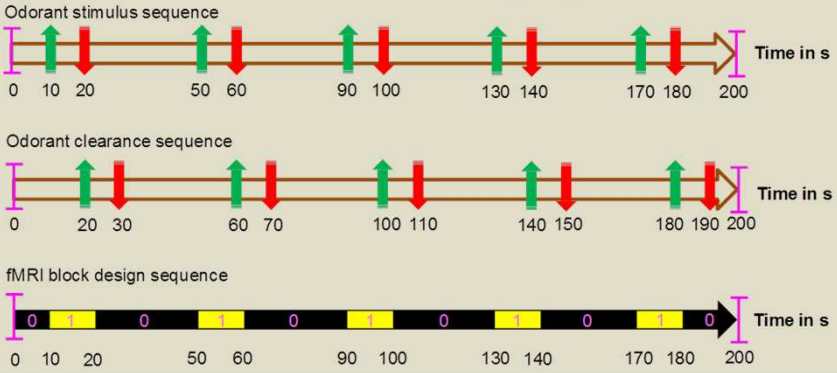
General Scanning Sequence

- Structural MRI scans to acquire anatomical reference
  Magnetization-prepared rapid gradient echo (MPRAGE) 104 slices
- Odorant / no odorant functional MRI scans
  echo-planar imaging (EPI) sequence for blood oxygenation level dependent contrast (BOLD)

OR

- Odorant A / no odorant / odor B randomized fMRI scans
- Resting state functional MRI scans

Odorant stimulation fMRI scanning sequence



Spatial Normalization Approach

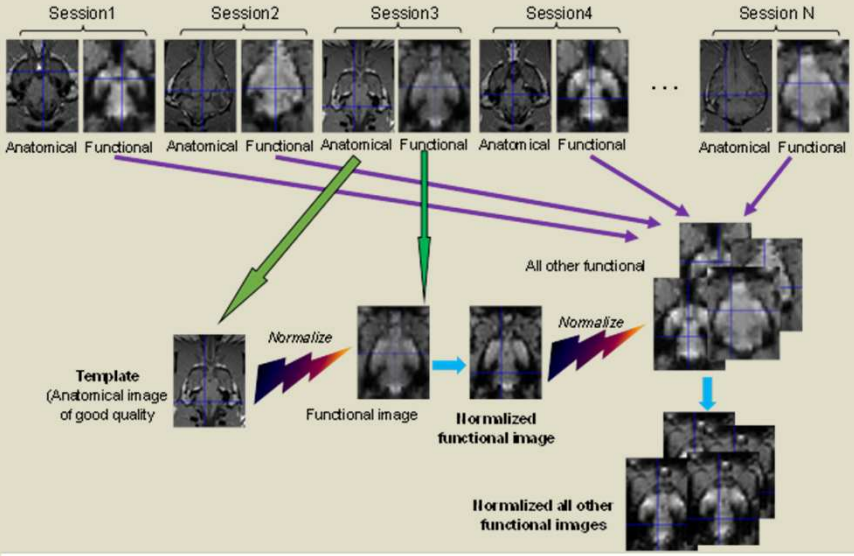
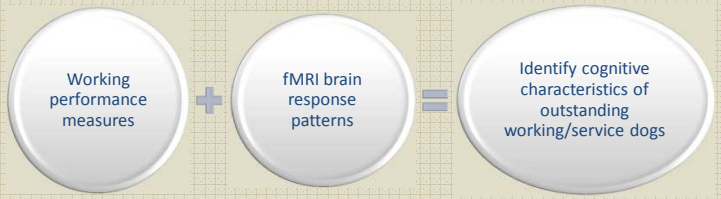


Figure 11 *Flow chart of proposed spatial normalization procedure. A good quality anatomical image was chosen as the template from a given session. Then one functional image from the same session was chosen and normalized to the template. Subsequently, this transformed functional image was used as a template to normalize other functional images of other sessions.*

Relationship Between Brain Activity and Measures of Working Dog Performance



- fMRI of awake dogs' response to discriminative vs. non-discriminative odor
  - Magnitude & location neural activation discriminative vs. non-discriminative odor
  - Pattern of activation to odor stimulation & working dog performance measures
- Resting state (RS) fMRI of dogs
  - RS brain activity patterns indicative of traits and cognitive performance in humans (e.g., problem solving, response to stimuli, extroversion/introversion etc.)
  - Relationship between working dog performance measures and resting state brain patterns

Relationship Between Brain Activity and Measures of Working Dog Performance

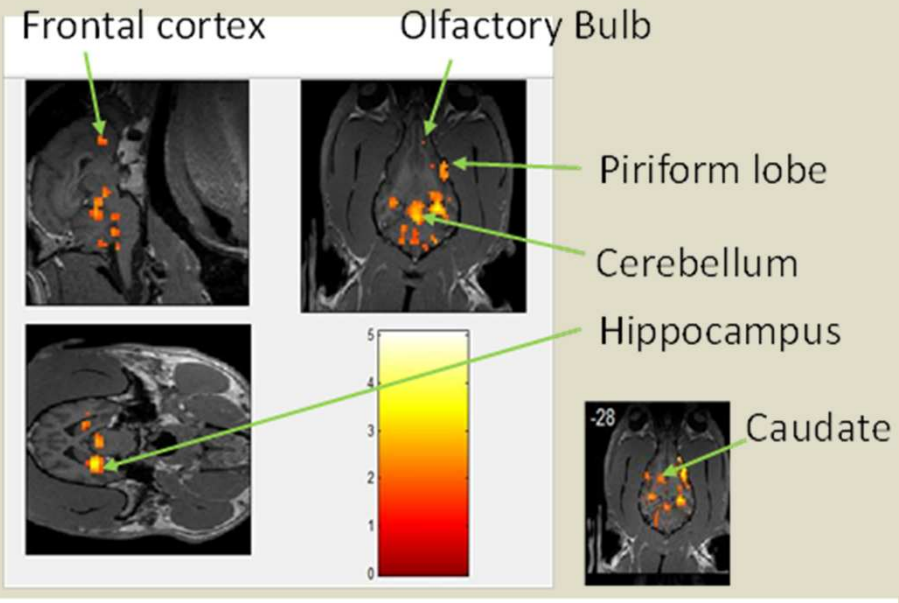
Dog performance measures

- Typical detector dog acquisition assessment
  - Retrieving, hunting, & environmental soundness (visual & auditory startle, people, etc.)
  - 1-3 (low, medium, high) score for each, combined into integrated behavioral score
- Ease of training for awake imaging task
  - Time to learn routine, time to first successful scan, time of maintenance training to scan
  - Rank order dogs on each then combined rankings for overall "training ease" metric

Correlated fMRI metrics

- Activation magnitude to discriminative odor in brain regions that showed higher response to discriminative vs. non-discriminative odor
  - 6 Dogs (1 M GSD, 1 M English Springer, 1 M GSP, 1 M Malinois , 1 M /1 F Lab)
  - ½ trained alert to ethyl butyrate, ½ to eugenol (passive exposure to E & EB respectively)
- Functional connectivity magnitude to posterior cingulate cortex & caudate nucleus during rest (6 dogs in odor activation plus rest data from 6 dogs in previous study)
  - Posterior cingulate connectivity implicated in working memory functionality
  - Caudate nucleus implicated in reinforcement sensitivity and learning

Regions of Awake Dog Brain Significantly More Activated for Discriminative vs. Non-discriminative Odor



Activation by Discriminative vs. Non-Discriminative Odor

- Correspond closely to those reported in similar human study on olfactory familiarity (Plailly et al., 2005, NeuroImage)

Piriform lobe & Hippocampus

- Recognition memory

Cerebellum

- Implicated in sniffing and odorant threshold detection in humans (Sobel et. al., 1998, Nature)

Olfactory bulb

- Suggests possible top-down modulation during signal transduction

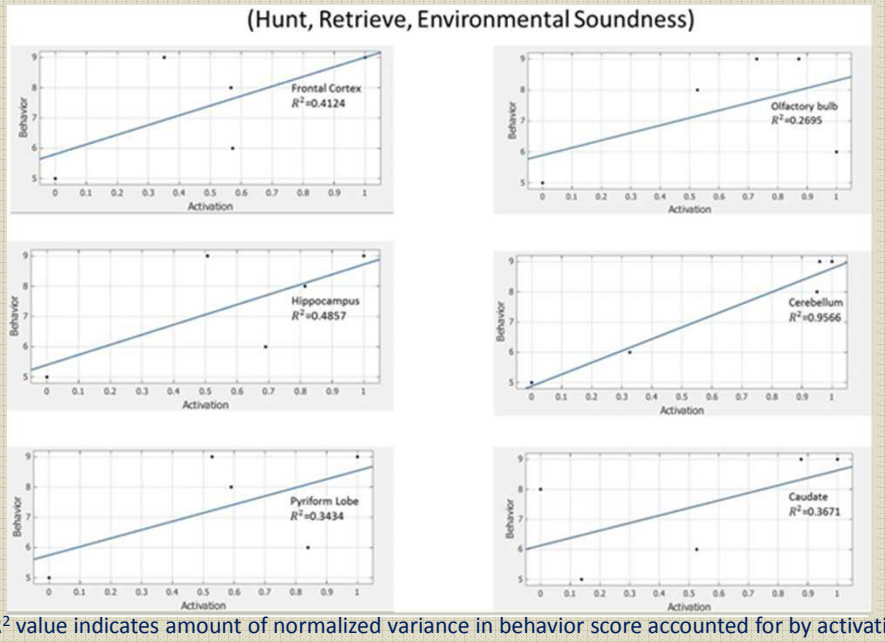
Frontal Cortex

- Possible consequence of additional cognitive processing demands of discriminative odor

Caudate nucleus

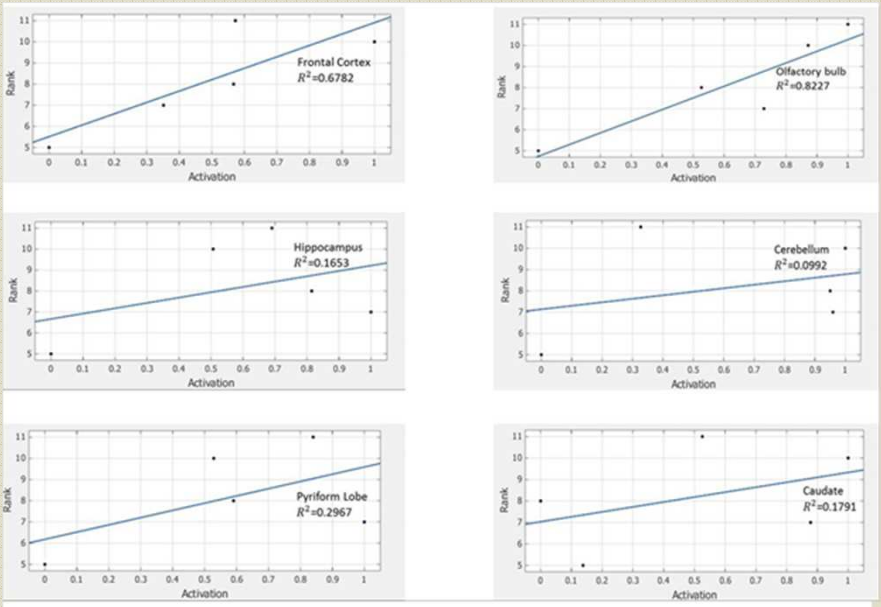
- Considered central to contingency-based learning and discriminative odor a component of a behavioral contingency

Correlation between activation during odor presentation & behavior score for brain regions more activated by discriminative as compared to non-discriminative odor



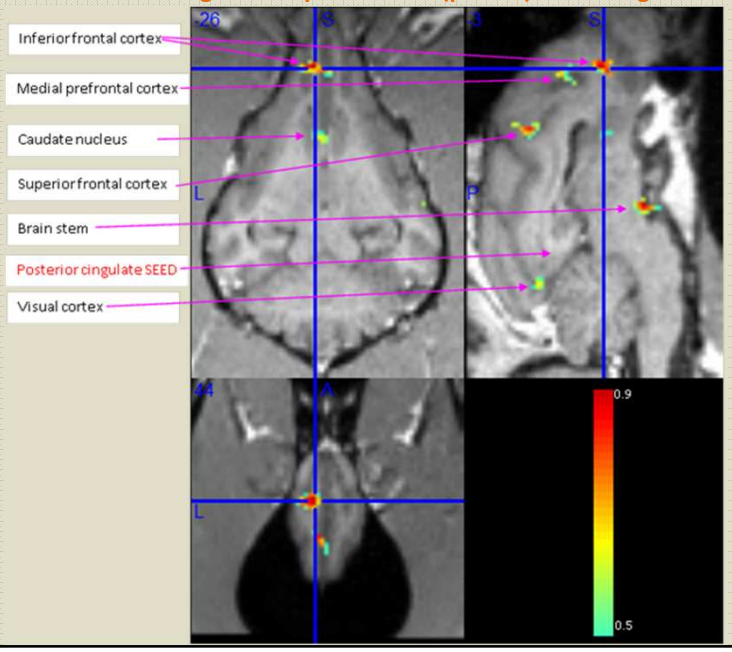
R^2 value indicates amount of normalized variance in behavior score accounted for by activation

Correlation between activation during odor presentation & MRI "training ease" score for brain regions more activated by discriminative as compared to non-discriminative odor

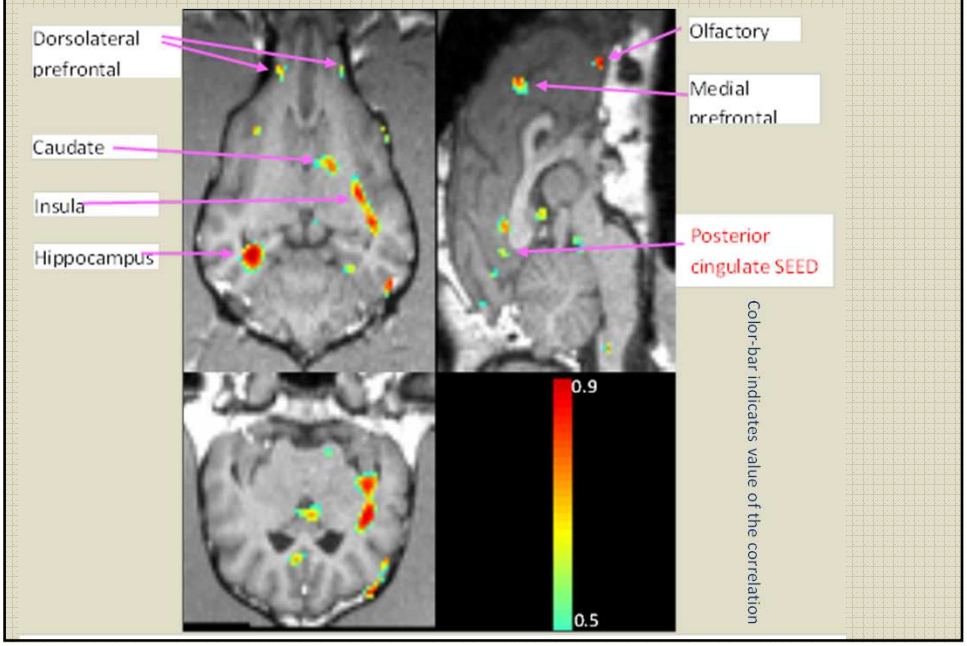


R^2 value indicates amount of normalized variance in training-ease score accounted for by activation

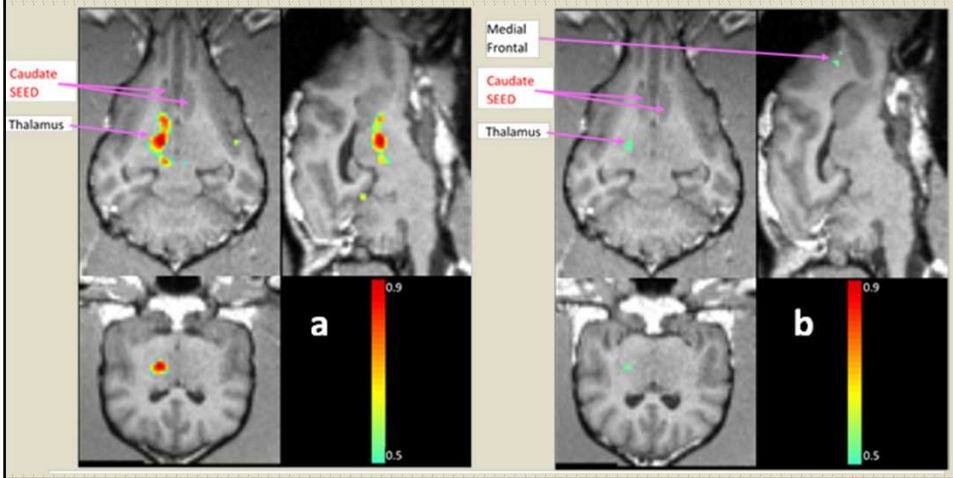
Awake dog brain regions where resting state connectivity with the posterior cingulate cortex was significantly correlated (p<0.05) with integrated behavior score



Awake dog brain regions where resting state connectivity with the posterior cingulate cortex was significantly correlated (p<0.05) with MRI "training ease" score



Awake dog brain regions where resting state connectivity with the caudate nucleus was significantly correlated ($p<0.05$) with the integrated behavior (a) and MRI "training ease" (b) scores



Color-bar indicates value of the correlation

Relationship Between Brain Activity and Measures of Working Dog Performance

- Differential activation by discriminative vs. non-discriminative odors suggests fMRI of odor stimulation in awake dogs may provide a means to explore processing of odor information
  - Could improve understanding of odor discrimination leading to enhancements of training and utilization practices
- No definitive conclusions about correlations of behavioral measures and brain activity due to small sample size
- Clear trend that dogs with greater activation to discriminative vs. non-discriminative odors scored higher in retrieval, hunt, & environmental soundness assessments and were more readily trainable for awake MRI
- If results hold true for larger sample, then fMRI of discriminative odor stimulation may provide a tool for understanding the fundamental basis of working dog performance

Relationship Between Brain Activity and Measures of Working Dog Performance

- High correlation of resting state connectivity between posterior cingulate and frontal cortices with behavioral measures suggests possibility of fMRI as means by which to screen for dogs with greatest working potential for varied tasks
  - Results correspond to human data showing co-variance of behavioral variables and connectivity in default mode and fronto-piritenal networks
- Covariance of behavioral measure and resting state connectivity with caudate nucleus is interesting given the strong implication of the caudate in learning
  - Resting state fMRI may provide means to explore the effects of different training experiences and enhance canine training procedures

Relationship Between Brain Activity and Measures of Working Dog Performance

- If relationships between brain activity and performance measures are shown to be consistent, then fMRI may provide phenotypic characteristics for which genetic marker(s) may be identified
  - Selection of working dogs and guidance for enhancing breeding of working dogs
- Although not a validation of working dog assessment procedures, does suggest that those assessment procedures are sensitive to some fundamental cognitive differences between dogs

Relationship Between Brain Activity and Measures of Working Dog Performance

Current/Future Canine fMRI Work

- Acquire more data for more dogs relating brain activity to behavioral measures
  - Longitudinal assessment scanning prior to , immediately after , and X time post training
- fMRI of awake dogs during stimulation with emotional faces of human
- Relationship between response to human gestures and fMRI resting state connectivity patterns associated with the amygdala (implicated in empathy and emotional reactivity)

Schematic of Planned Correlation Analyses Between Imaging Metrics and Behavior