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Visual Reflex Seizures Induced by Complex Stimuli

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Summary: Visual reflex seizures induced by complex stimuli may be triggered by patterned and flashing displays that are now ubiquitous. The seizures may be clinically generalized, but unilateral and bilateral myoclonic attacks also may be triggered, especially in patients with juvenile myoclonic epilepsy, and recently, clearly focal reflex occipital lobe seizures have been described. Some seizure-triggering properties of video displays can be identified, such as perceived brightness, pattern, flicker frequency, and color. Knowledge of these is useful in planning individual treatment and in designing regulations for screen content of television broadcasts or for other video displays. Some subjects will also be sensitive to cognitive or action-programming activation, especially when playing video games, and this can increase the chance of seizure triggering. Nonspecific factors such as sleep deprivation, prolonged exposure, and drug or alcohol use also may play a role in reflex seizure occurrence. **Key Words:** Reflex seizures—Visual sensitivity—Photosensitivity—Cognitive induction—Prevention.

All of human society is increasingly likely to come into contact with visual stimuli that can trigger epileptic seizures in susceptible individuals. Computers, television screens, videogames, and other video displays are inescapable in education, work, and entertainment. Other patterned and flashing light displays are part of everyday life as direction or warning signs, advertising, entertainment, and other forms of information: these technologies also have spread to developing countries. The sources of visual stimulation have been described elsewhere in this volume.

From the EEG era, photosensitivity was identified by the response to stroboscopic white flicker (intermittent photic stimulation: IPS) in the EEG laboratory. Flicker sensitivity is usual in patients with different types of seizures induced by visual stimuli, but subtypes in which patients are reproducibly sensitive to more complex stimuli can be distinguished. These stimuli usually add elements of pattern, color, flicker, or movement, often to the inherent flicker stimulation of displays such as domestic television (TV) screens. Other intrinsic factors not related to typical visual stimuli but adding to the seizure-generating properties of stimuli such as videogames include cognitive activity, thinking with action programming, and reading. Kasteleijn-Nolst Trenité et al. (1) showed that in subjects known to have seizures induced by videogames, more were sensitive to playing rather than simply to viewing the game under test conditions, and 14% could not be shown to be photosensitive (1). In daily life, extrinsic nonspecific factors such as sleep deprivation, prolonged and close exposure to the stimulus, and drug or alcohol use may also increase the risk of a seizure. Some will occur by chance.

Seizures evoked by these visual stimuli were formerly thought to be generalized almost exclusively, although asymmetric myoclonus could occur. More recently, induction of partial seizures by visual stimulation, including typical complex partial seizures, has been studied in detail by several groups; see for review (2). Ferrie et al. (3) found that 29% of a group of subjects with videogame-induced seizures had photosensitive partial seizures. Earlier reports often did not consider these specifically, and thus visually induced seizures have been reported to be typically generalized tonic–clonic from their onset, as in 84% of Jeavons and Harding's patients (4), whereas absences occurred in only 6%; partial motor seizures, possibly a mix of asymmetric myoclonus and true partial seizures, in 2.5%; and myoclonic seizures in 1.5% of patients. However, these proportions are subject to bias: diagnosis is often made after a florid myoclonic seizure or convulsion in front of the computer or television, but many less obvious unobserved partial or generalized reflex seizures may have already occurred.

Although much variability is found among patients sensitive to complex visual stimuli, we can identify some characteristics that strongly influence the likelihood of

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reflex seizures in daily life and that should be considered in developing preventive methods and individualized treatment.

COMPLEX VISUAL STIMULI

The role of brightness

In general, brighter stimuli are more likely to induce seizures. "Brightness" is, however, subjective and not measurable: it can be approximated by several different standard measures applied to light. Ricci and Vigevano (5) found that videogames with a steady maximal brightness of >100 lux (or lm/m^2, a measure of illuminance, describing illumination of a surface by a light source) were more likely to induce seizures and recommended that these be considered "potentially dangerous." More recently, Funatsuka et al. (6) suggested that brightness perception was important in a specific group of photosensitive patients in whom frontal predominance of the photoparoxysmal response was found. Television guidelines (7) aim in part to prevent broadcast of sudden and marked changes in screen luminance (measured in cd/m^2, units of luminance produced by a diffuse surface), thus avoiding flash effects, even when baseline luminance is low, as is usual for domestic TV.

The role of pattern

Pattern-sensitive epilepsy consists of seizures triggered by viewing patterns, typically stripes. Almost all such patients are sensitive to IPS, and about one third of photosensitive patients may have epileptiform EEG abnormalities on viewing stationary black-and-white striped patterns in the EEG laboratory. The characteristics of these have been reviewed (8): of importance to consider here is that discharge probability increases with pattern size and that peripheral and central pattern stimuli are equivalent when corrected for cortical magnification factor. Pattern sensitivity also is much enhanced if the pattern vibrates or flickers. Monocular viewing reduces pattern sensitivity. Sensitivity to pattern is usual in patients whose seizures are precipitated by videogames unless the seizure has occurred by chance or is unrelated to photosensitivity. Although striped patterns also are ubiquitous in everyday life, many are stationary or distant and are thus less likely to induce seizures than are those with the underlying flicker added by the video screen or by the screen content. Some subjects sensitive to pattern are not sensitive to flicker (9).

The role of flash frequency

Flicker frequency is the most important factor in sensitivity to video screens. The flash frequencies most likely to elicit a photoparoxysmal response (PPR) to IPS range typically from nine to 18 flashes/s. Only $\sim$3% of the photosensitive population is sensitive at 1–3 flashes/s. It is important to note that $\sim$48% are sensitive at 50 flashes/s and that $\sim$15% are sensitive at 60 flashes/s (4), which are also the approximate field rates of European, and Japanese and North American domestic TV screens, respectively. Even without an image, an operating TV screen delivers the equivalent of IPS at the field rate, and a slower 25- or 30-frames/s stimulation, which is a flickering pattern of horizontal lines produced by the raster and resolved at close viewing distances. Increasing the field rate by using 100-Hz screens reduces but does not eliminate the likelihood of triggered seizures during TV viewing or videogame play . Flashing screen content can still trigger seizures, even on high-frequency TV screens or noninterlaced computer displays without perceptible intrinsic screen flicker: this risk is the basis for some of the adaptive filter mechanisms (11) and safety regulations applied to screen content.

The role of duration

Experience and EEG data both suggest that duration of viewing of provocative stimuli can contribute to triggering clinical seizures. Some drugs, notably valproate, reduce photosensitivity. In untreated sensitive subjects, clinical seizures can be triggered with only momentary stimulation. How long a stimulation is needed has been little studied: Appleton et al. (12) showed that many subjects with photosensitivity and juvenile myoclonic epilepsy (JME) may require several minutes of stimulation before the generalized epileptiform response to IPS appears. Thus, brief IPS in the EEG laboratory, useful for screening untreated subjects, may not be adequate if the history suggests visual sensitivity or if the patient is taking antiepileptic drugs (AEDs).

The role of color

Red flicker and especially alternating red and cyan or blue flicker is especially provocative in photosensitive subjects, even at the low luminance typical of the home TV screen and with isoluminant stimuli. This mechanism was partially responsible for the potency of the notorious Pocket Monsters program in Japan in triggering photosensitive seizures (13,14). Compound color filtering and intensity-reducing lenses provide useful reduction in screen sensitivity (15).

The role of cognitive processes and action programming

Ricci and Vigevano (5) found that some videogames were more provocative of seizures and related this to illuminance ("brightness"), pattern sensitivity, and game content. Puzzle games tested on a 50-Hz screen could be quite provocative even without flashing images: they related this to patterned screen content and a possible sensitivity to cognitive activity or action programming. Photosensitivity is common in idiopathic generalized epilepsy (IGE) syndromes, recently reported in 5.6% (16), and is more frequent in JME (Herpin-Janz syndrome). These syndromes—and especially JME—are also associated

with sensitivity to cognitive stimuli. Triggered seizures range from brief unilateral myoclonus to generalized convulsions. Matsuoka et al. (17) found that 24.7% of a series of IGE patients and 46.7% of their JME subgroup were sensitive to such tasks. Rates for photosensitivity in JME depend on how and when assessment is made, but range in recent reports from 17.4% (16) to 90% (12). Matsuoka et al. (17) found that 36.4% of subjects with JME and activation by thinking or action-programming also were photosensitive: of interest is that photosensitivity was as frequent in subjects not activated by these tasks and thus that these are likely independent mechanisms that often coexist. Even with detailed testing by experienced investigators, it was found that some subjects referred for TV- or videogame-induced seizures could not be shown to be photosensitive (1,3). Thus, a major role for seizure induction by cognitive stimuli and especially by action programming must be considered in these patients, especially if seizures were induced by videogames. Tasks that evoke these seizures typically involve spatial information, writing, or calculating. In the laboratory and in daily life, these commonly require use of the hands, and videogame play would thus be expected to be effective in triggering seizures in susceptible individuals. Similar to occipital triggering in pattern sensitivity, one can argue that such "nonlesional reflex epilepsy evoked by nonlinguistic higher cerebral activities" (18) (praxis induction) depends on enhanced functional or regional hyperexcitability in the rolandic areas if myoclonus is triggered, in addition to any other regional or network hyperexcitability that may be present, including photosensitivity. Frontocentral regional hyperexcitability also seems to be a feature of JME clinically and electroencephalographically (19,20), and recent imaging and quantitative magnetic resonance (MR) studies also suggest morphologic changes compared with normal subjects, especially when myoclonus is present (21).

Prevention of such attacks during game play raises issues different from those of screen content and TV screen properties, which can be addressed by guidelines and by devices such as electronic filters and colored spectacles, because the seizures are triggered by the subject's participation rather than by passive exposure to the screen. Not playing videogames is an obvious solution, but adolescent and young adult patients may not comply with this advice. Some risk is unavoidable if the subject plays at all: this would presumably be reduced but not eliminated by drug treatment, avoiding factors such as prolonged play, sleep deprivation, drugs, and alcohol; and by stopping play if absence or myoclonus occurs, although triggered absences may not be noticed. We also suggest that patients who continue to play these games not play alone.

REFERENCES

1. Kasteleijn-Nolst Trenité DGA, Silva AM, Ricci S, et al. Video-game epilepsy: a European study. *Epilepsia* 1999;40(suppl 4):70–4.
2. Hennessy M, Binnie CD. Photogenic partial seizures. *Epilepsia* 2000;41:59–64.
3. Ferrie CD, De Marco P, Grunewald RA, et al. Video game induced seizures. *J Neurol Neurosurg Psychiatry* 1994;57:925–31.
4. Jeavons PM, Harding GFA. *Photosensitive epilepsy*. London: Heinemann, 1975.
5. Ricci S, Vigevano F. The effect of video-game software in video-game epilepsy. *Epilepsia* 1999;40(suppl 4):31–7.
6. Funatsuka M, Fujita M, Shirakawa S, et al. Study on photo-pattern sensitivity in patients with electronic screen game-induced seizures (ESGS): effects of spatial resolution, brightness, and pattern movement. *Epilepsia* 2001;42:1185–97.
7. Independent Television Commission guidelines: www.itc.org.uk/uploads/Guidelines_for_assessing_flashing_images_&_regular_patterns_in_television.pdf (accessed 2002;05–12).
8. Binnie CD, Wilkins AJ. Visually induced seizures not caused by flicker (intermittent light stimulation). In: Zifkin BG, Andermann F, Beaumanoir A, et al., eds. *Reflex epilepsies and reflex seizures: advances in neurology*. Philadelphia: Lippincott-Raven Press, 1998:123–38.
9. Harding GFA, Jeavons PM. *Photosensitive epilepsy*. London: MacKeith Press, 1994.
10. Ricci S, Vigevano F, Manfredi M, et al. Epilepsy provoked by television and video games: safety of 100-Hz screens. *Neurology* 1998;50:790–3.
11. Nomura M, Takahashi T, Kamijo K, et al. A new adaptive temporal filter: application to photosensitive seizure patients. *Psychiatry Clin Neurosci* 2000;54:685–90.
12. Appleton R, Beirne M, Acomb B. Photosensitivity in juvenile myoclonic epilepsy. *Seizure* 2000;9:108–11.
13. Shirakawa S, Funatsuka M, Osawa M, et al. A study of the effect of color photostimulation from a cathode-ray tube (CRT) display on photosensitive patients: the effect of alternating red-cyan flicker stimulation. *Epilepsia* 2001;42:922–9.
14. Takahashi T, Tsukahara Y. Pocket Monster incident and low luminance visual stimuli: special reference to deep red flicker stimulation. *Acta Paediatr Jpn* 1998;40:631–7.
15. Takahashi Y, Sato T, Goto K, et al. Optical filters inhibiting television-induced photosensitive seizures. *Neurology* 2001;57:1767–73.
16. Shiraishi H, Fujiwara T, Inoue Y, et al. Photosensitivity in relation to epileptic syndromes: a survey from an epilepsy center in Japan. *Epilepsia* 2001;42:393–7.
17. Matsuoka H, Takahashi T, Sasaki M, et al. Neuropsychological EEG activation in patients with epilepsy. *Brain* 2000;123:318–30.
18. Inoue Y, Seino M, Tanaka M, et al. Epilepsy with praxis-induced epilepsy. In: Wolf P, ed. *Epileptic seizures and syndromes*. London: John Libbey, 1994:81–91.
19. Panayiotopoulos CP, Obeid T, Tahan AR. Juvenile myoclonic epilepsy: a 5-year prospective study. *Epilepsia* 1994;35:285–96.
20. Wolf P. Regional manifestation of idiopathic epilepsy: introduction. In: Wolf P, ed. *Epileptic seizures and syndromes*. London: John Libbey; 1994:265–7.
21. Woermann FG, Free SL, Koepp MJ, et al. Abnormal cerebral structure in juvenile myoclonic epilepsy demonstrated with voxel-based analysis of MRI. *Brain* 1999;122:2111–8.