Short communication

Stimulus-induced gamma activity in the electrocorticogram of freely moving rats: The neuronal signature of novelty detection

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ABSTRACT

To investigate the cortical activity pattern associated with the exploration and identification of a novel object we recorded the intracranial electrocorticogram (ECoG) in the barrel cortex of freely moving adult rats using wireless technology. We report here that the exploration and detection of a novel object correlate with a transient increase of synchronized oscillatory activity in the 40–47 Hz frequency band. This specific cortical activity pattern occurs 200–300 ms after the first sensory contact with the novel stimulus and decreases in power in the subsequent recording sessions with the same object. During the first explorative session the increase in 40–47 Hz is associated with a simultaneous decrease in the 30–37 Hz band, which increased to a stable level already after one session. Our results indicate that synchronized gamma activities in primary sensory cortex may represent the neuronal signature for the detection of a novel object.

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The gamma rhythm (30–80 Hz) is selectively enhanced in different brain areas during perception tasks [5,18,22–24] and involved in neuronal processes such as attention, learning and memory [5,9,10]. It has been further proposed that synchronized neuronal firing in the gamma frequency range may be crucial to produce a coherent object representation [5,19] and gamma as well as beta oscillatory activity accompanies the presentation of a novel auditory stimulus in the human electroencephalogram (EEG) [7]. Furthermore, it has been shown in human auditory target detection tasks that novel sounds elicited a scalp recorded potential that peaked around 200–300 ms after the presentation of the target, the so-called “novelty P3” [17]. This novelty-related activity is larger over the central and frontal areas and has been observed in many different species [25,26]. In addition, in a visual detection task a relationship between the firing rate of prefrontal cortical neurons and the presentation of a novel object has been documented in primates [16]. These observations indicate that distinct oscillatory activity patterns correlate with the detection and perception of a novel object. It has been recently demonstrated in freely moving mice that beta2 oscillations (23–30 Hz) recorded in the hippocampus are transiently and selectively increased during the exploration of a novel environment [4]. These novelty-evoked oscillations only occurred when the mice were actively moving through the novel environment. Although functional studies on neocortical activity patterns in similar behavioural conditions are still missing, structural data indicate that the cerebral cortex may be also specifically activated during exploratory behaviour in a novel environment. In the somatosensory cortex of freely exploring rodents immunocytochemical studies revealed a prominent and highly specific increase in the expression of inducible transcription factors, such as c-fos, after a single exploration in a novel environment [14,20]. However, so far no experimental study, neither in humans nor in animals, addressed the question which large-scale neuronal network activity in the cerebral cortex may be correlated with the exploration and detection of a novel object. To address this question, we used our telemetric recording system [13], which allows electrocorticogram (ECoG) recordings from unrestrained freely moving rats under video control during an explorative task. Wireless technology has been shown to minimize the stress artefacts unavoidable in conventional in vivo electrophysiological recordings [11]. Therefore telemetric recordings represent a more appropriate technique to record neuronal activity during natural explorative behaviour.

All experiments were conducted in accordance with the national and European (86/609/EEC) laws for the use of animals in research and were approved by the local ethical committee (Landesuntersuchungsamt Koblenz, 23 1 77-07/G07-1-001). Five Male Wistar rats weighing 300–400g were used for this study. The animals were housed individually in standard plastic cages (42 cm × 26 cm × 20 cm) under a 12 h light-dark cycle (lights on at 7 a.m.). The room temperature was maintained at 21 ± 2 °C and relative humidity at 50 ± 5%. Standard rodent food and tap water were available ad libitum. The animals were handled for 2 days
by the experimenter who would perform the recordings. After this period the animals were placed two times 10 min/day (respectively between 09:00–11:00 and 14:00–16:00) for 4 days in an open field (60 cm × 70 cm) with one “training object” (a metal cube, Supplementary Fig. 1a) always positioned at the same location near the wall. All behavioural experiments were performed under infrared light emitting diodes in an isolated room and everything was cleaned between trials with 0.1% acetic acid.

The surgical method and the impact of the implanted system on the behaviour have been described by us in detail previously [13]. Briefly, the animals were deeply anaesthetised with chloralhydrate, a transmitter was placed in the abdominal cavity and wires were slipped between muscles and skin up to the head. The wires were soldered to three stainless steel screws (0.5 mm diameter). The recording electrode was placed in contact with the dura above the barrel cortex (L = Bregma + 5.5 mm, AP = Bregma − 2.3 mm) [15], the reference and the ground electrodes were placed in contact with the dura above the cerebellum (L = Bregma + 2 mm, AP = Bregma − 11.5 mm and L = Bregma − 1.5 mm, AP = Bregma + 11.5 mm, respectively). This assembling was fixed with grip cement (Dentsply Caulk International, Milford, USA). Both incision sites were closed using 4–0 Resolon (Resorba, Nürnberg, Germany). Surgery lasted a maximum of 3 h from induction of anaesthesia.

After surgery, a recovery period of 5 days was given to the animals before starting the first recording session, corresponding to the time needed to gain the pre-surgical weight. ECoG signal (recorded continuously at a sampling rate of 1000 Hz) and video data (25 frames/s, 720 × 576 pixels) were collected simultaneously and stored on a personal computer via CED and Spike2 software (Cambridge Electronic Design, Cambridge, England). In order to define the whisker-object contacts a CCD camera with progressive-scan sensor (JAI M105X-C, Stemmer Imaging, Germany) was used with a fixed shutter-speed (1/250 s) to record 25 high-resolution pictures per second. The rats were placed for 2 days in the open field two times for 10 min/day with the “training object” at the same place as before (first session always between 09:00 and 11:00 and second session between 14:00 and 16:00) (Supplementary Fig. 1a and b). In the following 2 days the object was substituted by a “new object” before a new object exchange. The objects were chosen to be as different as possible to each other and to the objects the animals were exposed in the standard animal facility. Each rat was recorded 120 min in total corresponding to 40 min per object.

A video analysis was then performed to define 1 exploration trials starting every time the animal moved toward the object and touched the object with the vibrissae contralateral to the cortical recording site. The eight successive recording sessions with the two new objects (four per object) were analysed for each animal, whereas the four recording sessions with the “training object”, were not considered for this study (Supplementary Fig. 1b). These 8 sessions were separated into 2 groups: the first session for each of the 2 new objects were averaged, pooled together in the “novel condition” (n = 2 sessions per animal) and the 3 following sessions for each of the 2 objects in the “familiar condition” (n = 6 sessions per animal). Trials with ECoG artefacts were rejected. Gamma oscillations were then analysed on 5.6 ± 0.4 contacts per 10 min session (from a total average of 12.8 ± 0.7 contacts for all sessions and animals). The data were imported to MatLab (MatLab 7, The MathWorks Inc., Natick, USA) and further data analysis has been described in detail previously [12,18]. Briefly, the signal was band-pass filtered (20–80 Hz) using a Butterworth 3rd order filter and a Hilbert transform was applied on each trial followed by a pseudo-Wigner-Ville transform (time–frequency toolbox, http://tfb.nongnu.org). The resulting time–frequency maps were normalized (using maximum and minimum peaks for each map) and averaged over trials (n = 63 and 156 trials for the novel and familiar conditions, respectively) and animals (n = 5). Further statistical analyses were performed in 5 Hz frequency bands that were extracted from these maps with an overlap of 2.5 Hz. P values were calculated with parametric unpaired samples t-tests (Systat Version 10, Systat Software, Erkrath, Germany) after testing the Gaussian distribution of the time–frequency relative power samples. After analysing all frequencies in the complete gamma band, only the bands showing significant differences between novel and familiar conditions were taken into account and further analysed session by session. P values were then calculated with a Dunnnett’s multiple comparison tests after testing the Gaussian distribution of the samples and calculating a one-way ANOVA.

The total time spent on the objects during the first and second session as well as the number of object explorations, defined as a movement toward the object followed by whiskers contact, were calculated as a measurement of novelty detection [6] and level of exploratory activity, respectively. P values were calculated with pairwise test after testing the Gaussian distribution of the samples. Values throughout this report are given as mean ± S.E.M.

It has been previously documented that rats spend significantly more time in exploring a new object as compared to a familiar one [21]. Therefore we measured the total time spent by the animals exploring the new object during the first two experimental sessions. The exploration time spent during the first session amounted to 51.6 ± 11.2 s (n = 10 sessions) and was significantly (P = 0.0314) longer as compared to the second session recorded 5 h later (31.1 ± 4.4 s). This result could not be explained by a reduction of the overall activity during the second session, since the animals presented a similar exploratory activity during the first (11.7 ± 1 exploration occurrences) and the second (12.6 ± 1.2 exploration occurrences) session. These behavioural data indicate that the animals perceived the object as novel only during the first session.

The averaged time–frequency maps revealed prominent differences in the ECoG activity during exploration of a novel versus a familiar object in the first 500 ms (see Fig. 1). We could distinguish one distinct activation period 200–300 ms after the initial contact of the whiskers with the novel object. The relative power of each frequency in the ECoG during this time window displayed two major differences between explorations of a novel versus a...
Fig. 2. Statistical analyses of the novel object-related gamma peak in the 40–47 Hz frequency band. This band frequency was one of the only two bands showing significant differences between novel and familiar conditions after testing the broadband gamma range. (a) The time courses of the averaged relative power of the 40–47 Hz band for the novel (n = 63 trials) and familiar (n = 156 trials) condition are plotted (50 points smooth) from 250 ms before to 500 ms after the first contact with the object. (b) The time courses are then plotted for the duration of 500 ms after the contact with S.E.M. for each ms. One distinct peak in the novel condition is observed with a significantly higher power between 220 and 285 ms (grey rectangle) after the first contact of the whiskers with the object. c) The relative power of the band frequency is first compared between novel (n = 63 trials) and familiar (n = 156 trials) conditions using an unpaired t-test (upper histogram). The familiar condition was then decomposed in the different sessions (lower histogram), every bar corresponding to the average of 2 recording sessions (one per object; session 1 = 63, session 2 = 50, session 3 = 55 and session 4 = 51 trials) in five recorded animals and P values were calculated with a Dunnett’s multiple comparison test (\(P < 0.05\), \(**P < 0.01\), \(***P < 0.001\))

Fig. 3. Raw and filtered ECoG traces after contact of the whiskers with a novel object. Three 500 ms ECoG traces are displayed corresponding to three successive contacts performed by the same animal during one session with a novel object. For each trial the filtered trace between 40 and 47 Hz using a Butterworth 3rd order filter is shown below. Induced oscillations in the gamma range can be observed between 200 and 400 ms after the first contact with the novel object (grey rectangles).

familiar object. The first one is a peak at \(\sim 45\) Hz specific to the novel condition (Fig. 1a). After analysing in detail all frequencies in the complete 20–80 Hz frequency range we noticed that this activity was restricted to a relatively narrow gamma frequency band between 40 and 47 Hz (see Fig. 2a and b for the time course). This activity with a maximum frequency of \(43.3 \pm 0.26\) Hz (n = 63 contacts) peaked at \(\sim 255\) ms after the first contact of the whiskers with the novel object and was highly specific to the novel condition (\(P = 0.0084\)) (Fig. 2c, Supplementary video 1 and 2). The analysis of this band during the successive recording sessions revealed that this response slightly, but not significantly, decreased during the second session and significantly declined in the subsequent two sessions (between 220 and 285 ms; Fig. 2c). This induced synchronized activity could be seen in the filtered 500 ms raw signal (Fig. 3) to consist of at least five cycles. This activity was accompanied by a decrease in the low gamma range (Fig. 1), which was more precisely a general decrease of the 30–37 Hz band during the first 400 ms (Fig. 4a and b) with a robust and significant (\(P = 0.0007\)) decrease in the relative power between 200 and 290 ms (34.6 \(\pm 0.25\) Hz peaked at \(\sim 254\) ms, n = 63 contacts) when compared to the familiar condition (n = 156 contacts) (Fig. 4c). This activity significantly increased immediately during the second session and remained stable in the two subsequent sessions.

The novel object related increase in the 40–47 Hz and decrease in the 30–37 Hz bands could be only observed for the first session with the new object and were independent of the interval between the four successive recording sessions. These data indicate a strong relationship between these two neocortical activity patterns associated with the detection of a novel object.

To our knowledge this is the first report demonstrating that the detection of a novel object during a free explorative task can be clearly associated with a highly specific neocortical activity pattern. Our results indicate that the detection of a novel object is accompanied by a rapid and transient synchronized increase of the gamma activity (40–47 Hz) in rodent primary sensory cortex. This network activity may represent the optimal oscillatory pattern for the propagation and storage of the new information in memory-related comparing each session to the first one (novel condition) after calculating a one-way ANOVA. The observed response slightly, but not significantly, decreased during the second session and significantly declined in the subsequent two sessions.
circuit as the hippocampus. A latency of ∼200 ms after the first sensory contact as well as the frequency range of this cortical pattern correspond well to human neocortical EEG activity and event-related potentials in response to a novel auditory stimulus [1,7,17]. It corresponds also to activity patterns with comparable latencies in visual perception tasks in humans [3,10,18,22–24]. These data indicate that the gamma activity at 200–300 ms corresponds most likely to the period of object perception (for review [5]). Already during this early recognition phase a novel object is differentiated from a familiar one, suggesting that memory-related circuits such as the prefrontal-perirhinal cortices, shown to be involved in recognition memory [2,16], are co-activated. In addition, the burst of activity described here is well suited to induce plastic and long-lasting modifications in neuronal circuits [8]. In our experiments, the 40–47 Hz burst activity is already replaced after one session by a 30–37 Hz band, which may correspond to the network activity associated with the memorized object.

Our present work provides further evidence that neuronal network activity in the gamma frequency range plays an important role in the neocortical processing of sensory stimuli and in higher cognitive function. Previous reports elucidated the role of gamma activity in the processing and perception of visual stimuli (for review Singer et al. [19]; Tallon-Baudry and Bertrand [22]), but their contribution in the processing of tactile stimuli in the somatosensory cortex was not exactly known. Our results indicate that the broadband gamma activity between 30 and 80 Hz most likely contains relatively narrow band frequencies involved in different behavioural tasks and distinct cognitive operations.

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**Author contributions:** D.L. designed and conducted the experimental studies, analysed the data and wrote the paper. J.B. developed and provided the telemetric recording systems. H.J.L. supervised all parts of the study and wrote the paper.

**Appendix A. Supplementary data**


**References**


