Reproduction of direct imaging of neuronal activity (DIANA) in mice at 11.7T

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Objective

Direct imaging of neuronal activity (DIANA) is promising for elucidating the spatiotemporal dynamics of brain networks. Here we report a replication of the DIANA study using forelimb electrical stimulation of medetomidine-anesthetized mice at 11.7T.

Methods

DIANA with millisecond resolution in mice at 11.7T.

Results

We first performed BOLD-fMRI experiments using forelimb electrical stimulation with an oblique slice encompassing the thalamus and forelimb somatosensory cortex (S1FL) areas of medetomidine-anesthetized mice (Fig.1A-B). We observed BOLD responses in the contralateral thalamus and S1FL about 0.5~1%, whereas there were almost no responses in ipsilateral areas (Fig.1C-E).

In DIANA experiments, we used the same acquisition scheme as the study by Toi et al.[1] (Fig.2A) and collected time series of 40 images at 5ms temporal and 0.2mm spatial resolutions (0.8mm thickness) on the same slice used in BOLD-fMRI (Fig.2B-C). As a result of averaging all 40 trials/mouse across 6 mice, we observed sequential DIANA responses in the contralateral thalamus and S1FL with signal changes of ~0.1%, peaking at 15 and 35ms, respectively

(Fig.3A, *n*=6), showing a statistically significant difference from the ipsilateral responses (Fig.3B,C).

Discussion and Conclusion

We reproduced the DIANA study using forelimb electrical stimulation in medetomidine-anesthetized mice at 11.7T. Peak latencies of DIANA responses in the contralateral thalamus (15ms) and S1FL (35ms) were consistent with previous studies[2–5]. The signal change here was ~0.1%, which is slightly smaller than the result reported at 9.4T[1]. This may be due to the use of different anesthetics (ketamine vs. medetomidine) as well as forelimb stimulation to which the mouse brain is less sensitive than whisker-pad stimulation. The BOLD signal change (0.5~1%) here was also smaller than the result at 9.4T (~2%)[1]. Whereas we averaged all trials across all mice, DIANA sensitivity may be improved by more effective data analysis methods, including objective methods to distinguish between good- and poor-responding trials or mice.

References

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Figures

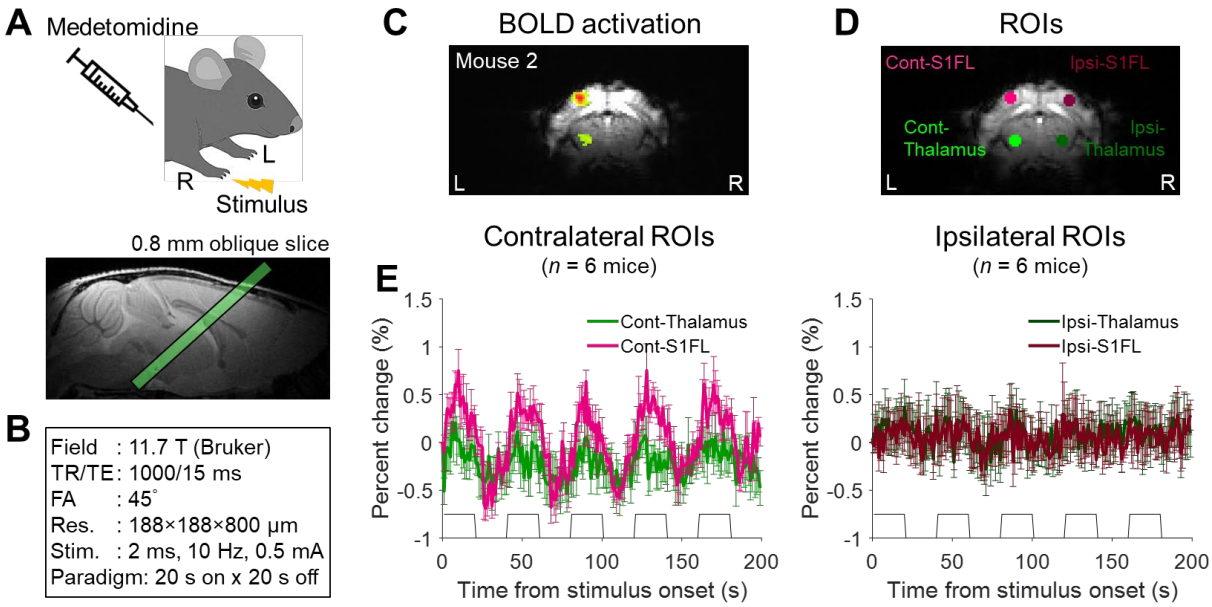
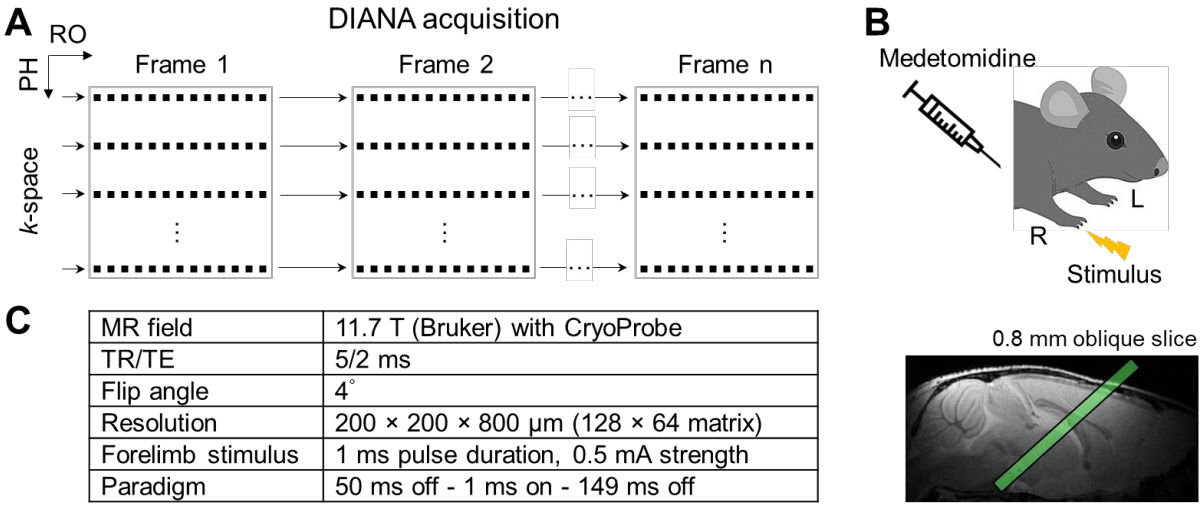


Figure 1. BOLD fMRI using forelimb electrical stimulation in anesthetized mice at 11.7 T for reference. (A) Illustration of BOLD fMRI experiment using forelimb electrical stimulation in mice anesthetized with medetomidine (top), acquiring images from a single oblique slice containing the thalamus and S1FL areas (bottom). (B) Scan and stimulation parameters for BOLD experiments. (C) BOLD activation map from a representative mouse ($p < 0.05$). (D) Regions of interest (ROIs) for extracting time courses. (E) Averaged BOLD time courses in the contralateral (left) and ipsilateral (right) thalamus and S1FL ($n = 6$ mice).



C

MR field	11.7 T (Bruker) with CryoProbe
TR/TE	5/2 ms
Flip angle	4°
Resolution	200 × 200 × 800 μm (128 × 64 matrix)
Forelimb stimulus	1 ms pulse duration, 0.5 mA strength
Paradigm	50 ms off - 1 ms on - 149 ms off

Figure 2. DIANA experiment using forelimb electrical stimulation in anesthetized mice at 11.7 T. (A) DIANA acquisition scheme, which was the same as the study by Toi et al.[1] (B) Illustration of DIANA experiment using forelimb electrical stimulation in mice anesthetized with medetomidine (top), acquiring images from a single oblique slice containing the thalamus and S1FL areas (bottom). (C) Scan and stimulation parameters for DIANA experiments.

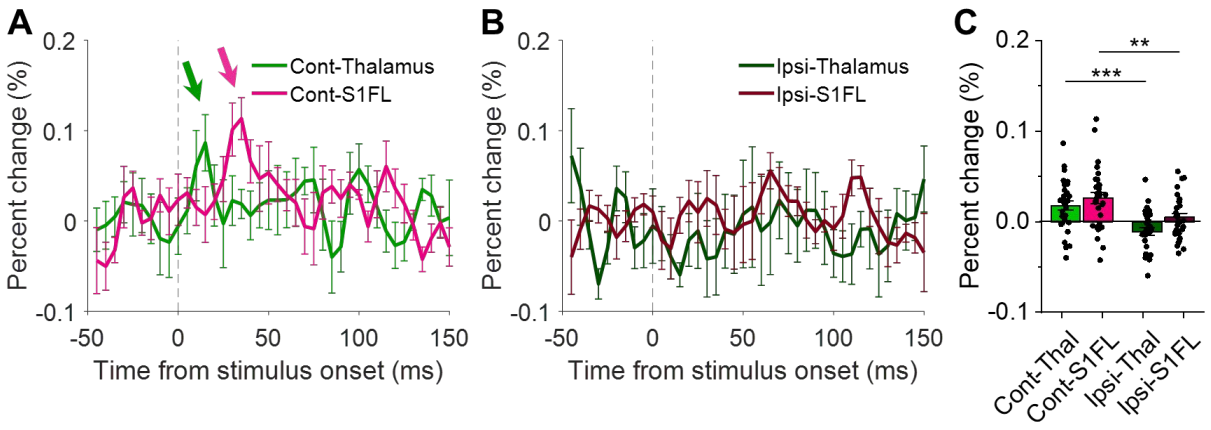


Figure 3. DIANA responses to forelimb electrical stimuli. (A) Averaged DIANA time series in the contralateral thalamus and S1FL (n = 6 mice). All 40 trials per mouse were averaged across 6 mice. Sequential DIANA responses peaked at 15 ms in the contralateral thalamus (green arrow) and at 35 ms in the contralateral S1FL (magenta arrow). (B) The same as (A), but for the ipsilateral thalamus and S1FL. (C) Statistical comparison of the means of post-stimulation signals between contra- and ipsilateral thalamus, as well as between contra- and ipsilateral S1FL in (A) and (B). Dashed lines indicate the forelimb stimulation onset time. ** $p < 0.01$, *** $p < 0.001$ for paired Student's t-test.