SPIKE–WAVE DISCHARGES: ABSENCE OR NOT, A COMMON FINDING IN COMMON LABORATORY RATS

Behavioral Detection of Tactile Stimuli during 7-12 Hz Cortical Oscillations in Awake Rats

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Prominent 7- to 12-Hz oscillations in the primary somatosensory cortex (S1) of awake but immobile rats might represent a seizure-like state (1) in which neuronal burst firing renders animals unresponsive to incoming tactile stimuli; others have proposed (2–4) that these oscillations are analogous to human μ rhythm (5–7). To test whether rats can respond to tactile stimuli during 7- to 12-Hz oscillatory activity, we trained head-immobilized awake animals to indicate whether they could detect the occurrence of transient whisker deflections while we recorded local field potentials (LFPs) from microelectrode arrays implanted bilaterally in the S1 whisker representation area. They responded rapidly and reliably, suggesting that this brain rhythm represents normal physiologic activity that does not preclude perception.

COMMENTARY

Animal modeling of absence seizures has been conducted in numerous studies. The defining EEG event in these models is a generalized spike–wave discharge (SWD), recorded variably at 7–12 Hz. During the many years' use of SWDs as a model of absence seizures, a persistent debate has existed regarding whether these discharges truly represent ictal events, during which the animal's level of consciousness is markedly impaired, or simply a rhythmic physiologic discharge (1,2) that does not preclude normal perceptive abilities.

This fundamental question was addressed in an imaginative study by Wiest and Nicolelis. The authors tested the hypothesis that trained rats could discern a tactile stimulus during a SWD and respond to it to obtain a learned reward. They elegantly demonstrated that the animals were not only able to discern small whisker deflections and respond rapidly, by licking for a liquid reward, but that the tactile stimulus or initiation of the licking movement coincided with desynchronizing the SWD. This provocative result indicated that perception was retained during SWDs and is qualitatively similar to the findings reported in a recent study assessing auditory information processing during SWDs (3), reviewed previously in this journal (4).

Because of the importance of the basic issues raised by the present study, a brief review is offered of the behavioral characteristics associated with SWDs and the numerous rat strains that demonstrate them. In general, SWDs are episodes of abrupt onset, variable duration (seconds to minutes), and abrupt termination, which usually occur during passive wakefulness and light sleep (5,6). The episodes are characterized by decreased responsiveness (behavioral arrest), with or without rhythmic whisker twitching (6,7). Additional behavioral features that may accompany SWDs include accelerated breathing, head tilt, eye twitching (5), as well as head and neck twitching associated with gradual head lowering (8). SWDs can be seen in both inbred and outbred rat strains. Wistar-derived inbred strains include GAERS (genetic absence epilepsy rats from Strasbourg) and WAG/Rij (Wistar Albino Glaxo strain, bred in Rijswijk, Netherlands). Wistar-unrelated inbred strains include Fischer 344, Brown Norway, and dark agouti (5,6,9). Common outbred strains include Sprague-Dawley, Wistar, and Long-Evans (1,6–8).

In their study, Wiest and Nicolelis present examples of 7- to 8-Hz SWDs recorded as local field potentials by microelectrode arrays positioned in the primary somatosensory cortex (S1) of Long-Evans rats; however, they avoid the use of the term "spike–wave discharges," electing to describe the discharges as cortical "oscillations." The difference in terminology does not appear to be semantic because the authors conclude that 7- to 12-Hz oscillations define a nonepileptic state in outbred rats and are a functional analog of the physiologic mu rhythm observed in humans. However, human mu rhythm is a suppressible rhythmical alpha discharge, not a SWD. In support of the idea that the "oscillations" do not represent ictal activity, the authors draw on the common distinction made between nonepileptic rat strains and those made epileptic with SWDs by successive inbreeding (e.g., GAERS and WAG/Rij). This distinction may be more apparent than real. Although the GAERS and WAG/Rij strains demonstrate a high rate of SWDs, often of long duration (5,10), the discharges and associated behavioral semiology can be virtually indistinguishable from that demonstrated by nonepileptic strains, including Sprague-Dawley (11,12), F344 (11), and the authors' own Long-Evans strain. The widespread prevalence of SWDs in common laboratory rat strains has become increasingly recognized by the availability and increased use of long-term digital video-EEG recording systems applied to rodent models. The apparent ubiquity of these discharges begs the question of whether SWDs can truly be a distinguishing marker of epileptic versus nonepileptic animal strains.

An important point raised by Stafstrom (4) with regard to clinical absence seizures is the potential variability of cognitive impairment experienced by a given patient from one absence seizure to the next. If this premise is accepted, then the experimental results demonstrated in the present study and by Drinkenburg et al. (3) support, rather than contradict, the validity of SWDs as a reasonable model of absence seizures. Regardless, the careful and beautifully crafted work of Wiest and Nicolelis has advanced our knowledge of these EEG phenomena and may spawn more imaginative clinical testing to improve our understanding of cognitive capacities and their underlying mechanisms during absence seizures.

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References

1. Semba K, Szechtmann H, Komisaruk BR. Synchrony among rhythmical facial tremor, neocortical "alpha" waves, and thalamic non-sensory neuronal bursts in intact awake rats. Brain Res 1980;195:281–298.
2. Kaplan BJ. The epileptic nature of rodent electrocortical spiking is still unproven. Exp Neurol 1985;88:425–436.
3. Drinkenburg WH, Schuurmans ML, Coenen AM, Vossen JM, van Luijtelaar EL. Ictal stimulus processing during spike-wave discharges in genetic epileptic rats. Behav Brain Res 2003;143:141–146.
4. Stafstrom CE. Information processing during spike-wave seizures. Epilepsy Curr 2004;4:15–16.
5. Coenen AML, Drinkenburg WHIM, Inoue M, van Luijtelaar ELJM. Genetic models of absence epilepsy, with emphasis on the WAG/Rij strain of rats. Epilepsy Res 1992;12:75–87.
6. Willoughby JO, Mackenzie L. Nonconvulsive electrocorticographic paroxysms (absence epilepsy) in rat strains. Lab Anim Sci 1992;12:75–86.
7. Buzsaki G, Laszlovsky I, Lajthma A, Vadasz C. Spike-and-wave neocortical patterns in rats: genetic and aminergic control. Neuroscience 1990;38:323–333.
8. Vergnes M, Marescaux C, Micheletti G, et al. Spontaneous paroxysmal electroclinical patterns in rat: a model of generalized nonconvulsive epilepsy. Neurosci Lett 1982;33:97–101.
9. van Luijtelaar ELJM, Coenen AML. Two types of electrocortical paroxysms in an inbred strain of rats. Neurosci Lett 1986;70:393–397.
10. Rudolf G, Bihoreau MT, Godfrey RF, Wilder SP, Cox RD, Lathrop M, Marescaux C, Gauguier D. Polygenic control of idiopathic generalized epilepsy phenotypes in the genetic absence rats from Strasbourg (GAERS). Epilepsia 2004;45:301–308.
11. Kelly KM, Kharlamov A, Hentosz TM, Kharlamov EA, Williamson JM, Bertram EH, Kapur J, Armstrong DM. Photothrombotic brain infarction results in seizure activity in aging Fischer 344 and Sprague Dawley rats. Epilepsy Res 2001;47:189–203.
12. Kharlamov EA, Jukkola PI, Schmitt KL, Kelly KM. Electrobehavioral characteristics of epileptic rats following photothrombotic brain infarction. Epilepsy Res 2003;56:185–203.