Saccadic modulation of neural activity in the human anterior thalamus during visual active sensing

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Abstract

Humans and other primates explore visual scenes by *active sensing*, using saccadic eye movements to relocate the fovea and sample different bits of information multiple times per second. Recent reports indicate that saccades induce a phase reset of ongoing neuronal oscillations in a distributed network including primary and higher-order visual cortices and medial temporal lobe. As a result, neuron ensembles in these regions are shifted to a momentary high excitability state at the time visual input enters the system; i.e., just after fixation; among other things, this would amplify the neuronal response to visual input. The extent of the brain's circuitry modulated by saccades is not yet known. Here, we evaluate the possibility that saccadic phase reset impacts the anterior nuclei of the thalamus (ANT) using field potential recordings in the ANT in three surgical patients undergoing deep brain stimulation for treatment of epilepsy. Given that ANT are strongly connected to frontal/prefrontal cortex, hippocampus and cingulate cortex - brain networks that support active sensing, we hypothesized that ANT would display similar saccade-related modulation of excitability. In all three patients, we found saccade-related phase concentration, peaking at 3-4 Hz, coincident with suppression of Broadband High frequency Activity (BHA; 70-150Hz), a signal that correlates with local neuronal spiking activity. Our results provide evidence for saccade-related modulation of neuronal excitability dynamics in the ANT, consistent with the idea that these nuclei are part of the brain circuitry underlying visual active sensing.

Introduction

Both human and non-human primates sample visual scenes actively by systematically shifting eye gaze several times per second (Yarbus, 1967; Gilchrist et al., 1997). These eye movements modulate neural activity along the visual pathway from the lateral geniculate nucleus (e.g., Lee and Malpeli, 1998; Reppas et al; 2002; Sylvester et al., 2005; Sylvester & Rees, 2006; McFarland et al., 2015) through ascending stages of visual cortex (Purpura et al., 2003; Rajkai et al., 2008; Bartlett et al., 2011; Ito et al., 2011; Hamamé et al., 2014; Zanos et al., 2015; 2016; Barczak et al., 2019) up to the medial temporal lobe (MTL) including the hippocampus and enthorhinal cortex (Killian et al., 2012; Hoffman et al., 2013; Jutras et al., 2013; Killian et al., 2015; Staudigl et al., 2017; Meister & Buffalo, 2018; Staudigl et al., 2018; Katz et al., 2018; Doucet et al., 2019; for a recent review see Leszczynski and Schroeder, 2019).

Earlier studies of the effects of saccades in the dark (Ringo et al., 1994; Sobotka & Ringo, 1997; Lee and Malpeli, 1998; Sylvester et al., 2005; Sylvester & Rees, 2006; Royal et al., 2006; Rajkai et al., 2008; Kagan et al., 2008; Nakamura & Colby, 2000), and more recent studies that minimize saccade-related visual input by various means (McFarland et al., 2015; Barczak et al., 2019) confirm the proposition that nonretinal “corollary discharge” (CD) signals generated in parallel to saccades, modulate the excitability of neurons in visual pathways structures (Sommer & Wurtz, 2008). Most recently, Barczak et al (2019) showed that nonretinal saccadic signals reset ongoing excitability fluctuations (oscillations) in V1 neuron ensembles to a high excitability phase, and that this effect amplifies their response to visual inputs arriving immediately after the saccade (i.e., at fixation onset). This phase modulation is primarily observed in theta and alpha ranges - key physiological signatures of active sensing (Ahissar and Arieli, 2001; Szwed et al., 2003; Kleinfeld et al., 2006; Leszczynski and Schroeder, 2019).

Interestingly, many of the areas displaying saccadic phase modulation lie outside of the classic visual system - higher order regions with multiple sensory and cognitive functions like the MTL. However, aside from the tectal nuclei (e.g., Lee et al., 1988; Munoz & Wurtz, 1995; Werner-Reiss & Groh et al; Sommer & Wurtz, 2008) and the lateral geniculate nucleus of the thalamus (Lee and Malpeli, 1998; Reppas et al., 2002; Sylvester et al., 2005; Sylvester & Rees, 2006; Royal et al., 2006; McFarland et al., 2015), the degree to which saccade-related signals impact other subcortical structures has not been systematically investigated. As a step toward addressing this question, we leveraged a unique dataset: intracranial electroencephalography (iEEG) recordings from anterior nuclei of the thalamus (ANT) in patients implanted for deep brain stimulation treatment of epilepsy (see e.g. Lehtimäki et al. 2018; see Figure 1A).

Based on the interconnectivity of the ANT with other brain regions like the hippocampus and anterior cingulate cortex (Bubb et al., 2017; Zikopoulos and Barbas, 2006) as well as its apparent receipt of direct retinal afferents (Itaya et al., 1986) we hypothesized that neuronal excitability in the ANT should be modulated by saccade-related signals. We tested three specific predictions: **1)** Saccades should perturb ongoing field potential activity in the human ANT; **2)** The phase of low frequency oscillations should cluster around saccade/fixation onset; **3)** Broadband High-frequency Activity (BHA; 70-150 Hz), a measure of neuronal processes correlated with neuronal spiking (Mukamel et al., 2005; Niessing et al., 2005; Nir et al., 2007; Ray et al., 2008; Leszczynski et al., 2019), should be systematically modulated by saccades. Our findings provide support for all three hypotheses. Thus, in addition to a range of other functions, the ANT appear to be part of the brain networks underlying active sensing.

Results

Fixation and saccade related field potentials in human ANT

Using frontal scalp EEG and EOG electrodes we detected time points of fixation and saccade onsets (Figure 1B-D; see Methods). This is possible because eye movements generate large magnitude electric field fluctuations that are measurable by scalp EEG across multiple frontal channels (Lins et al., 1993). Combining simultaneous EEG and direct ANT recordings we could thus study the impact of eye movements (as detected from EEG) on neural activity in human anterior nuclei of the thalamus.

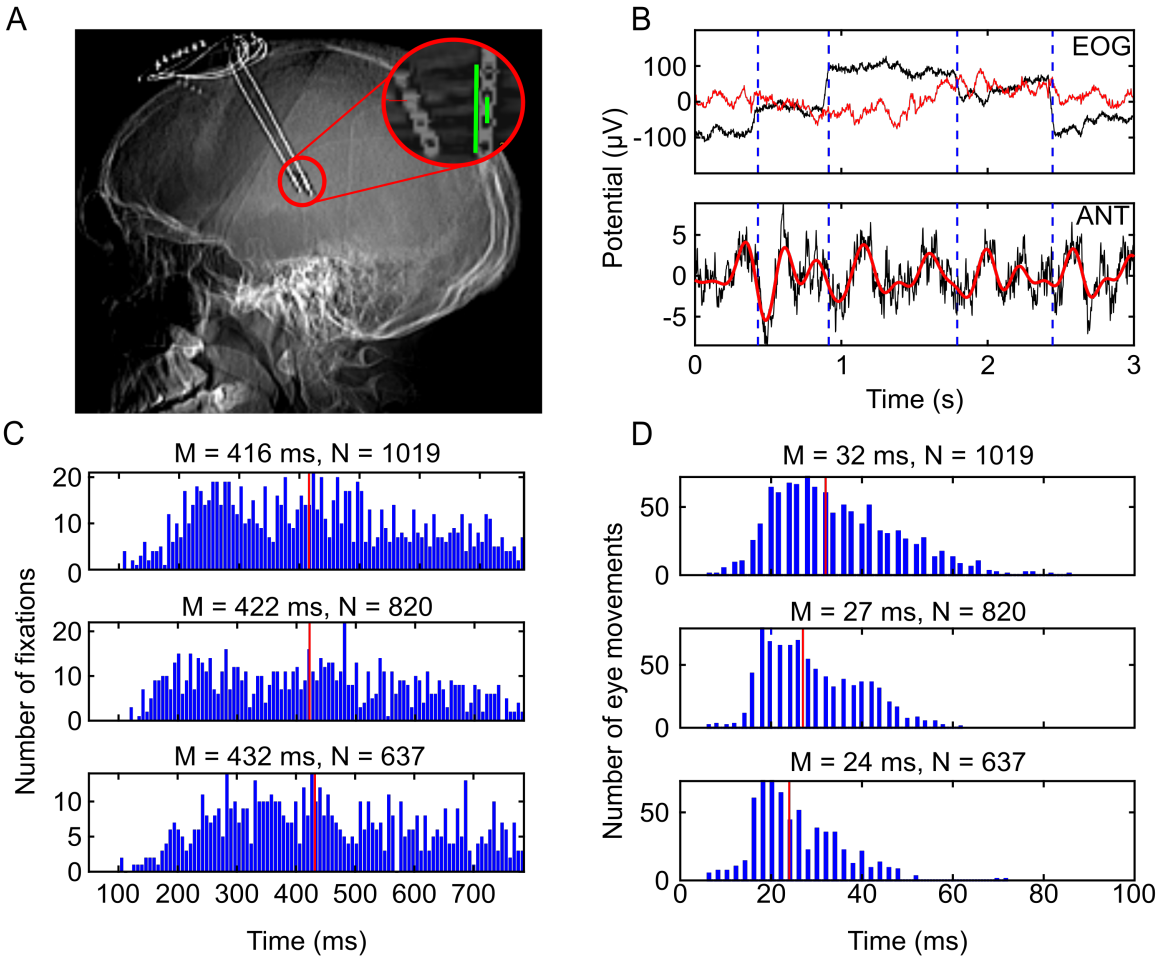

***Figure 1. Implantation trajectory, example field potential trace and behavior**. **(A)** Bilateral leads into the anterior nuclei of the thalamus marked with red in a single patient (4 contacts per side). Inset shows two shafts. Shorter green line depicts inter-contact space of 3 mm (contact height of 1.5 mm with 1.5 mm spacing). Longer line marks the total active span of 10.5 mm **(B)** An example of 3*

seconds long recording trace with signals from EOG (black trace) and Fp1 (red trace). Horizontal dashed lines indicate fixation onset time points (upper panel). The same interval of 3 seconds field potentials from an example site in the ANT. Black trace presents raw signal; red trace shows signal filtered in 2-5 Hz (lower panel). ***(C)*** *Distribution of fixation durations for each of three patients. Vertical red line indicates median duration.* ***(D)*** *Distribution of saccade durations for each of three patients. Vertical red line indicates median duration. Because we used the EOG signal to define time points of fixation and saccade onsets, it is possible that smaller eye movements were not detected (see Limitations).*

First, we tested whether fixation onset-related potentials (FRP) are modulated relative to a surrogate distribution. The surrogates (N=1000) were created by locking intact segments of ANT field potentials to pseudo-fixations (i.e., random time points uniformly distributed across the entire recording session; see Methods). We observed that the magnitude of fixation onset-related potentials departs from the surrogate distribution at multiple time points (permutation test; $p < 0.05$; FDR controlled for multiple comparisons; see Methods). An initial positive deflection around 100 ms before fixation onset was followed by a negative deflection peaking at 40-50 ms after fixation onset and another positive deflection peaking around 160 ms after fixation onset (Figure 2A). We also observed that FRP exceeded the surrogate distribution in 15 out of 18 channels (83%) in each of three patients (6, 5, 4 channels per patients 1-3, respectively).

We observed similar effects when locking analyses to saccade rather than fixation onsets (see Figure 2 E). The magnitude of saccade-related potential (SRP) also differed from the surrogate distribution across multiple time points (permutation test; $p < 0.05$). An initial positive deflection in the SRP peaked around 80 ms before fixation onset followed by a negative deflection 80 ms after fixation onset and another positive going deflection around 200 ms after fixation onset (Figure 2 E). We observed

that SRP exceeded surrogate distribution in 15 out of 18 channels (83%) in each of the three patients (6, 5, 4 channels per patients 1-3, respectively). As expected, locking our analyses to saccade as compared to fixation onset results in temporal shift of potential waveforms of about 25-30 ms, largely corresponding to the duration of eye movements.

Fixation- and saccade-related low frequency phase, power and BHA

Next, we investigated how fixation and saccade onsets influence spectral phase and power in the ANT. To this end, we studied inter-fixation phase coherence, perisaccadic power spectra across a range of low frequencies (1-30 Hz) and BHA power (70-150Hz; see Methods). Overall, we found that fixation-locked phase coherence increased above the 95th surrogate percentile (corresponding to $p < 0.05$; FDR controlled for multiple comparisons) across multiple time and frequency points with strongest effects of phase clustering at 3-4 Hz around 120 ms after fixation onset (see Figure 2B). This effect was evident in 15 out of 18 (83%) channels across all three patients (6, 5, 4 for patients 1-3, respectively). The effects were similar when we time locked analyses to saccade onset. The strongest phase coherence was observed at 3-4 Hz around 150 ms after saccade onset (Figure 2F). Saccade-locked phase clustering was evident in 16 out of 18 (88%) channels across all three patients (6, 6, 4 for patients 1-3, respectively). Despite the appearance of systematic trends, we detected no significant modulation of fixation- or saccade-related spectral power relative to their surrogate distributions (Figure 2C,G). We also found that both saccade- and fixation-locked BHA decreased below the 5th percentile of the surrogate distribution around 40-50 ms after fixation and saccade onset and increased above 95th percentile around 150 ms later (Figure 2 D, H). This effect although sparse was also evident in 4 out of 18 (22%) channels within each of our three patients.

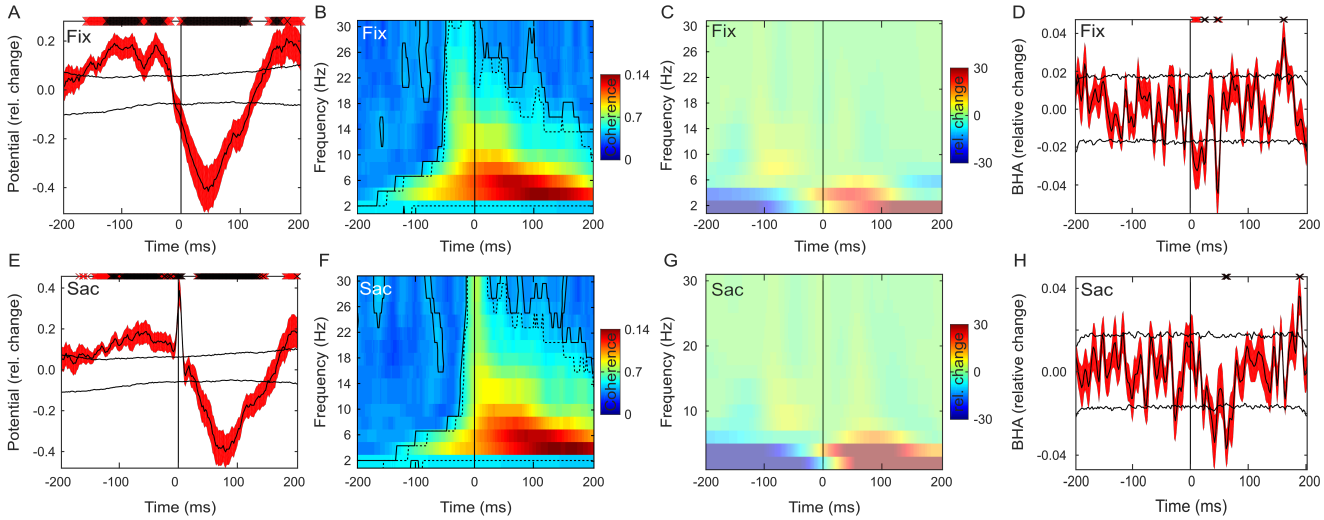

***Figure 2. Fixation- and saccade-related neural activity in human ANT**. **(A, E)** Grand average fixation- (A) and saccade-(E) related field potentials (N=18 ANT channels, 3 patients). Shading reflects standard error of the mean (SEM). Upper and lower black lines reflect 95th and 5th percentile of surrogate distribution (N=1000). Vertical black lines show the point of fixation/saccade onset. Red and black markers above indicate significant time points ($p < 0.05$, $p < 0.001$, respectively). **(B, F)** Color map shows inter-fixation (B) and inter-saccade (F) phase coherence (time on x-axis, frequency on y-axis). Contours depict significant time-frequency points (permutation test $p < 0.05$; $p < 0.001$ solid and dotted lines respectively). Vertical black line indicates fixation/saccade onset. **(C, G)** Color map shows fixation (C) and saccade (G) locked power relative to trial average (time on x-axis, frequency on y-axis). No change from surrogate distribution was detected (permutation test $p < 0.05$). **(D, H)** Fixation- (D) and saccade- (H) locked BHA (70-150Hz). Shading reflects SEM. Upper and lower black lines reflect 95th and 5th percentile of the surrogate distribution (N=1000). Vertical black line indicates fixation/saccade onset. Red and black markers above indicate significant time points ($p < 0.05$, $p < 0.001$, respectively). All results in panels A - H are controlled for multiple comparisons with Benjamini & Hochberg/Yekutieli false discovery rate procedure.*

Potential limitations of this study.

We analyzed data from only three patients. However, this in itself is not a critical limitation, as we have a large number of repeated measures within the individual patients (fixations/saccades: N = 1019, 820, 637) and our results are visible at multiple ANT channels and reproduced in each participant (Figure 3). A more obvious limitation is that while EOG-based eye movement detection provides great temporal precision and high accuracy in detecting large saccades, it is less sensitive to small eye movements. It is therefore possible that the current study underestimates the contribution of shorter saccades (and microsaccades) and over-estimates fixation durations. To ensure that our results are robust across fixation durations, we performed control analyses in which we limited maximum duration of fixation to 600 and 800 ms resulting in distributions with median durations centered at 300 ms or 500 ms (comparable to those known in real life visual exploration; e.g., Hayhoe et al., 2003). Both of these control analyses showed similar results – significant ERP deflection, increased phase coherence, decreased BHA and no detectable effect on power. A second limitation is that under the conditions of this study the EOG does not provide accurate information about the direction of gaze. Thus, while confirming significant saccadic modulation of ANT activity, our study leaves open the question of whether gaze direction is systematically reflected in saccade-related modulation of ANT activity. A final limitation is that we used Fp1 referenced to linked mastoids for detecting vertical part of EOG in patients 1-3 and bipolar EOG 2 - EOG1 in patients 1 and 3 and F7 – F8 in patient 2 for detecting horizontal EOG. EOG signals have been shown to spread across all these channels with varying magnitude (Lins et al., 1993). Despite these slight differences in electrode placement, we find consistent effects and similar eye movement distributions across all three patients, confirming that our results are robust across these variations in electrode position. Overall, there is no reason to think these limitations have a major influence on our main conclusions.

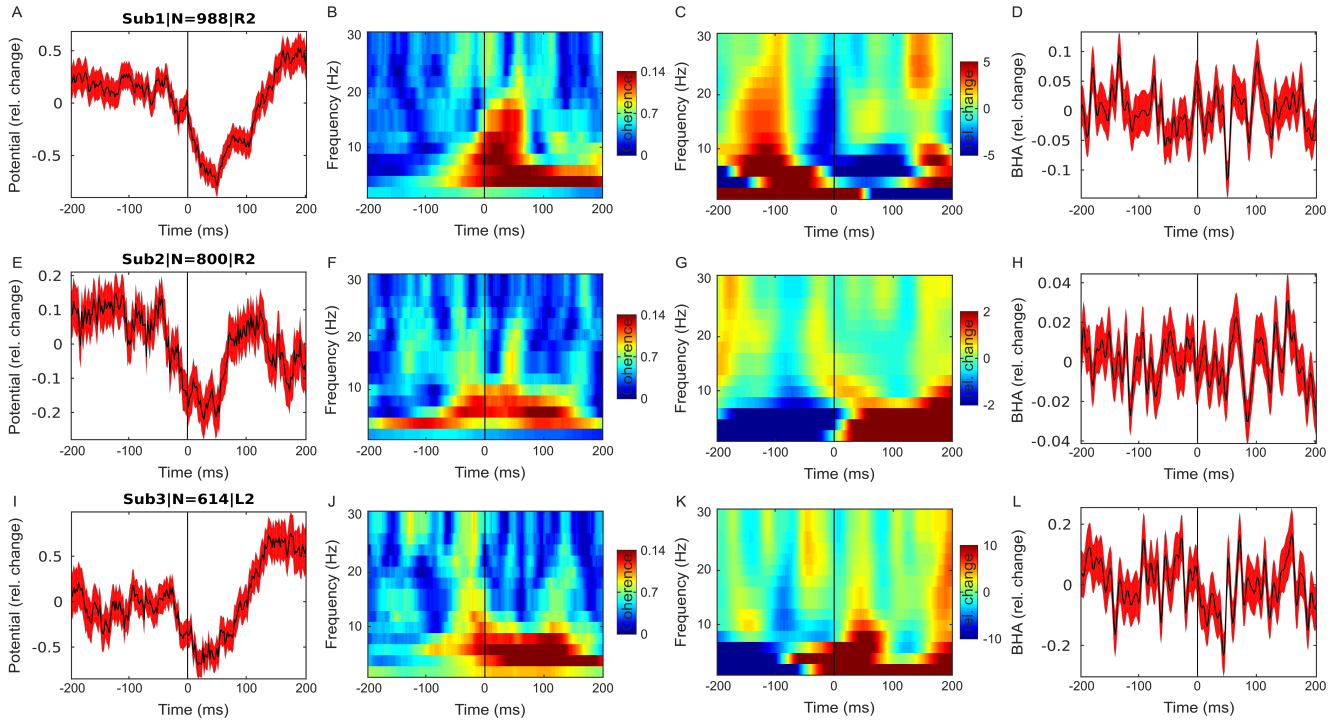

Figure 3. ***Fixation-related neural activity from individual channels in the ANT.***

(A, E, I) *Fixation-related field potentials from individual channels averaged across artifact-free epochs for participants 1-3, respectively. Shading reflects standard error of the mean (SEM). Number of artifact-free trials (N) for participants 1-3 used for the current analyses. Second bipolar channel on the right side (R) and left side (L) is presented. Vertical black lines indicate fixation onset.* ***(B, F, J)*** *Color map shows inter-fixation phase coherence for individual channels in participants 1-3 (time on x-axis, frequency on y-axis).* ***(C, G, K)*** *Color map shows fixation locked power from an individual channel calculated relative to the trial average for participants 1-3 (time on x-axis, frequency on y-axis).* ***(D,H, L)*** *Fixation-locked BHA (70-150Hz) from an individual channel averaged across artifact-free epochs for participants 1-3. Shading reflects SEM.*

Discussion

To evaluate the possible role of the ANT in visual active sensing, we studied neural dynamics surrounding saccades and consequent fixations during unconstrained free viewing, in three epilepsy patients implanted with ANT electrodes for clinical purposes. Comparing pre- and post-fixation measures to surrogate distribution, we found significant saccade-related increases in field potential magnitude and phase coherence, albeit without detectable concomitant changes in low frequency power. Saccade-related BHA, a measure of neuronal processes correlated with neuronal population spiking (Mukamel et al., 2005; Niessing et al., 2005; Nir et al., 2007; Ray et al., 2008; Leszczynski et al., 2019), showed decrease from the surrogate distribution peaking at around 50 ms after fixation onset, and rebound above the surrogate distribution at about 180 ms post-fixation.

Saccade-related phase concentration was strongest around the rate of saccades (3-4 Hz), peaking about 120 ms after fixation onset. The impact of saccades on oscillatory phase coherence in the ANT is consistent with findings from the MTL (Killian et al., 2012; Hoffman et al., 2013; Jutras et al., 2013; Killian et al., 2015; Staudigl et al., 2017; Meister & Buffalo, 2018; Staudigl et al., 2018; Katz et al., 2018; Doucet et al., 2019) and the visual system (Purpura et al., 2003; Rajkai et al., 2008; Bartlett et al., 2011; Ito et al., 2011; Hamamé et al., 2014; Zanos et al., 2015; 2016; Barczak et al., 2019). The dynamics of saccade-related excitability modulation in the ANT, with an initial dip in excitability around fixation onset followed by a later rebound, appear distinct from those reported for V1 (see e.g., Rajkai et al., 2008; Ito et al., 2011; Barczak et al., 2019). For example, Rajkai et al., (2008) observed the strongest suppression of neuronal firing *during* saccade and *before* the onset of fixation, and essentially the same thing was observed by Barczak et al., (2019). Interestingly, dynamics similar to those in the ANT have been noted in higher order visual areas. For example, Zanos et al., (2016) observed bimodal temporal distribution of suppression in V4 neurons, with late suppression being strongest after fixation onset.

What function might the ANT play in it visual active sensing? Although our findings do not directly address this question, the anatomical connections of the ANT provide some clues as to its position in the visual active sensing network. The ANT receive descending inputs from the subiculum and ascending inputs from the mammillary bodies forming a central component of the extended hippocampal–diencephalic system for episodic memory (Vann and Aggleton, 2004). The ANT also have dense reciprocal connections to cingulate areas including the anterior cingulate cortex, which are implicated in top-down cognitive control (for review see Bubb et al., 2017). Studies in non-human primates (Itaya et al., 1986) as well as tree shrews and rats (Conrad and Stumpf, 1975; Itaya et al. 1981) have also identified direct input pathways from the retina and pretectum (Sikes and Vogt, 1987) to the anterodorsal thalamus. Studies in nonhuman primates (Zikopoulos & Barbas, 2006) demonstrate that the many of the anterior thalamic nuclei have reciprocal connections to frontal and prefrontal areas, and through their intrathalamic connections, indirect access to posterior visual areas, placing the ANT within the circuits that could mediate top-down modulation due to both attention and eye movements.

Functional properties of ANT neurons are consistent with a role in the organization of sensing activities. In rodents, neurons in the ANT fire as a function of the animal's head direction (Taube, 1995; Tsanov et al., 2011; for review see Jankowski et al., 2013), providing crucial input during spatial navigation (Winter et al., 2015) by encoding animal's perceived directional heading relative to its environment (Taube, 2007). This is important to the present discussion, as rodents tend to favor head movements over saccades in active sensing. Although vestibular inputs are critical for generating head direction firing, the directional signal appears to also involve the motor system (Taube, 2007). Taube & Burton (1995) showed that preferred direction firing is stable as the animal "actively" moves from one environment to another. However, "passive" transportation of an animal between two environments distorts directional firing and this distortion seems to be independent of the visual input (Stackman et al. 2003; for review see Taube, 2007). Overall then, the interconnectivity patterns of the ANT together

with the functional properties of ANT neurons suggest that the ANT contribute more to top-down control, than to bottom-up input processing in active sensing.

How does mediation of control functions in active sensing fit with other functions that have been attributed to the ANT? The ANT have been proposed to contribute to a range of cognitive functions including learning and memory (Aggleton and Brown, 1999; Warburton et al., 2001; Vann and Aggleton, 2004) as well as attention (Bourbon-Teles et al., 2014; Wright et al., 2015; see also Leszczynski and Staudigl, 2016). Damage to the ANT or its inputs from the mammillary bodies leads to episodic memory deficit observed in Wernicke-Korsakoff and thalamic stroke patients (Kerrigan et al., 2004). Interestingly, along with other cognitive deficits, both Wernicke-Korsakoff and thalamic stroke patients have difficulty in motor sequence programming (Ghika-Schmid and Bogousslavsky, 2000; see also Carrera and Bogousslavsky, 2006). This last may be a key observation, because overt active sensing depends on motor sampling routines - sequences of movements by the eyes, whiskers, head, hands and breathing musculature. In an active sensing framework, these motor sequences imbue individual's sampling strategy with momentary predictions and allow to transcribe the sensory world into a set of neural representations that the brain can use to generate perception and to guide further adaptive behavioral routines (Ahissar and Arieli, 2001; Szwed et al., 2003; Kleinfeld et al., 2006; Schroeder et al., 2010; Leszczynski and Schroeder, 2019).

Methods

Participants. Depth field potentials along with the surface EEG were recorded from 3 pharmacoresistant epilepsy patients (age range from 22 to 52, 2 male and 1 female) implanted with electrodes targeted to the anterior nucleus of the thalamus for treatment of epilepsy. Recordings were performed at the Department of Epileptology, University of Bonn, Germany. The study was approved

by the Ethics Committee of the University of Bonn Medical Center and all patients gave written informed consent.

Electrophysiological recordings. The data were recorded using bilaterally implanted multi-contact (4 channels per shaft) depth electrodes and simultaneous scalp surface EEG electrodes (Fp1, Fp2, F3, F4, C3, C4, 'P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Cz, Fz, Pz, T1, T2, Cb1, Cb2) in patients 2 and additionally EOG1, EOG2 in patients 1 and 3 placed according to the 10-20 system. The depth electrodes' contacts (Medtronic 3387) were of 1.5 mm height with an inter-contact center-to-center spacing of 3 mm. All data were sampled at 1kHz, on-line band pass filtered between 0.01Hz (6dB/octave) and 300Hz (6dB/octave), off-line down-sampled to 500Hz. The ANT depth channels were re-referenced to its neighbor using bipolar montage to increase local specificity of the signal. This results in 3 bipolar pairs per subject per side. In total we analyzed 18 bipolar pairs (3 pairs on shaft x 2 sides x 3 subjects). The data consist of continuous 1 hour long unconstrained recordings during which participants performed various cognitive tasks involving presentation of visual stimuli on a laptop computer, interacted with experimentators and members of the hospital staff.

Data analyses. All data were processed offline using Fieldtrip toolbox (Oostenveld et al., 2011) and MATLAB (MathWorks). Pre-processing was performed at single electrode level. Continuous data were down-sampled to 500Hz. To remove line noise we used butterworth filter (4th order) at 50 Hz, 100 Hz, 150 Hz. Next, we created bipolar montage to maximize spatial specificity of the signal and also to decrease common noise and contributions from distant sources through volume conduction. To this end, we subtracted signals from neighboring contacts on the electrode (i.e., ANTR0 – ANTR1, ANTR1 – ANTR2, ANTR2 – ANTR3 for right side contacts and ANTL0 – ANTL1, ANTL1 – ANTL2, ANTL2 – ANTL3 for left side contacts, respectively). ANTR0 is the deepest contact on the right shaft. Next, to calculate Broadband High-frequency Activity (BHA), we band-pass filtered (70 - 150 Hz) and hilbert-

transformed continuous data. The complex-valued signal was then rectified and squared to extract power of the BHA. Low frequency activity (1-30Hz) was extracted from continuous data with 3 cycles Wavelets.

Next, we used scalp channels to create continuous signal maximizing vertical and horizontal component of the EOG. To this end, we used Fp1 channel (referenced to linked mastoids) for vertical component in all three patients and bipolar EOG2-EOG1 for patients 1 and 3 as well as F7-F8 for patient 2. Selection was based on channel availability per patient and known scalp distribution of the EOG gradient (Lins et al., 1993). To define fixation and saccade onsets, we used a probabilistic algorithm for detection of EOG events (Toivanen et al., 2015) which has been shown to achieve very high sensitivity and precision for detecting saccades and fixations - over 96% for saccade larger than 4.3 degrees of visual angle and over 90% for saccades larger or than 2.9 degrees of the visual angle; see Toivanen et al., 2015). We used initial 20 % of data (i.e., 12 minutes) for unsupervised training period which is required by the algorithm. The eye events were than detected in remaining 80% of data (48 minutes) which entered further analyses. We detected 1959, 1868 and 1635 number of eye events for patients 1-3, respectively.

Continuous BHA, complex-valued time-frequency series and raw field potentials were segmented into 400 ms long non-overlapping windows relative to each eye event (saccade and fixation) with 200 ms before and 200 ms after each event. For further analyses we only considered fixations that were not preceded or followed by another fixation within the +/-200ms window of interest. Based on previous studies we further constrained fixation durations to last below 800 ms (e.g., Hayhoe et al., 2003). We reasoned that longer fixations were likely spurious due to intervening small saccades that were undetected with the current setup. This resulted in 1019, 820, 637 epochs per patients 1-3, respectively. We defined epochs containing artifacts as these with gradient of field potential exceeded 5 standard deviation of the trial mean. On average (across patients) this criterion marked about 3% of epochs as containing artifacts. These segments were removed from further analyses. Phase locking

value was used to quantify phase coherence in each time-frequency point. To this end, we used segmented complex-valued signal and previously described formula (Lachaux et al., 1999) with the following Matlab implementation:

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PLV = abs(mean(exp(1i * angle(complex-valued signal))
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We tested whether fixation- and saccade-locked field potentials, BHA, PLV or power in frequencies 1-30 Hz differed from what would be expected by chance. To test this, we created surrogate distributions (N = 1000 permutations) for each of the signals of interest (i.e., field potentials, BHA. PLV, power). The surrogate distributions for field potentials, BHA, PLV and power were created by locking intact segments of ANT signals to pseudo-events (i.e., random time points uniformly distributed across the entire recording session). For each permutation we randomly selected “pseudo-events” - these were random time points from our 1 hour long recording session which matched the number of eye events. Next, we created surrogate data segments by extracting 400 ms time epochs around each “pseudo-event”. We used the same procedure of artifact rejection to remove artifacts from our surrogate distribution as we did from our empirical data. Next, each empirical signal (fixation-/saccade-onset locked field potential, PLV, BHA, power) was tested against its surrogate distribution with significance threshold set to 5th and 95th percentile (corresponding to $p < 0.05$). We used False Discovery Rate (FDR) correction for multiple comparisons across time (field potentials, BHA) and time-frequency (PLV, power; Benjamini and Hochberg, 1995).

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Author Contributions

ML and CES designed the study. ML and LC collected the data. ML performed analyses. ML, CES and TS wrote the manuscript. All authors contributed to the discussion and interpretation of findings, and edited the manuscript.

Declaration of Interests

The authors declare no competing interests.

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