

Life-threatening cardiac arrhythmia and sudden death during electronic gaming: An international case series and systematic review

Claire M. Lawley, MBBS, BSc(Med)Hons, PhD, FRACP,^{*†‡} Matthew Tester, BSc,[§] Shubhayan Sanatani, BSc, MD, FHRS,[§] Terence Prendiville, MD,^{||} Cheyenne M. Beach, MD,[¶] Jeffrey M. Vinocur, BA, MD,^{¶#} Minoru Horie, MD, PhD,^{**} Jae-Sun Uhm, MD,^{††} Apichai Khongphatthanayothin, MD,^{†‡##} Mark D. Ayers, MD,^{§§} Luke Starling, BSc(Hons), MBBS, FRCPCH,[‡] Yoko Yoshida, MD,^{|||} Maully J. Shah, MBBS, FHRS,^{¶¶} Jonathan R. Skinner, MBChB, FHRS, MD,^{*} Christian Turner, MBBS, FRACP^{*}

From the ^{*}The Heart Centre for Children, Sydney Children's Hospitals Network, Sydney, New South Wales, Australia, [†]The University of Sydney Children's Hospital Westmead Clinical School, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, Australia, [‡]Department of Paediatric Cardiology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom, [§]Children's Heart Centre, The University of British Columbia, Vancouver, British Columbia, Canada, ^{||}Department of Cardiology and Cardiac Surgery, Children's Health Ireland at Crumlin, Dublin, Republic of Ireland, [¶]Department of Pediatrics, Division of Pediatric Cardiology, Yale University School of Medicine, New Haven, Connecticut, [#]Department of Pediatrics, University of Rochester School of Medicine and Dentistry, Rochester, New York, ^{**}Department of Cardiovascular Medicine, Shiga University of Medical Science, Shiga, Japan, ^{††}Department of Cardiology, Yongin Severance Hospital, College of Medicine, Yonsei University, Yongin, Gyeonggi-do, Republic of Korea, ^{‡‡}Department of Cardiology, Yongin Severance Hospital, College of Medicine, Yonsei University, Yongin, Gyeonggi-do, Republic of Korea, ^{§§}Department of Pediatrics, Division of Pediatric Cardiology, Pediatric Electrophysiology, Indiana University School of Medicine, Indianapolis, Indiana, ^{|||}Department of Pediatric Electrophysiology, Osaka City General Hospital, Miyakojima-hondori, Miyakojima-ku, Osaka, Japan, ^{¶¶}Department of Pediatrics, University of Pennsylvania Perelman School of Medicine, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, and ^{##}Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

BACKGROUND Electronic gaming has recently been reported as a precipitant of life-threatening cardiac arrhythmia in susceptible individuals.

OBJECTIVE The purpose of this study was to describe the population at risk, the nature of cardiac events, and the type of game linked to cardiac arrhythmia associated with electronic gaming.

METHODS A multisite international case series of suspected or proven cardiac arrhythmia during electronic gaming in children and a systematic review of the literature were performed.

RESULTS Twenty-two patients (18 in the case series and 4 via systematic review; aged 7–16 years; 19 males [86%]) were identified as having experienced suspected or proven ventricular arrhythmia during electronic gaming; 6 (27%) had experienced cardiac arrest,

and 4 (18%) died suddenly. A proarrhythmic cardiac diagnosis was known in 7 (31%) patients before their gaming event and was established afterward in 12 (54%). Ten patients (45%) had catecholaminergic polymorphic ventricular tachycardia, 4 (18%) had long QT syndrome, 2 (9%) were post-congenital cardiac surgery, 2 (9%) had "idiopathic" ventricular fibrillation, and 1 (after Kawasaki disease) had coronary ischemia. In 3 patients (14%), including 2 who died, the diagnosis remains unknown. In 13 (59%) patients for whom the electronic game details were known, 8 (62%) were war games.

CONCLUSION Electronic gaming can precipitate lethal cardiac arrhythmias in susceptible children. The incidence appears to be low, but syncope in this setting should be investigated thoroughly. In children with proarrhythmic cardiac conditions, electronic war games in particular are a potent arrhythmic trigger.

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KEYWORDS Arrhythmia; Syncope; Sudden cardiac death; Electronic gaming; Adolescent

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Introduction

There have been recent case reports of children and adolescents experiencing suspected or proven cardiac arrhythmia during electronic gaming.^{1,2} Subsequent proarrhythmic cardiac diagnoses have had significant implications for these children and their families. The pathophysiological basis for this phenomenon is attributed to adrenergic stimulation related to the emotionally charged electronic gaming environment.^{1,2}

While competitive sport and certain high-risk activities³ are known to precipitate arrhythmic events in susceptible individuals, electronic gaming has not typically been included in the counseling provided to families with proarrhythmic diagnoses. Electronic gaming is a prevalent pastime in children and adolescents. In adolescents deemed to be at risk during competitive sporting activity, electronic gaming may be encouraged under the false premise that it may represent a safe alternative to higher-risk sports. The prevalence of electronic gaming–induced cardiac arrhythmia has not been investigated and would provide important background information for such counseling.

The primary purpose of this study was to seek further examples of electronic gaming–induced cardiac arrhythmia, identify the population who may be at particular risk, identify the types of arrhythmias seen and the nature of the electronic games most commonly implicated, and gauge the significance of the problem.

Methods

Case series

A multisite case series of children and adolescents experiencing suspected or proven cardiac arrhythmia during electronic gaming was undertaken. Case identification was undertaken via direct report by practitioners involved in the diagnosis and treatment of children and adolescents with heart rhythm disorders. An international callout via e-mail, word of mouth at scientific meetings, and in professional discussions for cases was made. In 1 instance, the authors were contacted directly as a result of a previous publication on the topic.¹

Electronic gaming was defined as playing any game that used electronics to create a system with which a player can interact. This included handheld electronic games, console-based electronic games, and games based on a computer and stand-alone systems such as electromechanical arcade games. The term “suspected or proven cardiac arrhythmia” was left broad and included symptoms that might represent an arrhythmia such as palpitations or syncope and any arrhythmia documented via an automated external defibrillator, insertable cardiac monitor, implantable cardioverter-defibrillator (ICD), or external cardiac rhythm monitoring

(such as a Holter monitor or surface electrocardiogram) at the time of event.

Participating centers undertook required institutional ethics standards for inclusion in an international case series including informed consent of the patients and families involved.

Centers provided de-identified information regarding patient demographic characteristics, the nature of the event during gaming, underlying cardiac diagnosis, family history, and subsequent clinical course. De-identified data were then evaluated.

Systematic review

A systematic search of Medline, PubMed, Embase, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Library was undertaken to identify relevant studies including cases of arrhythmic events during electronic gaming. Search terms included “video games” AND (‘syncope’ ‘faintness’ OR ‘arrhythmias, cardiac’ ‘heart arrhythmia’ OR ‘death, sudden, cardiac’ ‘sudden cardiac death’ OR ‘heart arrest’, OR ‘tachycardia, ventricular’ ‘heart ventricle tachycardia’ OR ‘ventricular fibrillation’ ‘heart ventricular fibrillation’). The “explode” function was used in each case. Language restrictions were not applied. Duplicates were removed. If cases were already included in the case series, the article was excluded. Article titles and abstracts were evaluated for suitability of inclusion. The full text of these remaining studies was reviewed. Reference lists were searched for other relevant articles. Eligible study types were randomized controlled trials, clinical trials, cohort studies, cross-sectional studies, case series, and case reports.

The primary outcome of interest was the occurrence of an arrhythmic event, syncope, or cardiac arrest during electronic gaming. Data extraction from each identified article was undertaken. Information extracted included patient demographic characteristics, the nature of the event during electronic gaming, underlying cardiac diagnosis including genetic results, initial management, and the subsequent clinical course. Extracted data were tabulated.

Genetic variants

The reporting of genetic variants from different centers was variable. For cases with sufficient information about the variant, no classification, or a “variant of uncertain significance” (VUS) classification, variants were reassessed using VarSome (<https://varsome.com>; accessed February 2, 2022⁴) with the inclusion of known clinical data.

Results

Systematic review results

Through the database search, 69 articles were identified. After exclusion of duplicates, there were 51 unique records.

These 51 records were screened (review of titles and/or abstracts), with 6 relevant articles identified. Two contained cases included in the case series and as such were excluded.^{1,2} Data retrieval was undertaken from the remaining 4 records.^{5–8} No randomized controlled trials, clinical trials, cohort studies, or cross-sectional studies were identified. The articles consisted of case series and case reports. Figure 1 outlines the process of selection of the studies for the systematic review.

Cases

Eighteen patients experiencing suspected or proven cardiac arrhythmia during electronic gaming were identified through the case series. Combined with the 4 patients identified through systematic literature review, a total of 22 patients experiencing suspected or proven cardiac arrhythmia during electronic gaming were identified.

Of the 22 patients, 3 (14%) were female. Age at the time of the event ranged from 7 to 16 years. Reported events included palpitations and/or chest pain, presyncope, syncope with return of consciousness, cardiac arrest, and sudden death. Sudden death occurred in 4 (18%) patients. Examples of the arrhythmias documented are shown in Figure 2.

A total of 19 (86%) of the 22 patients had a proarrhythmic diagnosis. In 7 (32%) patients the diagnosis had been established before the event during electronic gaming. This included 3 (14%) patients with long QT syndrome (LQTS), 3 (14%) with catecholaminergic polymorphic ventricular tachycardia (CPVT), and 1 (5%) with “idiopathic” ventricular fibrillation with no relevant genetic variants identified. In 12 (55%) patients the diagnosis was made after the event during electronic gaming. Of the 19 (86%) patients with proarrhythmic diagnoses, 10 (46%) patients had CPVT, 4 (18%) patients had LQTS, 2 (9%) patients had post-cardiac surgery, 2 (9%) patients were diagnosed with idiopathic ventricular fibrillation, and 1 (5%) patient had an anterior myocardial infarction due to a large left coronary aneurysm attributed to “missed” Kawasaki disease. In 2 deceased patients and 1 surviving patient, a diagnosis has not yet been reached. Patient characteristics, nature of the event during electronic gaming, and details of any cardiac diagnosis are summarized in Table 1.

In all instances, the game being played was console- or computer-based except 1 patient who was watching an arcade game. Information regarding the specific electronic game being played during the event was available for 13 (59) patients. In 8 cases this was a war game. The stage of play at the time of the event was known in 7 (32%) patients, 6 of whom had just won or lost and one of these was jumping up and down in excitement. The other patient was fighting with his sibling for the electronic game controller at the time of the event.

For patients without a previously established diagnosis, in keeping with previous guidelines for the investigation of syncope and suspected ventricular arrhythmia,^{9,10} patients typically underwent cardiac screening including a combination of electrocardiogram, echocardiogram, ambulatory monitoring, and stress testing (pharmacological or exercise) to help establish a diagnosis. Genetic investigations were performed at some centers. Subsequent testing of family members was undertaken in some instances, leading to diagnoses in multiple family members.

Management varied on the basis of the severity of the presenting episode, local institutional practice, and patient and family preference. Of the 7 (32%) patients with an arrhythmic diagnosis made before their event during electronic gaming, 6 were prescribed some form of β -blocker medicine at the time of their event. The use of medication in the seventh patient was not known: this patient was identified through the systematic review. Two patients already had an ICD in situ, and 1 had an insertable cardiac monitor. None had undergone a previous cardiac sympathetic denervation. At last follow-up, of the 18 surviving patients, an additional 8 (44%) had been implanted with an ICD and 2 had undergone cardiac sympathetic denervation. Seventeen (94%) were on some form of antiarrhythmic medication. Five (28%) patients had subsequent episodes of arrhythmia during electronic gaming; 4 of these were on treatment at the time. Diagnoses and management are summarized in Table 2.

Seventeen (77%) of the 22 patients had results of genetic testing available, with potentially relevant genetic variants identified in 14 (63%) patients. The genetic variants are outlined in Table 1, including reclassifications based on VarSome.⁴ It was not usually known whether the variants were de novo; de novo status would likely have contributed to variant classification achieving at least “likely pathogenic.”

Of the 10 patients with CPVT, 9 had a ryanodine receptor 2 RyR2 variant, classified as “pathogenic” in 1 patient, “likely pathogenic” in 3 patients, “likely pathogenic/VUS” in 4 patients, and not classifiable in 1 patient. One patient with CPVT had 2 RyR2 variants, the first classified as “likely pathogenic/VUS” and the second as “VUS.” One patient with CPVT had a *CALM2* variant, classified as “likely pathogenic.” All 4 patients with LQTS had *KCNH2* variants, which were classified as “pathogenic” in 3 patients and “VUS” in 1 patient. One patient had 2 *KCNH2* variants, the first of which was classified pathogenic and second of which was classified as “VUS” and 1 patient had a “pathogenic” *KCNQ1* variant, in addition to

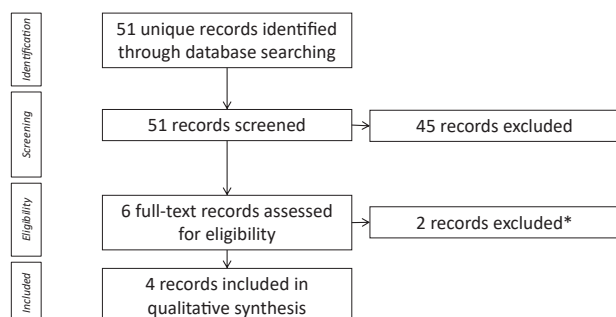


Figure 1 Process of selection of the studies for the systematic review.

*Records excluded as containing cases already included in the case series.

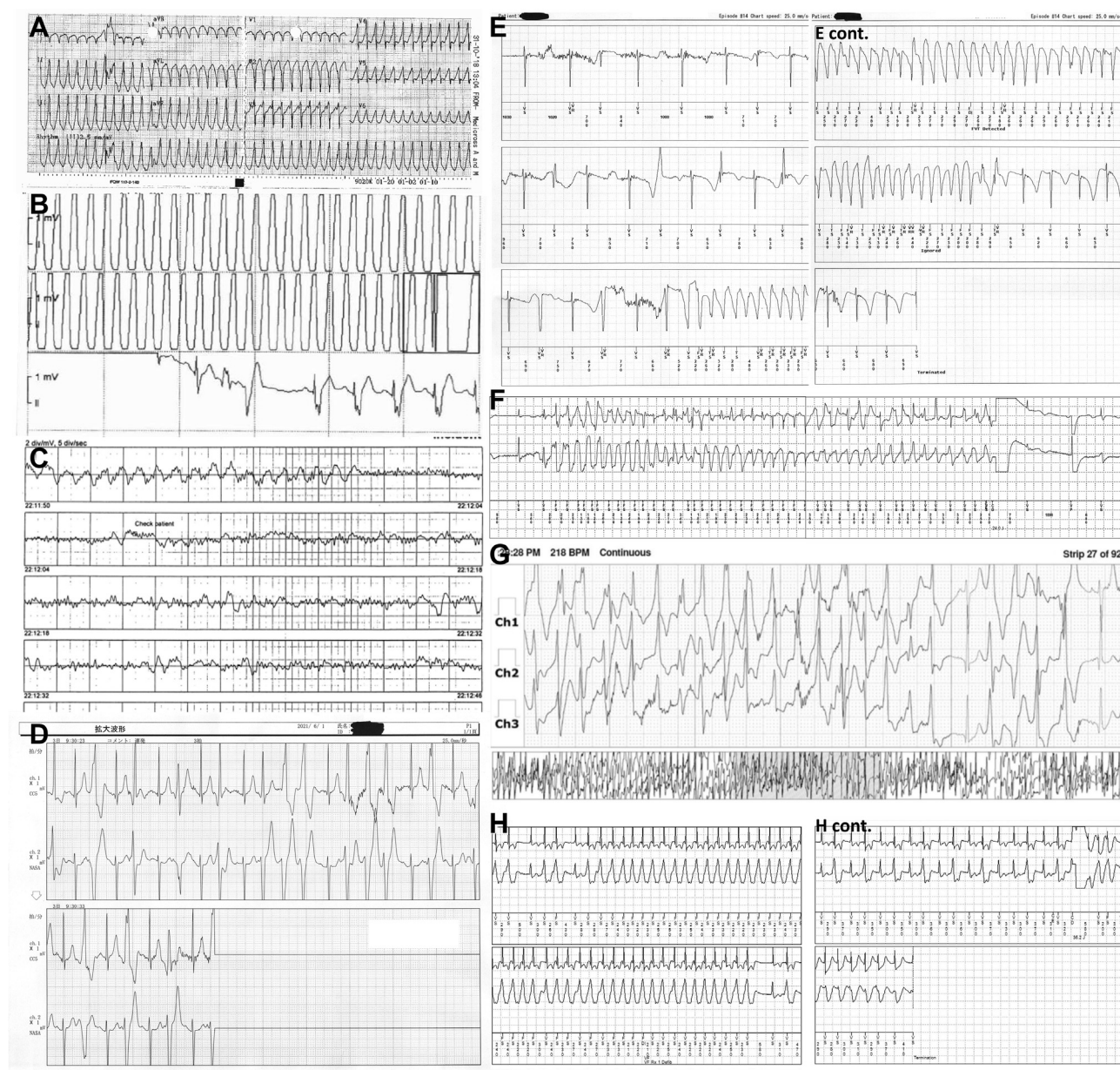


Figure 2 Examples of cardiac arrhythmia with onset during electronic gaming. **A:** Case 8: 12-lead electrocardiogram taken at the time of presentation to the emergency department with presyncope that started during electronic gaming, demonstrating ventricular tachycardia (VT). **B:** Case 8: implantable cardioverter-defibrillator (ICD) recording of VT and appropriate discharge at the subsequent event during electronic gaming. **C:** Case 10: automated external defibrillator recording at the time of arrest during electronic gaming, demonstrating ventricular fibrillation. **D:** Case 11: Holter during electronic gaming, demonstrating polymorphic ventricular ectopy/nonsustained VT. **E:** Case 12: implantable cardiac monitor during electronic gaming, demonstrating VT (torsades de pointes [TdP]). **F:** Case 13: ICD recording during electronic gaming, demonstrating VT (TdP). **G:** Case 15: Holter during electronic gaming, demonstrating polymorphic VT. **H:** Case 16: ICD recording during electronic gaming, demonstrating monomorphic VT and subsequent shock (delivered after reversion to sinus rhythm due to the programming algorithm).

a “pathogenic” *KCNH2* variant. Of the remaining 3 patients with genetic testing results available, 1 patient had a VUS in *RyR2* without a definite CPVT phenotype and in 2 patients no relevant variants identified. Five patients did not have genetic testing results; in 3, genetic testing was not undertaken because of another explanation for the arrhythmia (post-cardiac surgery in 2 and coronary artery-related ischemia in 1), and in 2 deceased patients, no genetic information was available.

Discussion Findings

This international case series and systematic review presents a total of 22 cases of suspected or proven cardiac arrhythmia during electronic gaming. It includes 6 resuscitated cardiac arrests and 4 sudden deaths. As far as we can ascertain, this is the first report of multiple sudden deaths occurring during electronic gaming. Given the large number of centers

Table 1 Patient characteristics, nature of the event during electronic gaming, and cardiac diagnosis

Case no.	Gender, age (y)	Preexisting arrhythmic cardiac diagnosis	Event (including rhythm if known)	Resuscitation	Cardiac diagnosis	Genetic variant found, classification
1	M, 13	N	Sudden death	CPR, unsuccessful	CPVT	RyR2:c.1069G>A, p.Gly357Ser, "pathogenic"
2	M, 15	N	Sudden death	CPR, attempted cardioversion unsuccessful		
3	M, 14	N	Cardiac arrest (VF)	CPR, adrenalin, cardioversion		Negative genetic panel
4	M, 16	N	Syncope	Spontaneously regained consciousness	CPVT	RyR2:c.13763T>C, p.Ile458Thr, "likely pathogenic,"* highly conserved position, not seen in gnomAD, in silico support
5	M, 10	N	Palpitations, syncope	Spontaneously regained consciousness	CPVT	RyR2:c.7600C>G, p.Leu2534Val, "likely pathogenic"
6	M, 11	N	Palpitations, syncope	Spontaneously regained consciousness	LQTS	KCNH2:c.2399-28 del, "pathogenic"
7	M, 15	Y	Palpitations	Spontaneously regained consciousness	CPVT	CALM2:c.248A>G, de novo, "likely pathogenic"
8	M, 15	N	Presyncope (VT)	Cardioversion	Repaired complex CHD	
9	F, 9	Y	Syncope	Spontaneously regained consciousness	LQTS	Two variants: KCNH2:c.1655T>A (p.Leu552 [†]), "pathogenic" and KCNH2:c.2128G>A (p.Gly710Ser), "VUS"
10	M, 10	N	Cardiac arrest (VF)	CPR, cardioversion	CPVT	RyR2:p.Met2192Leu, "VUS/likely pathogenic,"* highly conserved position, not seen in gnomAD, in silico support
11	M, 10	Y	Palpitation (VT)	Spontaneously resolved	CPVT	RyR2:c.14311G>A, p.Val4771Ile, "likely pathogenic"
12	F, 9	Y	Syncope (VT)	Spontaneously regained consciousness	LQTS	Two variants: KCNQ1:c.691C>T, p.Arg231Cys, "pathogenic" and KCNH2:c.1936_1936delC, "pathogenic"
13	F, 8	Y	Cardiac arrest (VF)	Cardioversion by ICD	LQTS	KCNH2:c.1864C>T, p.Leu622Phe, "VUS"
14	M, 7	N	Cardiac arrest (VF)	Cardioversion in the emergency department	CPVT	RyR2:c.1811A>T, "VUS/likely pathogenic,"* highly conserved position, not seen in gnomAD, in silico support
15	M, 9	N	Syncope	Spontaneously regained consciousness	CPVT	RyR2:c.12454A>C, p.Ile4152Leu, designated as "VUS" by the laboratory, but *highly conserved position, not seen in gnomAD, hot spot and in silico support, therefore designated "likely pathogenic"
16	M, 16	Y	ICD discharge (VT)	Returned to sinus rhythm after ICD discharge	Idiopathic VF	Nil detected (comprehensive arrhythmia and cardiomyopathy panel performed)
17	M, 10	N	Cardiac arrest (VF)	CPR, cardioversion	Idiopathic VF	RyR2:c.341T>A, p.Leu114His, heterozygous, also present in the mother designated "VUS" by the laboratory, but *highly conserved position, not seen in gnomAD, in silico support, therefore designated "VUS/likely pathogenic"
18	M, 15	N	Cardiac arrest (VF)	CPR, cardioversion	Postsurgical valve replacement in Marfan syndrome	
Gutierrez et al ⁵	M, 14	N	Chest pain, palpitations, eventual cardiac arrest (VT)	IV medication, successful DC cardioversion after arrest	Postinfarction [‡]	

(Continued)

Table 1 (Continued)

Case no.	Gender, age (y)	Preexisting arrhythmic cardiac diagnosis	Event (including rhythm if known)	Resuscitation	Cardiac diagnosis	Genetic variant found, classification
Ito et al ⁶ Takayama et al ⁷	M, 7 M, 12	N Y	Syncope Sudden death		CPVT CPVT	RyR2 missense variant Two variants: RyR2:p.Gln3304Glu, "VUS/likely pathogenic"* and RyR2:p.Ala4741Val, "VUS,"* not moderately conserved, but absent from gnomAD, in silico support Family had a negative genetic panel
Teman Yarden et al ⁸	M, 14	N	Sudden death			

CHD = congenital heart disease; CPR = cardiopulmonary resuscitation; CPVT = catecholaminergic polymorphic ventricular tachycardia; DC = direct current; F = female; ICD = implantable cardioverter-defibrillator; IV = intravenous; LQTS = long QT syndrome; M = male; N = no; RyR2 = ryanodine receptor 2; VF = ventricular fibrillation; VT = ventricular tachycardia; VUS = variant of uncertain significance; Y = yes.
*Pathogenicity assessed using VarSome (<https://varsome.com>; accessed February 2, 2022⁴).

[†]Predicted consequence only.

[‡]Missed Kawasaki disease with large left coronary artery aneurysm and transmural infarct of the basal anterior and anterolateral left ventricle.

approached for cases across the world, it is clear that this phenomenon is uncommon, but it is clearly prevalent internationally and may represent a meaningful issue in children with arrhythmic conditions. Electronic gaming can pose a significant arrhythmic risk; it can be lethal in children with predisposing (but often previously unrecognized) arrhythmic conditions.

In this series and subsequent systematic review, 14 patients (63%) were found to have potentially relevant genetic variants. All patients with diagnoses of CPVT or LQTS had potentially relevant genetic variant. Three patients had 2 potentially relevant variants. The relatively high yield of pathogenic/likely pathogenic variants seen, compared to previously published work on the individual conditions^{11–15} and the entity of sudden unexplained death,^{16,17} may be related to a relatively high pretest probability of identifying an inherited arrhythmia syndrome in patients presenting with arrhythmia during electronic gaming.

Proposed mechanisms

The mechanism by which electronic gaming precipitates cardiac arrhythmia remains incompletely understood. Electronic games increase the heart rate of participants without arrhythmic diagnoses.^{18,19} Mental stress and extreme emotion alter cardiac electrophysiological properties.^{20–22} Common sense observation and anecdotal descriptions lead to the inevitable conclusion that extreme excitement, possibly with added emotional stress with adrenaline release, triggers arrhythmic events during electronic gaming. The occurrence of suspected or proven arrhythmic events at times of heightened emotion during electronic gaming, such as when the participant is about to win or has just won or lost, is in keeping with this. The number of events seen when participating in electronic war games is of interest when considering the overrepresentation of cardiac events at times of mental and emotional stress in first responders and tactical athletes.^{23,24}

Uncontrolled intracellular sarcoplasmic calcium release due to adrenergic stimulation is a proven trigger for events in individuals with CPVT.^{25–27} A diagnosis of CPVT in 10 (45%) of the 22 cases reported here supports the theory that adrenergic stimulation plays a role in the pathophysiology of the arrhythmic events seen. Four subjects reported here had LQTS, with *KCNQ1* and/or *KCNH2* variants. Exercise and associated adrenaline release is a typical trigger for cardiac events in LQTS type 1.²⁸ Recent coculture of human pluripotent sympathetic neuronal cells with cardiac cells from the same patient has shown that there is a link between sympathetic stimulation and arrhythmia in LQTS type 1.²⁹ However, emotional excitement and startle are more typical for LQTS type 2; it is interesting that these 2 types are present here during electronic gaming. In addition, the presumptive reentrant-based ventricular tachyarrhythmias (occurring in individuals post-cardiac surgery and with myocardial ischaemia) also appear susceptible to the hyperadrenergic state, which is thought to exist during intense electronic gaming.

Table 2 Demographic characteristics, suspected or proven cardiac arrhythmic event during electronic gaming details, subsequent management, and outcome at follow-up

Demographic characteristic	n (%)
Female	3 (14)
Age range (y)	7–16
Sudden death	4 (18)
Proarrhythmic cardiac diagnosis	19 (86)
CPVT	10 (45)
LQTS	4 (18)
“Idiopathic VF”	2 (9)
Other*	3 (14)
Potentially relevant genetic variant identified	14 (63)
Management†	
Medical therapy	17 (95)
ICD in situ	10 (56)
Cardiac sympathetic denervation	2 (11)
Subsequent events during electronic gaming while on treatment‡	4 (22)

CPVT = catecholaminergic polymorphic ventricular tachycardia; ICD = implantable cardioverter-defibrillator; LQTS = long QT syndrome; VF = ventricular fibrillation.

*Other proarrhythmic diagnoses included arrhythmia in patients who had cardiac surgery (n = 2) and ischemic heart disease after missed Kawasaki disease (n = 1).

†Fslor 18 surviving patients.

‡One additional patient had further events during gaming before treatment commencement.

Recommendations

In light of this series, we advocate that a clinical history of syncope during electronic gaming mandates similar cardiac investigations to syncope during exertion, including, at a minimum, a family history, electrocardiogram, and stress test.^{10,30} This is important in children, where description of symptoms suggestive of cardiogenic syncope may be vague. Where a specific inherited primary arrhythmia is suspected or diagnosed, the authors advocate genetic counseling and targeted molecular testing,⁹ given its high yield in this series and the implications this has for predictive testing within families.

Recommendations for the treatment of specific proarrhythmic conditions is established.^{3,9} While there is good evidence that medication adherence reduces cardiac event risk during sport in patients with underlying channelopathies (particularly CPVT),^{31,32} it is unclear whether the same is true in the setting of electronic gaming; 4 children had further events during electronic gaming while prescribed antiarrhythmic medication. Our experience would suggest that pharmacotherapy alone in some situations may be insufficient and additional treatment such as a secondary prevention medical device and surgical strategies may be required. In addition, just as counseling regarding safe participation in high-risk activities such as competitive sport is a cornerstone of management of individuals once an arrhythmic diagnosis has been made,³ we purport that advice regarding safe participation in electronic gaming should be provided. This may entail ensuring adherence to medical therapies and

optimizing dosage through rhythm monitoring while playing. It may also involve avoiding a particular video game that triggered a previous collapse. Dissemination of this counseling need is particularly important as electronic gaming may have previously been viewed as a “safe” alternative to competitive physical sports.

Limitations

Limitations of this study include its “opt-in” nature, potentially leading to an underestimation of case numbers. The systematic review seeks to partially address this concern but is reliant on the identification and reporting of these events. Events occurring in adults are not addressed here. It remains unknown whether the adult population is also at risk of arrhythmias during electronic gaming—no cases were found in the systematic review. One might anticipate a different profile of patients at risk, such as those with underlying cardiomyopathies and coronary ischemia.^{20,33} In addition, information on potential cofounders such as additional medical diagnoses, sleep practices, or use of stimulants in the group was not available.

Conclusion

Electronic gaming can precipitate lethal cardiac arrhythmias in susceptible children, and syncope in this setting should be investigated. Clinical history taking regarding syncopal events in children should include details of participation in exciting and emotionally charged activities such as electronic gaming at the time of the event. Counseling regarding safe participation in electronic gaming should be considered after a proarrhythmic cardiac diagnosis, particularly CPVT, has been made.

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