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A Prospective Study of Loss of Consciousness in Epilepsy Using Virtual Reality Driving Simulation and Other Video Games

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Abstract

Patients with epilepsy are at risk of traffic accidents when they have seizures while driving. However, driving is an essential part of normal daily life in many communities, and depriving patients of driving privileges can have profound consequences for their economic and social well being. In the current study, we collected ictal performance data from a driving simulator and two other video games in patients undergoing continuous video/EEG monitoring. We captured 22 seizures in 13 patients and found that driving impairment during seizures differed both in terms of magnitude and character, depending on the seizure type. Our study documents the feasibility of the prospective study of driving and other behaviors during seizures through the use of computer-based tasks. This methodology may be applied to further describe differential driving impairment in specific types of seizures and to gain data on anatomical networks disrupted in seizures that impair consciousness and driving safety.

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Keywords

Epilepsy; consciousness; driving; EEG; SPECT; virtual reality; computer games

Introduction

Loss of consciousness during seizures is a major mechanism of morbidity and mortality in epilepsy. Patients with epilepsy are at increased risk of serious automobile accidents, accidental suffocation, and drowning compared to the general population, presumably due to temporary impairment in their ability to interact consciously with their environment during seizures [1–3]. Furthermore, impaired consciousness interferes with patients' daily activities, diminishes school and work performance, and leads to social stigma [4,5].

The question of when to restrict driving is emblematic of the dilemmas faced by regulators, patients and their clinicians related to impaired consciousness in epilepsy [6]. On the one hand, a significant body of evidence suggests that patients with epilepsy are at elevated risk of collisions causing injury or death [3,7]. On the other hand, restricting driving can devastate patients' careers, finances, and social lives. Furthermore, not all studies have found evidence of increased overall accidents or traffic fatalities in epilepsy, and several investigators have noted that other variables, including age, gender, and other medical conditions account for far more collisions than does epilepsy [1,2,8]. Though laws vary, many jurisdictions have addressed these competing priorities by requiring patients to have a seizure-free interval, usually one year, before resuming driving [9]. Such rules aim to allow patients to drive when their seizures are well-controlled, but to keep them off the road when they are most likely to be involved in an accident.

Several problems exist with this approach, however. First, many patients do not abide by their driving restrictions [10,11]. Patients may see driving bans as unfair and may fail to report seizures to their physicians and/or motor vehicle authorities. Furthermore, one-size-fits-all waiting periods fail to account for the vast differences between different seizure syndromes, especially in terms of their impairment of consciousness. If loss of consciousness is a primary mechanism by which seizures lead to motor vehicle collisions, those seizure types causing the greatest impairment in consciousness are likely the greatest risk to drivers, passengers, and pedestrians.

There is some evidence that different seizure types do indeed entail graded driving risk. For example, a retrospective study of seizures occurring behind the wheel showed that complex partial seizures were more likely to cause collisions than simple partial seizures [12]. Similarly, seizures preceded by auras were found to be less likely to cause collisions than those not preceded by auras [12]. Some motor vehicle authorities have attempted to account for these differences between seizure types by allowing certain categories of patients, such as those with myoclonic seizures, to drive. Similarly, in the Netherlands and in most of the United States, patients with simple partial seizures are allowed to drive [2]. Nevertheless, the most common approach to dealing with driving in epilepsy remains seizure-free interval requirements which lump all or most forms of epilepsy together.

Both physicians and regulators are called upon to make decisions regarding driving safety in epilepsy without detailed data linking specific seizures to driving risk. Though the available evidence generally supports the notion that seizure types involving a greater loss of consciousness are most likely to cause collisions, to our knowledge no one has directly observed patients driving or performing driving-like tasks during seizures to determine if there are differential effects of different seizure types on driving ability. However, driving

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simulators and instrumented vehicles have been used successfully to study the mechanisms and effects of other conditions associated with driving safety problems, such as alcohol intoxication, Alzheimer disease and excessive daytime sleepiness [13–16].

Similarly, although recent work in our laboratory and others has shed light on the anatomy and mechanisms of impaired consciousness in epilepsy, human studies specifically linking impaired consciousness and proposed seizure mechanisms have been largely retrospective. Based on the available data, our group has proposed the "network-inhibition hypothesis," which suggests that impaired consciousness in epilepsy is mediated by disruption of normal cortical-subcortical interactions. Specifically, partial seizures leading to impaired consciousness, but not those which do not impair consciousness, have been found to involve reduced cerebral blood flow and ictal slow activity on EEG in frontal and parietal association areas [18,22–23]. Our group has suggested that these changes are caused by ictal disruption of subcortical activating systems and that they prevent affected association cortices from performing integrative function necessary for normal consciousness [25,26]. Similar mechanisms may also play a role in generalized absence and tonic-clonic seizures [17,19–21,24,27,28]. However, this model has not yet been tested in prospective study of patients' ability to continue performing cognitive tasks during seizures.

In the current study, we designed a prospective experiment in which patients undergoing continuous video/scalp or intracranial EEG-monitoring and ictal SPECT played video games, and their game performance during seizures was analyzed. Whereas previous studies of consciousness in epilepsy have relied mainly on retrospective data, in which evidence of patients' impairment in consciousness was difficult to standardize, the current study allowed patients to choose from one of three pre-determined tasks, each of which required continuous interaction with a video game console. One of these tasks, a realistic driving simulator, was chosen in part for its relevance to the issue of driving performance.

The purpose of the study was to establish feasibility of the prospective study of driving performance and impaired consciousness during seizures through the use of video games and to gain insight into whether different types of seizures have different effects on driving ability. We hypothesized that this type of study would indeed be feasible and that seizure types known to impair consciousness (e.g. absence, complex partial, secondarily generalized) would affect driving ability to a greater degree than those not considered to impact consciousness (e.g. subclinical, simple partial).

Methods

Subjects and Recruitment

91 inpatients undergoing continuous audio-visual/EEG monitoring were recruited to the study. An additional 11 patients participated during the pilot phase for technical development (data not included in analysis). Informed consent was obtained from all subjects in accordance with NIH and Yale Human Investigations Committee procedures. All patients had known epilepsy, as defined by International League of Against Epilepsy (ILAE) criteria [29,30]. Exclusion criteria included non-epileptic (e.g. psychiatric) episodes and cognitive or motor impairment which prevented patients from understanding instructions or performing tasks. Seizures were induced with sleep deprivation, photic stimulation, deep breathing, and withholding of medications only by patients' clinical care providers, and the research team had no role in these decisions. Patients were paid a baseline of $20 for participation, with an additional $10/hour of play, up to maximum earnings of $100. In the driving game, one cent was deducted from earnings for each time the vehicle had a collision.

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Tasks

Patients were offered the following three games to play: (1) rFactor, a driving simulator, (2) SNIP, an open-source, generic version of Tetris, and (3) Frets on Fire, an open-source, generic version of Guitar Hero. rFactor was available for a longer period of time during the study, with the other two games added more recently, so that most patient data were obtained with rFactor. Patients played games on a modified hospital table with a laptop computer and relevant accessories attached (described below). Members of our research team instructed patients on how to play the games they chose and observed patients using the controls until they were comfortable playing on their own. Patients were encouraged to play as much as possible and to try to continue playing if they had a seizure.

rFactor (http://www.rFactor.net/) (Image Space Incorporated, Ann Arbor, MI) is a customizable racecar driving game designed to be a realistic representation of automobile racing. The game allows users to choose from a variety of vehicles and tracks, as well as to design their own. Cars are controlled by a steering wheel, gas pedal (throttle), and brake pedal (Logitech® MOMO® Racing Force Feedback Wheel, Fremont, CA) which attach to a USB port. We chose an easy-to-control racing roadster for patients to drive. During pilot testing, track and vehicle settings were adjusted such that a novice player could navigate the track, typically with less than one collision per minute. However, all tracks had frequent turns, in order to insure that continuous interaction was required to avoid collisions and maintain forward progress. Most patients drove on a custom track designed during pilot testing to maximize these features. The game recorded a large amount of data on driver performance, including the position of the steering wheel from left to right (on a scale from −1 to +1), velocity, vehicle position, throttle, and the timing of collisions.

SNIP (http://snip.sourceforge.net/) is a generic version of the familiar game Tetris, which involves objects of various shapes falling from the top of the screen to the bottom of the screen. Patients' task was to use buttons on a computer keyboard to rotate and move the objects so that they landed in positions where they fit with existing shapes in order to form complete lines across the bottom of the screen. Frets on Fire (http://www.unrealvoodoo.org/projects/fretsonfire/) is a generic version of the popular video game Guitar Hero, which involves listening to popular rock and roll songs and playing along in rhythm with the songs' guitar parts by pressing a particular key, or set of keys on the computer keyboard, as indicated on the screen. Like rFactor, the SNIP and Frets on Fire games were programmed to collect data continuously on patient performance, and were synchronized with the video/EEG data acquisition.

Data Collection

A 27-channel video/EEG monitoring system (BioLogic, Knoxville, USA) was used to record continuous EEG and video data from adult subjects age 18 years and older. Pediatric subjects below the age of 18 underwent 21-channel EEG monitoring using the same system. Electrodes were placed according to the international 10–20 system under bipolar montage. An Ipela camera and microphone system (Sony of America, New York, NY) was positioned on a wall of the hospital room. All the video/EEG data were recorded and reviewed using Ceegraph vision software (7.15.06.i06 Model 811 Rev A). A video monitoring technician watched patients from a neighboring room 24 h/day, adjusting the camera to record the patients' behavior and speaking with patients and nurses over an intercom during seizures.

All games output an electrical timing (TTL) pulse that was recorded on an unused lead of the EEG to facilitate synchronization of game data with that of the clinical data collection system. This pulse was generated by an external chip (Brainstem Moto 1.0 Module) connected to the computer through a USB port, and it generated a series of pulses encoding

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the computer clock's time every 30 s. For electrical safety, the TTL pulse was isolated from the EEG recording system using a custom-built photodiode-based isolator, and signal attenuator. All game data were recorded automatically by the laptop computer. Video-EEG data were archived and analyzed for each patient extending from 20 min before each playing start time to 20 min after each playing stop time.

EEG and Behavioral Analysis

All patients' EEGs and video-behavioral recordings were reviewed by neurologists specializing in epilepsy at our institution. Seizure onset time was defined by the earliest time with behavioral or electrographic evidence of seizure, and offset time was defined as the latest time with such evidence. Events were classified as: 1) interictal activity, 2) subclinical seizures, 3) auras, 4) partial seizures, 5) absence seizures or 6) secondarily generalized tonic-clonic seizures. Classification of partial seizures, absence seizures, and secondarily generalized seizures were done according to the criteria established by the International League Against Epilepsy [29,30]. Interictal activity was defined as brief epileptiform activity on EEG, with no clinical signs or symptoms, and which did not progress in location or frequency. Subclinical seizures were defined as events with epileptiform activity on EEG which progressed in either frequency or location in a characteristic ictal pattern, but had no clinical signs or symptoms [31]. Auras were defined as seizure warnings reported by patients verbally or by pressing the event button with no other overt behavioral changes.

Our research team further reviewed video recordings of each seizure which occurred while patients played one of the games. Patient behavior was described during the events, with particular attention paid to whether patients appeared to continue playing during the events (i.e. looking at the screen, interacting with game controls, etc.). In addition, certain time periods of some seizures were excluded from further analysis based the occurrence of confounders, such as family members or hospital personnel removing game controllers from patients during the seizures. Because of the large number of interictal events that occurred and their relatively brief duration, behavior was not analyzed in detail during interictal activity, but these will be investigated through an ongoing separate study in the future.

Performance and Game Data Analysis

For seizures occurring while patients played rFactor, which accounted for most of the seizure events, Matlab version 7.5 (Mathworks, Natick, MA) was used to plot the following variables over time: steering wheel velocity, throttle (gas pedal) position, car position and car velocity. Seizure onset time, offset time, and any collisions were also marked. Each seizure was then analyzed for evidence of impairment in one of four variables during the period from 1 s before the seizure onset to 1 s after seizure offset, using the following criteria:

1. Collisions: occurrence of any collisions
2. Decreased steering wheel velocity: drops below 0.1 for more than 10 s
3. Decreased throttle: drops below 0.05 on a scale from 0–1 for more than 10 s
4. Decreased car velocity: drops below 1 for more than 10 s.

All units were arbitrary game units. Seizures with either a collision and/or impairment in any of these variables were classified as showing evidence of impairment, whereas those with no collisions and no variable meeting impairment criteria were classified as not impaired.

In order to validate our impairment criteria, we selected a random four min period with no epileptiform activity for each patient who had been deemed to be impaired in steering wheel velocity, throttle position and/or car velocity during a seizure. We then examined the data

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from these randomly chosen time windows to see if the variables which previously met criteria for impairment during a seizure would also meet our criteria during these interictal periods.

Because fewer data were available with SNIP and Frets on Fire, we analyzed performance on SNIP by simply looking at the number of times game keys were pressed, and analyzed performance on Frets on Fire by looking at the omissions (missed key pressing when supposed to press), and commissions (key pressing when not supposed to press).

Results

Participation and Feasibility

A total of 91 patients participated in this study. The mean age was 30.9 years (range 7 to 64), with 18 pediatric patients aged 7–17 years (19.8%) and 73 adults aged 18–64 years (80.2%). Subjects included 45 males (49.5%) and 46 females. 12 patients (13.6%) were left-handed. 83 (91.2%) were undergoing scalp EEG alone, seven patients (7.7%) were undergoing ictal SPECT analysis along with scalp EEG, and one patient (1.1%) was undergoing intracranial EEG.

Table 1 shows clinical information for the 13 patients who had seizures during game playing. Based on these data, 4 patients' (2,5,8,9) epilepsy was localized to the left hemisphere, while 7 patients' (3,4,6,7,10,11,12) epilepsy was localized to the right hemisphere. Patients 1 and 13 could not be definitively localized based the available data. Of note, ictal SPECT was obtained in two patients while they participated in our tasks (patients 6 and 7).

Patients in the study played for a total of 24,388 min (406.5 hours (h)). The mean time of participation per patient was 268 min (range 2–1,300). Adults played for a mean of 281 min (range 2–1,300), and pediatric patients age 17 and younger played for a mean of 189 min (range 14–474). Females played for a mean of 258 min (range 7–1,108) and males played for a mean of 278 min (range 2–1,300). There were no significant differences in playing time based on adult vs. pediatric patients or based on gender. rFactor was the first game introduced and accounted for 59.1% of playing time (14,413 min). SNIP and Frets on Fire were introduced subsequently and accounted for 39.7% and 1.2% of playing time, respectively.

A total of 13 patients (14.3% of participants) had seizures while playing games. The overall number of seizures captured while patients played games was 22, an average of one seizure every 1109 min (18.5 h) of game play. Table 2 shows the total number of patients and number of seizures for each seizure type discussed above in the Methods. In addition, there were a total of 105 interictal discharges in 14 patients while playing three games (data not shown in Table). There were 86 interictal events which occurred in 12 patients while playing rFactor, 10 interictal events in four patients playing SNIP, and nine interictal events in two patients playing Frets on Fire. Five of the patients with interictal events also had seizures.

Behavioral Observations Based on Video Review

Review of the 22 seizures listed in Table 2 using the clinical video/EEG recordings revealed variable behavioral changes while playing the games.

During subclinical seizures (Table 2), patients by definition had no identifiable signs or symptoms of their seizures. Analysis of their audio-visual recordings during the seizures revealed that both patients continued to interact with game controllers during subclinical seizures.

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During 40% of auras, patients continued to play the video games. The first patient was playing rFactor during his aura (Table 2). He pushed the event alert button, had an appropriate conversation with the monitor watcher, and then continued to drive. The second patient had two auras while playing SNIP. During both of these auras, she suddenly paused the game, saying things such as, “The screen blanked out…” and “I got very nauseous.” Another patient also had two auras while playing SNIP. During the first aura, the patient pushed the event alert button twice and immediately continued to play SNIP. During the second aura, she suddenly hit the escape key to end the game and then looked for the event button.

Ictal behavior varied greatly during partial seizures (Table 2) while performing our tasks. In two of seven seizure events (28.6%), patients continued playing games throughout their seizures. For example, during one seizure the patient (Patient 5) responded to questions over the intercom while continuing to drive, playing rFactor. As he conversed with the monitoring technician, the patient occasionally looked toward the intercom rather than the computer screen and briefly reduced his throttle and steering. During a different patient’s partial seizure while playing rFactor, the patient (Patient 6) said, “Ok… you wanted the aura of a seizure… I think I’m starting to feel it.” She continued steering while complaining that she could not drive through the seizure. She then stopped steering, saying, “I couldn’t see where I was going.” She noted to a nurse in the room that she was not sure if she could resume driving and that her foot was on the accelerator though she was not steering.

Patient 7 had a partial seizure while playing SNIP and stopped playing. Patient 4 had two partial motor seizures while playing rFactor. During one of these she continued to play the game, whereas in the other she pushed the game table away from herself. Patients 8 and 9 each had a partial seizure while playing rFactor, and both stopped playing the game.

During 60% of absence seizures (Table 2), patient 13 appeared to continue playing the video games. One of the seizures occurred during SNIP, and showed no behavioral impairment on video monitoring. While playing rFactor, two additional seizures also showed no evidence of behavioral impairment on the video monitoring. In another seizure occurring during rFactor, however, the patient stared straight ahead with her mouth open and rested her hands on the steering wheel for nearly 10 seconds, turning the wheel only once during this period. During the fifth seizure the camera did not capture the patient’s face and hands well enough to allow detailed description of her behavior.

In one secondarily generalized seizure (Table 2), patient 10 exhibited a dystonic posture, followed by sudden stiffening. The patient’s foot stopped pressing the throttle and his left hand stiffened and stopped steering, while his right hand continued moving the steering wheel back and forth. During the patient’s other secondarily generalized seizure, behavior was similar, except that his right hand came off the steering wheel and touched his chest several times before again grasping the steering wheel and turning it rapidly back and forth several times.

Driving Performance Based on rFactor Output Data

Seizures occurring while patients played rFactor were analyzed based on the game performance output data in detail, while data from other games was more limited and will be discussed only briefly. While playing rFactor, 11 of 16 seizures were included, as five had incomplete performance data due to TTL pulse malfunction or corruption of performance log files. As described in the Methods, each seizure was analyzed for impairment based on the presence of collisions and/or decreased steering wheel velocity, throttle position, or car velocity. Table 3 shows the proportion of events for each seizure type in which the patients had impairment in these rFactor output variables. For comparison, impairment on rFactor

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playing based on review of video behavior (described in the preceding section) is also listed (Table 3).

None (0%) of the subclinical seizures met our criteria for impairment in any of the rFactor output variables, and there were no collisions during any of these events. The only aura which occurred during rFactor was excluded for the technical reasons discussed above.

Three of four (75%) partial seizures met our criteria for impairment in at least one category. Indeed, three of four partial seizures (75%) involved at least one collision, and one seizure involved two collisions. The remaining variables were not analyzed for one seizure because the patient's mother moved the gaming table away from him. Among the remaining seizures, steering wheel velocity was impaired in one of three events (33%), whereas throttle and vehicle speed were impaired in two of three events (67%).

One of two (50%) absence seizures demonstrated impairment according to our criteria. Interestingly, neither of the absence seizures (0%) showed impairment in steering wheel velocity, throttle, or car velocity. However, there were three collisions during one of the seizures.

Both secondarily generalized seizures (100%) involved impairment of at least one variable. Steering wheel velocity was impaired in one of two seizures (50%), whereas in the other seizure the patient continued to move the steering wheel even after the vehicle had stopped. Throttle and vehicle speed were impaired in both secondarily generalized seizures (100%). There were no collisions during secondarily generalized seizures, since in both cases the vehicle fortunately stopped without striking any obstacles.

Fig. 1 shows examples of driving performance during different types of seizures. In the first example of a partial seizure (Fig. 1A), review of the audio-video EEG recording demonstrated the patient's ability to have an appropriate conversation with the monitoring technician, described above. Steering wheel velocity was maintained throughout the seizure. There was a brief deceleration after the throttle dropped to zero for several seconds (<10 s), but the car quickly started again. This deceleration occurred while the patient looked at the intercom and spoke with the technician. There were no collisions during this seizure.

The second example of a partial seizure (Fig. 1B) on video/EEG review demonstrated the patient complaining of impaired vision and inability to continue driving. Note that during this seizure the patient initially maintained the throttle, and velocity actually increased during the first 25 s of the seizure. However, despite continued steering, the patient had two collisions and subsequently the steering wheel velocity, throttle, and vehicle velocity dropped to zero for the remainder of the seizure. As discussed above, the patient complained that she could not see the track during the seizure.

During the example of an absence seizure (Fig. 1C), steering wheel velocity, throttle, and vehicle velocity were similar to the period before seizure onset, and showed no impairments. In the first several seconds of the seizure, the patient continued to push the throttle and increased velocity before having two accidents very close together. After the second collision, the steering wheel velocity and throttle dropped to zero. However, within <10 s the throttle and steering wheel velocity increased again and remained high for the rest of the seizure. The patient had a third collision just before seizure offset. Note that there were three periods, two before seizure onset and one during the seizure, during which the throttle dropped to zero for slightly less than 10 s. As discussed above, there was no clinical evidence of this absence seizure based on the video review, though the patient was facing away from the camera during the seizure.

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An example of driving performance data for a secondarily generalized seizure is shown in Fig. 1D. Within several seconds of seizure onset, the throttle dropped to zero and remained there for the rest of the event. The velocity also dropped to zero as the vehicle rolled to a stop without hitting anything. As discussed above, the patient's right arm continued to turn the steering wheel back and forth intermittently throughout the seizure, though the patient was not looking at the computer screen for most of this time, nor was the vehicle moving. This was reflected in maintenance of a positive steering wheel velocity throughout the event.

As described in the Methods, for each patient who met criteria for impaired steering, throttle, or car velocity during seizures we selected a random four min period with no epileptiform activity for comparison. Neither of the two patients who met criteria for impaired ictal steering met those criteria during the four minute interictal periods. Similarly, none of the three patients with impaired car velocity during seizures met criteria for impairment during the interictal periods. None of the three patients who met impairment criteria for throttle during a seizure met criteria at any point during the random interictal periods. Overall, these finding suggest that our criteria are at least a reasonable starting point for detecting seizure-related impairment.

Performance on SNIP—Game output results for SNIP were mixed. In some cases, button pushing decreased over time during seizures, whereas in other seizures the button pushing increased.

Performance on Frets on Fire—Patients had interictal epileptiform activity while playing Frets on Fire and showed no obvious impairment of game performance.

Discussion

In the current study, we captured 22 seizures in 13 patients playing video games while undergoing continuous video/EEG monitoring. We demonstrated that it is feasible to synchronize data on ictal performance of computer-based tasks with data from brain function studies including EEG and ictal SPECT. Though our sample size was small and our conclusions are preliminary, our initial analyses suggest that the impact on game performance of different types of seizures varies both in character and magnitude.

Feasibility

The results of our study demonstrate that it is possible to recruit patients undergoing continuous video/EEG monitoring for a prospective study and to capture seizures while patients perform a task. Based on our experience, it is reasonable to expect seizures from one out of approximately seven to eight patients recruited, or the equivalent of approximately one seizure every 18.5 h of game playing. Patients of all ages and both genders are suitable candidates for a study of this type.

Variable Impact of Types of Seizures on Driving Performance

Our results suggest that there are indeed differences between how different types of seizures affect driving ability. At one end of the spectrum, we found no evidence of impairment during subclinical seizures. At the other end of the spectrum, secondarily generalized seizures showed marked evidence of impairment. We found evidence of driving impairment in some, but not all, partial seizures and absence seizures. Future studies with a larger number of subjects and seizures are needed to confirm the trends seen in our small sample.

Among those seizures that did affect driving performance, ictal impairment was qualitatively different between different types of seizures. During secondarily generalized

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seizures, for example, ictal performance was characterized by sudden disengagement from driving simulator controls, which occurred within seconds of seizure onset. The notable exception to this was turning of the steering wheel during one seizure, which we interpreted as involuntary because it occurred while the vehicle sat still. In contrast, none of the absence seizures completely prevented the patient from continuing to engage the throttle, maintaining vehicle velocity, or turning the steering wheel. However, as exemplified in Fig. 1C., the occurrence of three collisions in rapid succession during one of the absence seizures suggests that the patient's driving safety and conscious interaction with the environment were impaired. Similarly, driving impairment in partial seizures manifested itself in a variety of ways. This ranged from sudden disengagement from game controls at the time of seizure onset in one patient, to increased engagement of the throttle in another patient. In the latter case, vehicle speed increased and lead to two high velocity collisions.

This diversity in performance among seizures is not surprising, given that different types of seizures (and different partial seizures) involve distinct brain networks. Furthermore, seizures can occur in many diverse driving environments, and the outcome of any seizure occurring while driving is likely determined by the interaction between seizure type and driving environment. For this reason, we found it most useful to analyze game performance during seizures by looking for evidence of impairment in any of several variables (i.e. steering wheel movement, throttle engagement, car velocity, and collisions).

Though preliminary, our results are largely consistent with previous work suggesting that different types of seizures pose different levels of risk to driving safety. Gastaut and Zifkin [12] found that three of four generalized tonic-clonic seizures (75%) occurring behind the wheel led to collisions. 53 of 88 complex partial seizures (60.2%) led to motor vehicle accidents, whereas only three of 11 simple partial seizures (27.3%) led to accidents. One of three (33.3%) absence seizures involved collisions. Our results are similar, in that secondarily generalized seizures were the most likely to show some evidence of impairment (100%), partial seizures were the next most likely (75%), and only 50% of absence seizures met our objective criteria for impairment. Differences in collision rates between the two studies may have been due to small sample sizes and differences between our driving simulator and real world driving.

The descriptions of individual seizures provided by Gastaut and Zifkin [12] also line up with our own results. For example, they describe a 19-year-old patient witnessed having an absence seizure while driving. This patient continued to drive in a straight line and did not have an accident because the road was straight and there were no other cars on it. As discussed above, a patient in our study also continued to drive during absence seizures, albeit recklessly.

Previous studies of consciousness in absence seizures have found that patients' impairment varies significantly from patient to patient and between episodes in a given individual (reviewed in [32]). Patients with absence seizures have previously been shown to continue some activities during seizures, especially in simple motor activities such as repetitive tapping. However, they have greater difficulty with applying sensory input and more complicated motor tasks. The driving behavior during absence seizures in both the Gastaut and Zifkin study and the current investigation are consistent with these previous descriptions of patients' abilities during absence seizures [32–37].

Gastaut and Zifkin [12] also found that partial seizures preceded by an aura were less likely to lead to accidents, presumably because patients had time to stop their vehicles safely before losing consciousness. This variable was not directly measured in the current study, because we instructed patients to try to continue driving during seizures. However, as

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discussed above, during one seizure (Fig. 1B), the patient mentioned that she was having an aura and said she doubted she could continue to drive. The collisions she had during this seizure might well have been prevented had the patient been instructed to stop the car safely at the outset of seizures rather than to attempt to continue driving.

Mechanisms of Driving Impairment During Seizures

Based on our current data, we have too little localizing information to propose a model for mechanisms of driving impairment during seizures. In considering future study, however, it is worth noting overlap between anatomical networks implicated in recent functional imaging studies of normal driving and those networks implicated in loss of consciousness in epilepsy. Both deficits in the *level* of consciousness, which includes mechanisms for maintaining an alert, attentive state, and the *content* of consciousness, which includes sensorimotor function, vision, and higher order integration, could adversely affect driving during seizures. Our initial data suggest impairment in different aspects of consciousness in different types of seizures. We can speculate, for example that driving is impaired in absence seizures due to decreased attention, in occipital lobe seizures due to impaired visual processing, and in tonic-clonic seizures due to both impaired alertness and loss of motor control. More data is needed, however, to further investigate specific impairment of these functions during seizures.

Spiers and Maguire (2007) completed an fMRI study of normal subjects driving in a simulator of central London and used video review and post-testing interviews to classify time periods as involving specific driving behaviors or categories of driving behaviors. The investigators then identified areas differentially activated by each type of driving behavior. For example, areas activated while performing prepared actions (e.g. stopping at a stop sign, turning at a corner) included pre-supplementary motor area/supplementary motor area, medial parietal cortex, and posterior cingulate, among others. Areas activated while swerving to avoid collisions included posterior parietal cortex, ventrolateral prefrontal cortex, anterior cingulate and other areas [38].

Regions implicated by this study as mediating various components of driving thus overlap substantially with the cortical-subcortical network implicated in impairment of consciousness during seizures, as discussed in the introduction [39,41]. Admittedly, Spiers and Maguire identified a long and diverse list of brain regions activated by various behaviors, and the true meaning of such results is unclear. However, their method of breaking driving behavior into its multiple subcomponents could be utilized to look for evidence of impairment in individual categories during seizures in a future study with a larger sample size.

In another fMRI study using driving simulators, Calhoun et al. similarly found activation of posterior parietal cortex during driving compared to rest. However, this activation was inversely correlated with vehicle speed [40]. Both the challenge and the opportunity going forward will lie in teasing out the meaning of changes in levels of brain activity in specific regions during task performance and/or seizures. Seizures involving posterior parietal cortex seem especially likely to be implicated, by further study, in impaired driving, but it may be difficult to tell if such impairment is due to impaired consciousness or to impaired spatial mapping. Or is spatial mapping a subcomponent of both normal driving and normal consciousness?

Recent work in our laboratory and others has begun to identify not only an anatomical network likely to be involved in seizures with impaired consciousness, but also the time course over which changes occur in different structures [20,27]. For example, in an fMRI study of childhood absence epilepsy, we found small increases in BOLD signal which

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occurred in frontal and parietal cortex more than five seconds before electrographic and behavioral evidence of seizure onset. These same areas showed profound decreases more than 20 seconds after seizure offset. Our current exploration of customizable video games with complex data output may offer opportunities to uncover subtle behavioral changes related to changes in specific structures at particular parts of a seizure.

In addition, it is important to address the implications of this study for driving licensure. Although our data showed that some absence seizures and some partial seizures did not have a significant impact on driving in this study, it would be improper to conclude these seizure types do not have a significant impact upon driving in reality. Indeed, it is possible that with a more realistic study paradigm and with a greater sample size, it might be found that these seizure types often do pose a threat to patients behind the wheel.

The current study was limited by its small sample size and small amount of localizing data during seizures. Future study could expand the overall sample size and focus on gathering ictal SPECT and intracranial EEG data to facilitate identification of brain regions involved in seizures which lead to driving impairment. Other studies, such as one in progress in our laboratory, could gather prospective data on ictal impairment of consciousness based on interactive patient examination, which may provide additional information on the specific deficits in patients who stop driving during seizures.

In summary, the current investigation has demonstrated the feasibility of studying driving performance and other measures of consciousness by recruiting patients to play video games during inpatient video/EEG monitoring. We have identified preliminary trends regarding the differential effects of different types of seizures on driving performance. These results could be extended to identify brain regions implicated in impaired driving performance during seizures. We hope that with further study, this approach will expand the prospective investigation of impaired consciousness in epilepsy, and eventually provide insight into mechanisms of differential driving risk among patients with different types of seizures. This information will be useful both to patients and to their health care providers in guiding decisions about driving, and ultimately may also facilitate the development of treatments that reduce driving risk in epilepsy.

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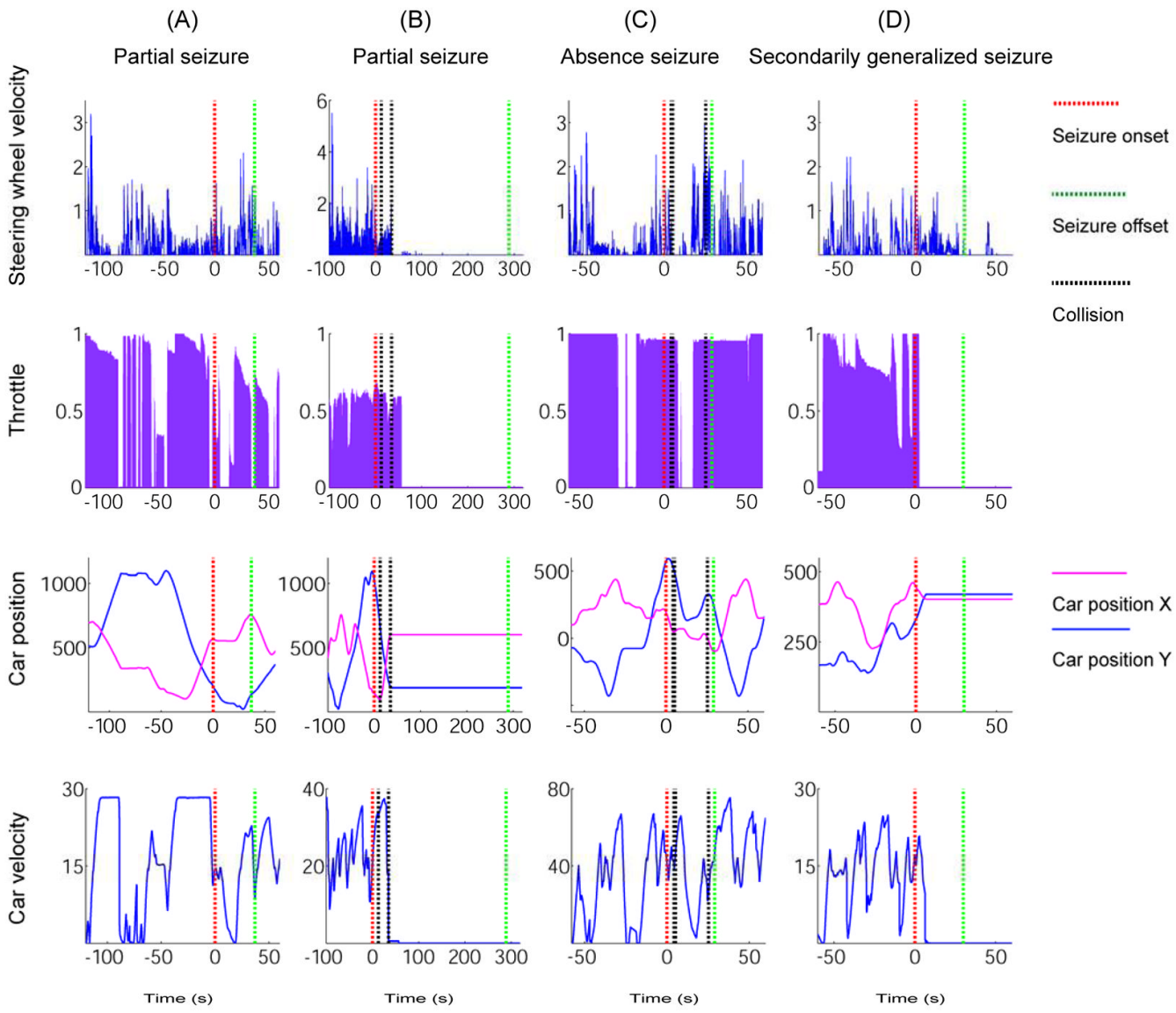

Fig. 1. Performance on rFactor driving simulator during different seizure types

Change in driving performance over time is shown for representative examples of different types of seizures. All of the variable units are arbitrary game units. (A) Partial seizure (Patient 5). (B) Partial seizure (Patient 6). Note that after the second collision the throttle remained depressed for a while but the car did not move since it had collided with a wall. (C) Absence seizure (Patient 13). Note that the first two collisions occurred very close together and appear merged at this time resolution. (D) Secondarily generalized seizure (Patient 10). Driving performance variables shown include the following: Steering wheel velocity (top row) is the absolute value of the derivative of the steering wheel position vs. time. This value represents the quantity of steering wheel position changes at each time point and was used as a measure of patients' engagement in avoiding collisions. Throttle (second row) shows engagement of the throttle, where 1.0 means the gas pedal is fully depressed and 0 means the patient's foot is off the pedal. Car position (third row) displays the location of the vehicle in terms of the game world grid, according to two dimensions x and y vs. time as the car travels around the track in the x-y plane. If the car is moving, then one or both of these values should change over time. Car velocity (fourth row) shows

vehicle's total speed as it moves along the track vs. time. In all plots, time is relative to seizure onset, which is set to time 0 s. The red line indicates seizure onset. The green line indicates seizures offset. Black lines represent collisions.

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Table 1

Clinical information for patients with seizures during game playing

Patient #	Number of seizures	Seizure category	MRI	PET hypometabolism	Ictal SPECT hyperperfusion	EEG localization[a]	EEG localization of seizure during task	Overall localization
1	2	Aura	N/A	N/A	N/A	No EEG changes	No EEG changes (auras 1 & 2)	N/A
2	1	Aura	L > R Bi F foci of T2 hyperintensity	N/A	N/A	L F	No EEG changes	L F
3	2	Aura	Normal	R T	N/A	R T	No EEG changes (auras1 & 2)	R T
4	2	Partial seizure	R > L H T2 increases and volume loss	R O, extends to R P & T	N/A	R H neocortical onset	R F-C sharp & slow waves (seizures 1 & 2)	R H
5	1	Partial seizure	Normal	N/A	N/A	L T	L T theta sharp waves	LT
6	1	Partial seizure	R HCA	R T	R O (while playing rFactor)	R P-O	Initially R T-P, then Bi T-P	R T-P-O
7	1	Partial seizure	R HCA	Bi T, R > L	R T (while playing SNIP)	Bi T, R > L	R T	R T
8	1	Partial seizure	L T atrophy	N/A	L F	Non- localized slowing	Non- localized slowing	L H
9	1	Partial seizure	Multiple cavernous hemangiomata	L T-P	N/A	L T-P	L T-P slow wave	L T-P
10	2	Secondarily generalized	Multiple white matter abnormalities	R F-T-P	N/A	Diffuse R F	R F to general (seizure 1), generalized SWD (seizure 2)	R H
11	1	Subclinical seizure	R T-P-O cortical thickening	R T-P-O	R O	R O	L O low amplitude 5 Hz spikes	R O
12	2	Subclinical seizure	R P nodular heterotopias	R T	N/A	Bi F-T	Repetitive 2Hz R H spikes (seizures 1 & 2)	R H
13	5	Absence seizure	Normal	L T	N/A	Generalized SWD	Generalized SWD	N/A

[a]Based on overall EEG of all seizures, not just seizure occurring during task. Abbreviations: HCA=hippocampal atrophy, R=right, L=left, O=occipital, T=temporal, P=parietal, F=frontal, Bi=bilateral, H=hemisphere, SWD=spike wave discharge.

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Table 2

Seizures during game playing

Type of event	Number of patients	Number of seizures	Game(s) played during events
Subclinical seizure	2	3	rFactor
Aura	3	5	rFactor, SNIP
Partial seizure	6	7	rFactor,SNIP
Absence seizure	1	5	rFactor, SNIP
Secondarily generalized seizure	1	2	rFactor
Total	**13**	**22**	

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Table 3

Impairment during seizures while playing rFactor

	Analysis of Video/EEG	Analysis of rFactor output variables					
Seizure type	**Behavioral description**	**At least one collision during seizure**	**Total collisions during seizures**	**Steering wheel velocity impairment**	**Throttle impairment**	**Car velocity impairment**	**Seizures with any evidence of impairment**
Subclinical seizures	0/3 stopped playing	0/3 (0%)	0	0/3 (0%)	0/3 (0%)	0/3 (0%)	0/3 (0%)
Auras[a]	0/1 stopped playing	--	--	--	--	--	--
Partial seizures[b]	4/6 stopped playing and behaved differently	3/4 (75%)	4	1/3 (33%)[c]	2/3 (67%)[c]	2/3 (67%)[c]	3/4 (75%)
Absence seizures[d]	1/4 stared and paused playing ~10 s, 1/4 off camera, (2/4 continued play)	1/2 (50%)	3	0/2 (0%)	0/2 (0%)	0/2 (0%)	1/2 (50%)
Secondarily generalized seizures	2/2 sudden tonic posturing and stopped playing	0/2 (0%)	0	1/2 (50%)	2/2 (100%)	2/2 (100%)	2/2 (100%)

For all entries, numerator is number of seizures and denominator is total number of seizures analyzed.

[a] One patient had an aura while playing rFactor but rFactor output variables could not be analyzed due to technical problems.

[b] Two partial seizures were analyzed by video/EEG review but could not be analyzed by rFactor output variables because of technical problems.

[c] Steering, throttle and car velocity were not analyzed for one partial seizure because the patient was stopped from playing by a family member. However, there was one collision before this happened.

[d] Two absence seizures were analyzed by video/EEG review but could not be analyzed by rFactor output variables because of technical problems.