

## INFORMATION PROCESSING DURING SPIKE–WAVE DISCHARGES

### Ictal Stimulus Processing During Spike–Wave Discharges in Genetic Epileptic Rats

Drinkenburg WH, Schuurmans ML, Coenen AM, Vossen JM, van Luijtelaar EL

Behav Brain Res 2003;143:141–146

In the present experiment, we investigated whether and to what extent auditory information processing is possible during the presence of spike–wave discharges in rats. To that end, WAG/Rij rats, which are an animal model for absence epilepsy, were provided with cortical electrodes for the registration of the electroencephalogram (EEG). The animals were first trained in an appetitemotivated conditioning paradigm to learn to discriminate between two auditory stimuli with equal duration and frequency but with different intensities. Next, the stimuli were presented in the test phase in pseudo-random order during spike–wave discharges. The reactivity of the ongoing EEG was analyzed. It was found that the presentation of the reinforced stimulus induced a larger number of aborted spike–wave discharges than that of the nonreinforced stimulus, regardless of the intensity of the stimuli. This implies that during generalized spike–wave discharges, the brain is still capable of evaluating the meaning of an ictally presented stimulus. It also shows that sensory, attentional, and mnemonic processes are at least partially intact during the occurrence of a spike–wave discharge. The results of the present study are largely in agreement with results on human spike–wave activity–related cognitive disturbances. Moreover, they may lead to a refinement of the concept of epileptic consciousness and may emphasize the heuristic value of rodent models for studying both ictal and interictal information processing.

### COMMENTARY

Absence seizures are operationally defined as episodes in which a patient's responsiveness is reduced during a run of spike–wave discharges. Clinical experience suggests that in

patients with primary generalized seizures, such as absence seizures, impairments are variable—a given patient may be partially responsive during some seizures and not at all aware or able to respond during other seizures. During runs of spike–wave discharges that underlie the clinical changes of absence seizures, is responsiveness totally impaired, or are only certain aspects of cognition reduced (e.g., ability to attend, estimate time, process sensory information)? Finally, does the degree of responsiveness depend on the type, extent, or duration of the discharge?

These and similar questions have been examined in both humans and animal models. Many previous studies have been flawed, in that the ability of a subject to respond was judged by a motor response, adding another layer of uncertainty as to whether cognition is purely affected.

This article approaches the question of ictal information processing by using the rat strain WAG/Rij, which displays spontaneous absence seizures accompanied by spike–wave discharges recorded in the cortical electroencephalogram (EEG). These seizures are considered a model of human absence epilepsy. Previous studies have shown that the rats are normal interictally, but during their spontaneous spike–wave discharges, sensory processing is altered, as assessed by auditory evoked potentials (1). In the present study, the investigators developed a paradigm in which EEG reactivity during spontaneous spike–wave discharges could be assessed directly (without an accompanying motor action) in response to reinforced (learned) or nonreinforced auditory stimuli.

Drinkenburg et al. trained rats by presenting two auditory stimuli that were identical in frequency and duration but differed in intensity (18 dB or 30 dB; that is, low “L” or high “H” intensity, respectively). Each rat was trained to receive a food reinforcement for either a L or H stimulus, but not for the other stimulus. Therefore rats were grouped into those that got a food reinforcement with a loud but not soft stimulus (H+/L–) and those that got the converse (H–/L+).

The authors then monitored the rats during EEG recording. When spontaneous spike–wave activity began on the EEG, an H or L stimulus was presented to the rat through loudspeakers, in a pseudo-random order, to see whether the stimulus affected the ongoing discharge. EEG reactivity to the stimulus was categorized as either “aborted” (the spike–wave discharge ceased within 0.5 seconds of the auditory stimulus) or “nonaborted”

(no change of resumption of the spike–wave discharge within 1 second of the stimulus). It was found that nearly 77% of all previously reinforced stimulus presentations aborted ongoing spike–wave discharges, whereas only 34.5% of previously non-reinforced stimuli were aborted. That is, rats were able to process (and respond to) two auditory stimuli that differed only in intensity, even during an absence seizure. This finding is highly significant. The results held regardless of whether the reinforced stimulus was H or L, suggesting that it was not just stimulus volume that “aroused” the rat during the spike–wave discharge. The authors conclude that rats can discriminate between two auditory stimuli of different intensities during ictal spike–wave discharges.

These intriguing results suggest that some information processing does occur during spike–wave discharges, at least in WAG/Rij rats. The mechanism underlying this ability to discriminate is not clear. Presumably, spike–wave discharges in these rats involve corticothalamic circuits, as in humans. The results cannot be explained as a simple effect on arousal, because a reinforced stimulus of either intensity was equally ef-

fective in aborting the spike–wave discharge, depending on the stimulus intensity on which the rat was trained. The detailed relation of sleep–wake cycle to these results requires further exploration.

Nevertheless, these results have implications for human absence epilepsy as well. In the human disorder, variability exists in cognitive responses, depending on some known factors (e.g., discharge duration) but mostly on unknown factors. This model offers the opportunity to explore ictal-related information processing in great detail, with the hope of better understanding the ictal deficits in humans as well.

by *Carl E. Stafstrom, M.D., Ph.D.*

## Reference

1. Meeren HK, van Cappellen van Walsum AM, van Luijtelaar EL, Coenen AM. Auditory evoked potentials from auditory cortex, medial geniculate nucleus, and inferior colliculus during sleep-wake states and spike-wave discharges in the WAG/Rij rat. *Brain Res* 2001;898:321–331.