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► **To cite this version:**

Ayan Sengupta, Rochelle Ackerley, Roger H. Watkins, Rosa Sanchez Panchuelo, Glover Paul, et al.. Global responses to microstimulation at 7T and comparison with vibrotactile stimulation. International Society for Magnetic Resonance in Medicine, Jun 2018, Paris, France. hal-02357525

HAL Id: hal-02357525

<https://hal.science/hal-02357525>

Submitted on 10 Nov 2019

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Global responses to microstimulation at 7T and comparison with vibrotactile stimulation

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International Society for Magnetic Resonance in Medicine (ISMRM)
16-21 June 2018, Paris, France

PURPOSE:

Intra-neural microstimulation (INMS) is a technique that allows the precise delivery of low-current electrical pulses into human peripheral nerves. Single unit INMS can be used to stimulate individual afferent nerve fibres during microneurography. Combining INMS with neuroimaging^{1,2} allows the unique monitoring of central nervous system activation in response to unitary, controlled tactile input, with functional magnetic resonance imaging (fMRI) providing high spatial localisation and sensitivity to brain activity.

Here, we report the application of INMS at ultra-high field (7T), and compare the global pattern of positive and negative BOLD response to INMS with that of perceptually matched vibrotactile stimulation of the skin.

METHODS:

Five subjects each participated in an ~4 hours scan session involving characterization of a single tactile unit; assessment of the effect of microstimulating the unit to ensure the location of the electrically-elicited sensation matched the location where mechanical stimulation of the skin generated a response; and concurrent INMS and fMRI². INMS was performed using a INMS system specifically designed to provide compatibility with ultra-high field (7T)³, a tungsten needle microelectrode was percutaneously inserting into the median nerve to stimulate and record from single afferent units. Each single unit was stimulated with short bursts of 60 Hz electrical pulses. INMS stimulation was then repeated at 30 and 90 Hz, with matched perceived amplitude for each frequency. In addition, fMRI data was collected using mechanical vibration applied to each of the unit's receptive field at matched perceptual threshold to the INMS.

fMRI paradigm: fMRI data was collected on a 7T Philips Achieva using a GE-EPI acquisition (Multiband factor 2, 1.25mm isotropic resolution, 40 axial slices, TE=25ms, TR=2s). The INMS protocol comprised a burst of 30, 60, or 90Hz 200 μ s current pulses of 1 s (0.5s on and 0.5s off) repeated 8 times, followed by a rest period of 23 s. This was repeated for a total of 8 cycles. Vibrotactile stimulation was applied at 60 Hz to each unit's receptive field using an identical paradigm to the INMS at the same perceived intensity to INMS. High resolution structural data were also acquired.

Data Analysis: fMRI data were analyzed using Freesurfer and FSL. No spatially smoothed was applied, a GLM analysis was performed in FSL to generate both positive and negative BOLD statistical parametric maps (SPMs) ($Z > 2.3$, $p < 0.05$ uncorrected). A fixed effects group analysis was performed of all units stimulated at 60 Hz, and group SPM formed of the response to 60 Hz vibration applied the same units' receptive fields. ROI analysis was performed to assess the beta values in primary and secondary somatosensory areas (SI and SII), and the default mode network (DMN).

RESULTS:

fMRI data were collected on 14 units (8 fast-adapting type 1 (FA1); 5 slowly-adapting type 1 (SA1) and 1 type 2 (SA2) units), Figure 1 shows the location and type of each of these units. The group SPM to 60 Hz INMS of the SA1 and FA1 units resulted in a positive BOLD responses in a number of sensory-related brain areas - SI, SII, premotor cortex (supplementary motor area (SMA), and dorsal premotor cortex (PMC)), primary motor cortex (MI), insula cortex (anterior (AIC) and posterior (PIC) parts), prefrontal cortex (PFC) and posterior parietal cortex (PPC), and a strong negative BOLD response in the DMN (Fig.2A). Vibrotactile stimulation generated a similar pattern of positive BOLD response (Fig.2B and C), and in addition a strong negative BOLD response ipsilateral S1 but no DMN response (Fig.2B). Figure 3 plots the mean beta values across units/vibration sites highlighting this difference in negative BOLD response between INMS and vibrotactile stimulation.

DISCUSSION:

We used an MRI compatible INMS system to assess fMRI responses during INMS at 7 T. Maps showed INMS and vibrotactile stimulation generate a similar pattern of positive BOLD response, but altered negative BOLD patterns. Vibrotactile stimulation led to strong ipsilateral negative BOLD response not seen for INMS. The negative BOLD response to vibrotactile stimulation has been widely reported previously and has been suggested to represent active inhibition of the ipsilateral cortex⁴ mediated by transcallosal mechanisms. In contrast, INMS generated strong negative BOLD response in the DMN, not seen in response to vibrotactile stimulation. The DMN has commonly been shown to display task-induced reductions in BOLD signal (DMN deactivations) concurrently with increased response to task⁵. The DMN deactivations were associated with increased BOLD signal in the fronto-parietal network (FPN), suggesting increased attentional demands or level of cognitive engagement⁵. No effect of stimulation frequency was found associated with unit type.

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Acknowledgements: This work was funded by MRC grant MR/M022722/1.

Figure 1: The location and type of each of units on which fMRI data was collected. Data was acquired from the left hand on 14 units comprising 8 fast-adapting type 1 (FA1); 5 slowly-adapting type 1 (SA1) and 1 type 2 (SA2) units.

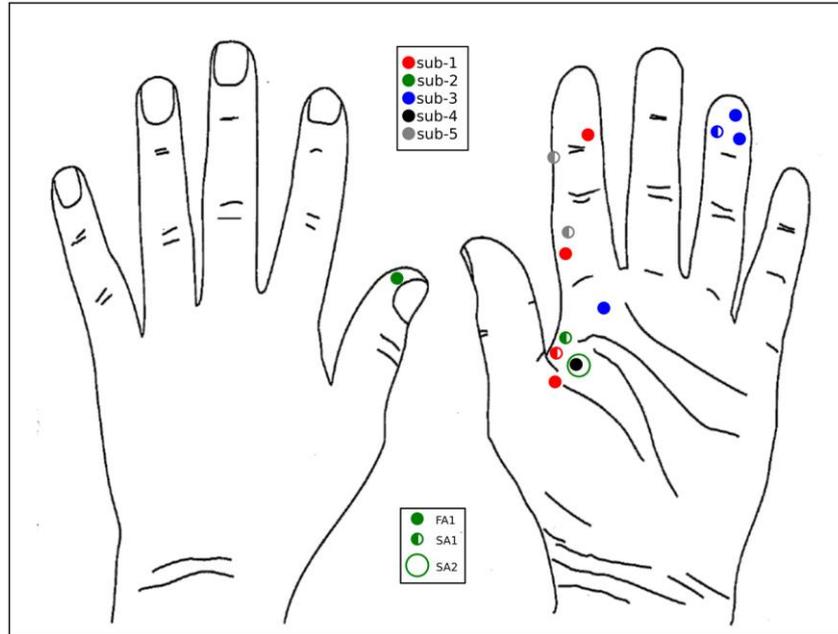
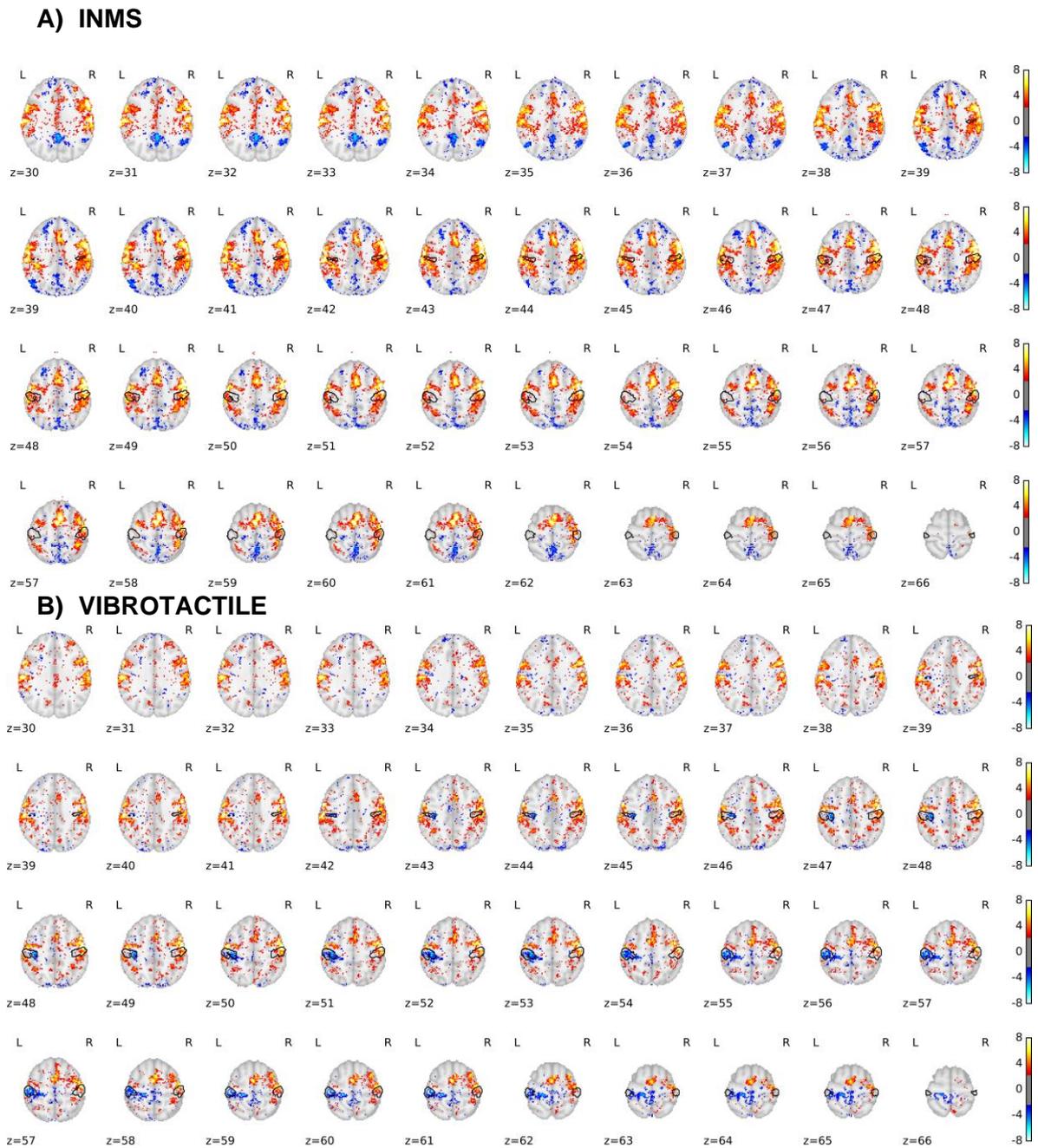


Figure 2: A) Group SPM to 60 Hz INMS of 13 SA1 and FA1 units. A positive BOLD response is seen in a number of sensory-related brain areas - SI, SII, premotor cortex (SMA and PMC), primary motor cortex (MI), insula cortex, prefrontal cortex (PFC) and posterior parietal cortex (PPC), and a strong negative BOLD response is seen in the Default Mode Network (DMN). **B)** Group SPM to 60 Hz vibrotactile stimulation. Note a similar positive BOLD response pattern, negative ipsilateral S1 response but no DMN activity. **C)** Conjunction map of INMS and vibrotactile, areas of overlap seen only for positive BOLD responses. Black outline show S1 hand area as defined from a travelling wave paradigm.



C) CONJUNCTION OF INMS AND VIBROTACTILE

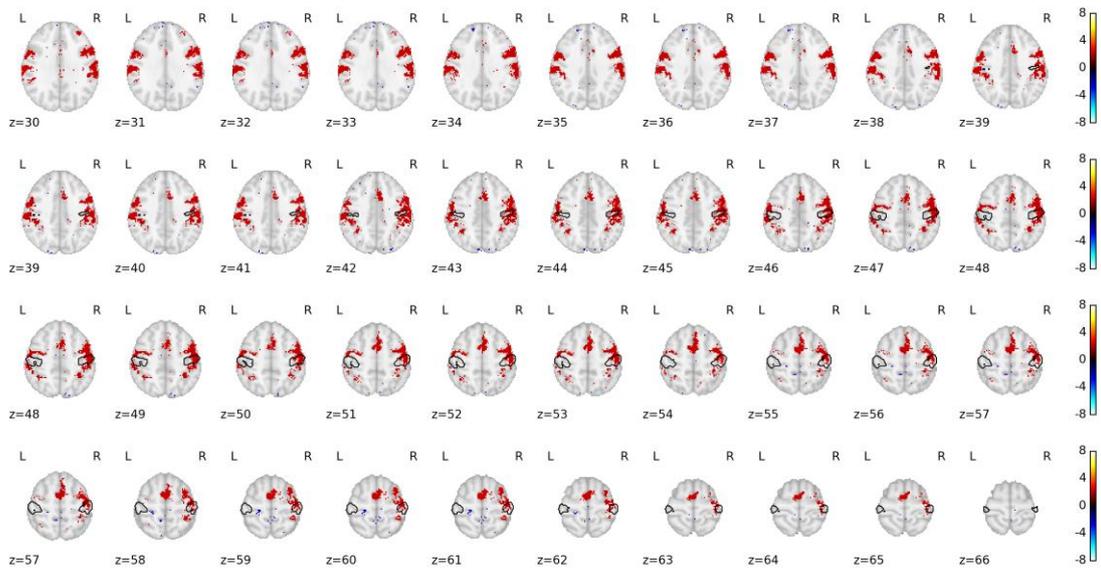


Figure 3: Mean beta values in ROIs of the contralateral and ipsilateral hand area (S1), secondary somatosensory cortex (OP1) and the default mode network (DMN). A Significant difference in beta values between INMS and vibrotactile stimulation was found in the DMN ($p=0.029$), with greater suppression of the DMN for INMS, and in the ipsilateral hand area which showed a negative BOLD response during vibrotactile stimulation and a positive response during INMS ($p=0.002$).

