How does whisker stimulation modulate ongoing electrophysiological signal? Implications for resting state fMRI

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Introduction Spontaneous fluctuations in the resting state fMRI time course have been shown to exhibit structured spatial and temporal patterns, and are modulated in a variety of diseases. These spontaneous BOLD fluctuations have electrophysiological origins (1-5). However, the underlying mechanisms are still poorly understood. A few recent human studies (6, 7) reveal that functional connectivity results from "pure" resting state scans are similar to those acquired with conventional block-design paradigms after the corresponding evoked fMRI responses have been regressed out, suggesting that the ongoing electrophysiological signal that underpins the spontaneous fluctuations observed in resting state fMRI is minimally disturbed by the task blocks. The goal of this study is to investigate how tasks modulate ongoing spontaneous fluctuations. We chose a rat whisker barrel (WB) stimulation model instead of the electrical forepaw stimulation model, because, unlike the latter one in which stimulation is typically delivered with electrical pulses, mechanical deflection of rat whiskers is more physiologically relevant and can be delivered continuously.

Methods A customized whisker stimulation apparatus was constructed. Sinusoidal pulses were generated by a computer, which was power-amplified to drive a piezoeletrical device. A comb connected to the piezoeletrical device was used to move rat whiskers along the rostral-caudal direction. The stimulation paradigm was a block design consisting of 32 sec ON and 32s OFF with 8 repetitions. During the ON-period, the comb was driven at 8Hz with an amplitude of 4 mm (peak-to-peak). Multi-channel epidural EEG signals were recorded from 9 rats using a Plexon system with semi-micro electrodes. Recording sites: bilateral whisker barrel cortex with the visual cortex serving as a control site. Data acquisition frequency was 4 KHz, down-sampled to 256 Hz during data analysis. EEG mean power, power time correlation and raw EEG signal coherence between electrode pairs were computed using the complex Morlet Wavelet analysis method. Matlab code for Wavelet analysis was provided by Grinsted et al. (http://www.pol.ac.uk/home/research/waveletcoherence/). EEG signal was classified into five conventional frequency bands (delta 1-4 Hz, theta 5-8 Hz, alpha 9-14 Hz, beta 15-25 Hz, gamma 26-50 Hz). Mean power and power correlation between the ON versus OFF periods were compared for each frequency band. Coherence between electrode pairs was calculated with 57 log-scales, ranging from 0.0078 to 1 (the corresponding Fourier frequency 124 Hz to 0.97 Hz).

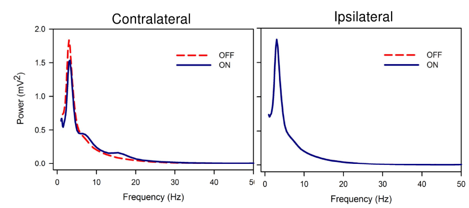

Figure 1. An example showing distinct power spectrum during whisker stimulation ON vs. OFF on the contralateral, but not the ipsilateral side.

Results Whisker stimulation induced EEG signal on the contralateral side manifest as a reduction in overall amplitude and an increase in higher frequency components. Figure 1 illustrates a comparison of power spectra between the contralateral and ipsilateral sides. Table 1 summarizes statistical results from 9 animals. Whisker stimulation induced power changes only on the contralateral, but not the ipsilateral side. It caused an enhancement in EEG power from theta to gamma bands, but a reduction only in the delta band. Such modulations were specific to the contralateral WB cortex as expected. Furthermore, power correlation between left and right WB cortex was reduced in both the theta and beta bands; spectral coherence was also reduced in both the beta and gamma bands. There was no significant change between either side of WB cortex and visual cortex in any frequency band.

Table 1. Statistical comparison of mean power, power correlation and coherence between the left-right whisker barrel cortex electrode pairs during the stimulation OFF vs. ON period.

	Delta (1-4 Hz)	Theta (5-8 Hz)	Alpha (9-14 Hz)	Beta (15-25 Hz)	Gamma (26-50 hz)
Change in power (OFF vs ON)	-9.3±5.6%*	21.8±19.4%*	61.3±32.2%*	330.6±204.1%*	164.3±100%*
Power Correlation					
OFF	0.49±0.12	0.29±0.08	0.22±0.10	0.23±0.08	0.16±0.10
ON	0.47±0.18	0.21±0.11*	0.20±0.12	0.11±0.11*	0.14±0.07
Coherence				**14-23 Hz**	**28-40 Hz**
OFF				0.23±0.02	0.23±0.02
ON				0.19±0.01*	0.19±0.02*

* Indicates significant difference during the ON vs. OFF period (Bonferroni corrected, $p<0.05$). Significant changes are seen ***only*** between the left and right whisker barrel cortex (WBC) electrode pairs. There is **no** significant difference in power change, power correlation or spectral coherence between the visual and either the left or the right WBC electrode pairs (data not shown).

Discussion Given the tight neurovascular coupling, it is likely that electrophysiological signals in every frequency bands have a hemodynamic signature, i.e. they are reflected in the fMRI signal. A key question, however, is what the major electrophysiological sources are that contribute to the resting state fMRI signal. Our data reveal that power correlation and/or coherence are modulated in the theta, beta and gamma bands, but not in the delta or alpha band. We reason that if signals in theta, beta and gamma bands are the major contributors to resting state fMRI signal, bilateral correlation of the fMRI signal should be significantly reduced during whisker stimulation. However, if delta and/or alpha signal is the major contributor, bilateral correlation of the fMRI signal should be similar between the ON and OFF periods. Recent human fMRI data seem to support the latter. Further fMRI experiments can be performed to test this hypothesis.

Acknowledgement This work was sponsored by the National Institute on Drug Abuse, Intramural Research Program, National Institutes of Health(NIDA/IRP/NIH).

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