# Possible effects of insufficient sleep on brain structure and sudden death linked to video games

**Ph.D. thesis booklet**

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# I. List of abbreviations

| | |
|---|---|
| AC-PC line | anterior and posterior commissural line |
| ACTH | adrenocorticotropic hormone |
| ANOVA | analysis of variance |
| AV node | atrioventricular node |
| DSM-5 | Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition |
| ECG | electrocardiography |
| FPS | first-person shooter |
| GH | growth hormone |
| ICSD | International Classification of Sleep Disorders |
| IGD | internet gaming disorder |
| MCI | mild cognitive impairment |
| MP-RAGE | magnetisation-prepared rapid gradient echo |
| MRI | magnetic resonance imaging |
| MOBA | multiplayer online battle arena |
| REM | rapid eye movement |
| RTS | real-time strategy |
| RPG | role-playing game |
| SCN | suprachiasmatic nucleus |
| SPSS | Statistical Package for Social Sciencies |
| SWS | slow wave sleep |
| TPS | third-person shooter |

# II. Introduction

Sleep is the resting state of the human body. During sleep, the body regenerates, sleep affects the functioning of the immune and nervous systems, influences stress tolerance, plays an essential role in the process of learning and remembering (memory consolidation), and in ensuring the body's homeostasis and metabolic processes. A sufficient amount of sleep is therefore essential, the lack of which can lead to the development of various somatic (e.g. cardiovascular diseases, tumors) and mental (e.g. depression) diseases.

The circadian (around 24-hour) rhythm of biological processes is a general feature of the living world, the most striking of which is the biphasic wake-sleep cycle. The cyclicity is controlled by the **suprachiasmatic nucleus** (SCN) located in the anterior hypothalamus, which is also called the pacemaker of circadian rhythms and the biological clock, and in addition to sleep-wakefulness, it also controls the circadian rhythm of many other physiological parameters (core temperature, ACTH, cortisol blood level).

### II.1. Sleep structure

During sleep, two main sleep phases can be distinguished, the so-called NREM (Non-Rapid Eye Movement) and REM (Rapid Eye Movement) phase. Based on the depth of NREM sleep, it can be further divided into 4 stages. The 1st-2nd stage is also called "superficial" sleep, which is clearly separated from „deep" sleep (the 3rd-4th stage). The latter is characterized by a predominance of slow delta waves, hence the name SWS (Slow Wave Sleep). In the physiological case, after falling asleep, the 1st REM phase is reached through the stages of NREM sleep, which deepens and then gradually becomes superficial, thus completing a sleep cycle (**Figure 1**). It lasts an average of 90 minutes and is repeated 4-6 times during a night's sleep. The first third of sleep is characterized by the dominance of deep sleep phases, and later on, the frequency and length of REM phases increase. 20-25 percent of total sleep in adults is REM sleep, the duration of which typically depends on age. In a newborn, for example, it makes up nearly 50 percent of the 17-18 hours of sleep.

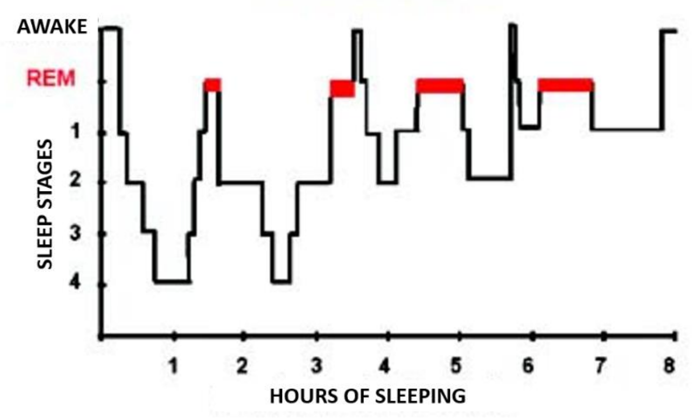



**Figure 1**: Sleep phases

## II.2. Sleep disorders

Based on the International Classification of Sleep Disorders (ICSD-3), we distinguish 6 main categories: insomnias, parasomnias (e.g. sleepwalking), sleep-related breathing disorders (e.g. obstructive sleep apnea syndrome), sleep-related movement disorders (e.g. restless legs syndrome), hypersomnias of central origin (e.g. narcolepsy) and circadian sleep disorders. They have many subgroups, on the basis of which we can distinguish about 90 sleep disorders. Two subgroups of circadian sleep disorders are more closely related to the topic of the dissertation, so I will discuss them in more detail.

Circadian sleep disorders:

- The characteristics of *Delayed Sleep Phase Disorder (DSPD)* are the following: The nighttime sleep period is at least 2 hours later than the socially accepted one. Sleep time is relatively constant, the sleep structure shows no abnormalities. As a result of the environmental pressure, a picture of chronic difficulty falling asleep and lack of sleep in the morning may develop. In the free-running position (holiday), the characteristic sleep period position is restored, and the patient becomes relaxed. The 24-hour rhythm is maintained. It mostly occurs in young people, often as a result of drinking coffee late, watching TV/internet at night. The core temperature curve is also postponed.
- During *Advanced Sleep Phase Disorder (ASPD)*, the nighttime sleep period is pushed forward by at least 2 hours. These individuals fall asleep too early and often wake up during the night. The length of sleep is also normal here, the sleep structure shows no abnormalities. It is mainly typical of the older age group. In the vast majority of cases, it shows familiarity (per2 gene mutation). The core temperature curve also moves forward.

Those who go to bed late are called "owls" and those who get up early are called "larks".

## II.3. Need for sleep, short and long sleepers

The average sleep time is 7-8 hours, those who sleep significantly less are called short sleepers, and those who sleep significantly more are called long sleepers. It is characteristic of short sleepers that they need no more than 5-6 hours of sleep. Their sleep is continuous, when they wake up they are fresh and rested, they are energetic during the day, and they feel good. The condition that begins in childhood or young adulthood is typical for

4% of the population. It is slightly more common in women and shows familial accumulation. Long sleepers, on the other hand, need 10-12 hours of sleep per day, after which they wake up refreshed and their daily performance is favorable. It affects 2% of the population, is noticeable since childhood, and has a discrete male predominance. Although they do not cause subjective complaints, both sleep patterns that differ from the average are difficult to reconcile with everyday life and social norms.

The above so-called natural short sleepers should be distinguished from individuals who cannot get enough sleep for some external reason (e.g. they can only go to bed late because of their duties and have to get up early for school/work) thereby suffering a lack of sleep.

### II.4. Harmful consequences of insufficient sleep

We have all experienced the unpleasant effects of acute or chronic sleep deprivation; difficulty to concentrate, reduced mental and physical performance, irritability, mood swings, to name just a few.

In addition to psychosocial aspects, insufficient sleep can also cause several metabolic and hormonal changes. With little sleep, the concentration of appetite reducing leptin can significantly decrease, while the level of appetite-stimulating ghrelin increases, which can lead to weight gain and obesity in the long term. Lack of sleep is accompanied by an increase in the level of the stress hormone, cortisol, and the sympathetic predominance of the vegetative nervous system as well, which can lead to carbohydrate metabolism disorders, reduced glucose tolerance and insulin sensitivity. While the hormonal effects of a single sleep deprivation are mostly resolved after the next restful sleep, the consequences of chronic sleep deprivation can be significantly more serious and are associated with an increased risk of cardiovascular and gastrointestinal diseases, diabetes and cancer.

In case of chronic sleep deprivation, structural brain anomalies can also be detected. In the first half of the thesis, we examined the role of sleep habits and sleep characteristics from this approach.

### II.5. Sleep insufficiency as a social problem

Compared to previous decades, both adults and children are sleeping less. Members of Generation Y (born between 1981 and 1995) encountered the Internet in their childhood, which is now part of their everyday life. The youngest members of Generation Z (born between 1995 and 2012) already have access to the Internet anytime, anywhere. According to The National Sleep Foundation's 2006 Sleep in America Poll, almost every adolescent typically has at least one electronic media device in their bedroom; and these are regularly used even after 9 p.m. The almost continuous online presence, stress, excitement, strenuous mental activity, frequent use of coffee and cigarettes, neglect of sleep hygiene rules increase arousal, i.e. raise the level of alertness, which leads to insomnia and frequent sleep interruptions, leads to shortening and insufficiency of sleep time.

Sleep deprivation due to overuse of electronic media devices can sometimes reach frightening proportions, and many such cases have been associated with serious health damage or death. In the second half of the thesis, we analyzed this topic.

## III. Relationship between sleep habits and hippocampal volume

### III. 1. Background

Hippocampal vulnerability has been demonstrated in several medical conditions including neurological and psychiatric disorders such as epilepsy, depression, schizophrenia and post-traumatic stress disorder. These conditions are also shown to be associated with multiple sleep alterations. Sleep disorders themselves may also be associated with decreased hippocampal volumes, a finding generally explained by chronic hyperarousal and associated elevations in the hypothalamus-pituitary-adrenal (HPA) axis-related hormones during sleep. So far only a single study has assessed the relation between sleep and hippocampal volumes in a non-clinical sample. This study demonstrated a positive correlation between sleep duration and bilateral hippocampal volume in healthy children. Studies investigating the relationship between sleep and specific brain volumes typically examine sleep duration but not other sleep measures. Since slow wave sleep (SWS) and rapid eye movement (REM) sleep differ in their physiological correlates and timing within the circadian cycle, a delay in sleep onset may alter sleep structure, which may have negative consequences. Sleep habits, such as timing of going to bed and waking up are known to be rather invariable within but variable between subjects. Here we sought to examine whether individual differences in regular bedtime, wake up time and sleep duration are associated with differences in hippocampal volumes in young healthy university students.

## III.2. Methods and subjects

*III.2.1. Subjects*

Based on an advertisement placed on notice boards at the University of Pécs, healthy right-handed, Caucasian university students without history of brain or sleep disorders, drug/alcohol abuse between age of 19 and 30 were recruited. Subjects completed a questionnaire about health issues and sleeping habits including regular bedtimes and wake up times. Sleep-related questions were focused on the last 12 months. 90 subjects were recruited (mean age ± SD: 23.1 ± 2.7 years), 37 males and 53 females. Subjects reported bedtime and wake up time in rounded hours. Sleep duration was calculated as a difference between the two. For each sleep variable we created three categories to include the extreme and medium values. For *bedtime* the early group included subjects going to bed at 21.00 or 22.00 hours, the medium group those going to bed at 23.00 or 00.00 hours (average time) while the late group included those going to bed at or later than 01.00 hours. For *waking up* the early group included those subjects waking up at 05.00 or 06.00 hours, the medium group those at 07.00, 08.00 or 09.00 hours (average time), while the late group included those waking up at or later than 10.00 hours. For *sleep duration* the short sleeper group contained those with sleep duration of 5 or 6 h, the medium group those with 7, 8 or 9 h, while the long sleeper group contained those with 10, 11 or 12 h of sleep. Cut-offs for creating these categories were determined to include about 15% of the subjects for the extreme categories. The study was approved by the Ethics Committee of the University of Pécs and all subjects gave written informed consent before each examination.

*III.2.2. MRI examinations*

All measurements were performed on the 3T Magnetom TRIO human whole-body MRI scanner (Siemens AG, Erlangen, Germany) with a 12-channel head coil in the Pécs Diagnostic Center. The total measurement time was approximately 7 minutes. For volumetric analysis, T1-weighted axial MPRAGE sequence was used. For standardized and accurate axial slice positioning the anterior and posterior commissural line (AC-PC line) was used as a reference determined by analysis of a T2-weighted turbo spin echo sequence measured in sagittal plane.

*III.2.3. MR data processing evaluation*

Freesurfer 4.4.0 was used for the whole evaluation. This software provides one of the most reliable automated brain segmentation methods for subcortical structures and allows us to assess the volume of the pre-defined brain structures in a large number of subjects.

Freesurfer's semi-automatic anatomical processing scripts were executed on all subjects' data. Manual verifications were performed after each script and manual adjustments were applied where it was necessary. To avoid bias due to differences in intracranial volumes, the volumes of right and left hippocampus was summed and divided by total intracranial volume. Thus, we used relative bilateral hippocampal volumes.

*III.2.4. Statistical analysis*

Statistical analyses were performed using SPSS 17.0 software. The relation between sleep variables and relative volume of the hippocampus was investigated using both univariate and multivariate models. First each sleep variable was analyzed in a separate analysis of variance (ANOVA) model with post-hoc t-tests to assess specific differences between groups. Then we constructed a multiple linear regression model to assess the independent contribution of bedtime and wake up time to hippocampal volumes. In the next step we entered sex and age as additional independent variables into the model to control for these potential confounders.

## III.3. Results

Number of subjects for each hour of the sleep variables is presented in **Figure 2**. Distribution of subjects with early, medium and late bedtimes and wake up times among the three sleep duration categories are shown in **Figure 3**. As can be seen the main difference between the sleep duration groups is that late bedtime occurs more frequently in the short sleeper group (as compared with the two other sleep duration groups) while late wake up is most frequent among long sleepers. There were more females than males in the study (37M/53F) and distribution according to sex was unequal according to the sleep variable groups: in the bedtime groups the ratio of males was 20, 42 and 56% in the early, medium and late groups, respectively. In the wake up groups male ratio was 15, 40 and 80% across early, medium and late groups. In the sleep duration groups male ratio was 44, 39 and 56% in the short, medium and long sleeper groups, respectively. Given the inhomogeneous distribution of genders among groups results were controlled also for gender effects in the multivariate analysis.

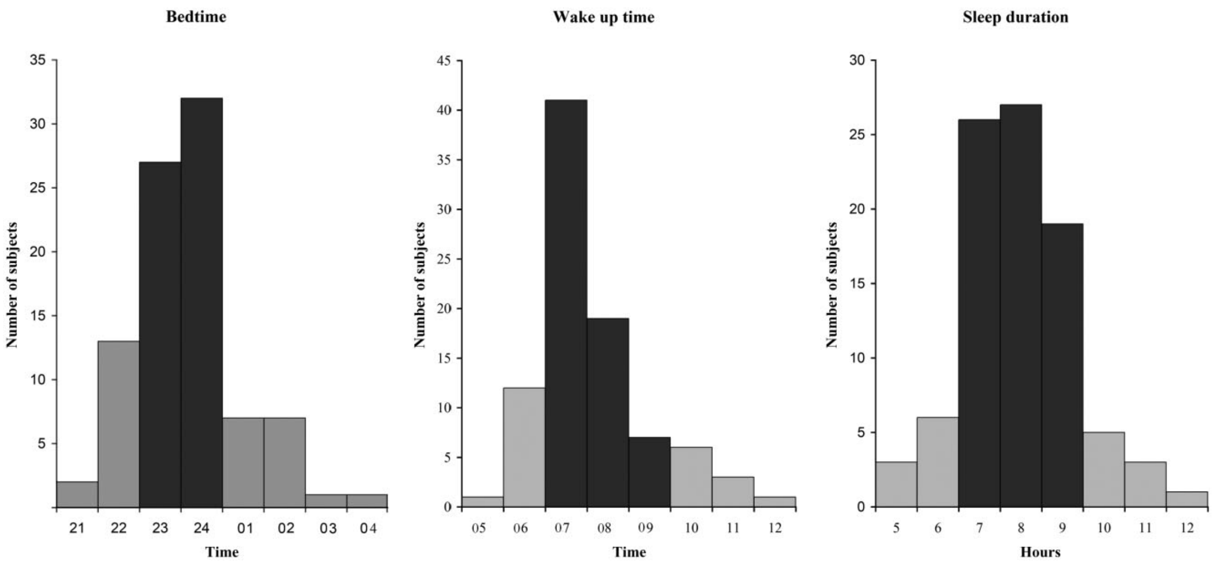
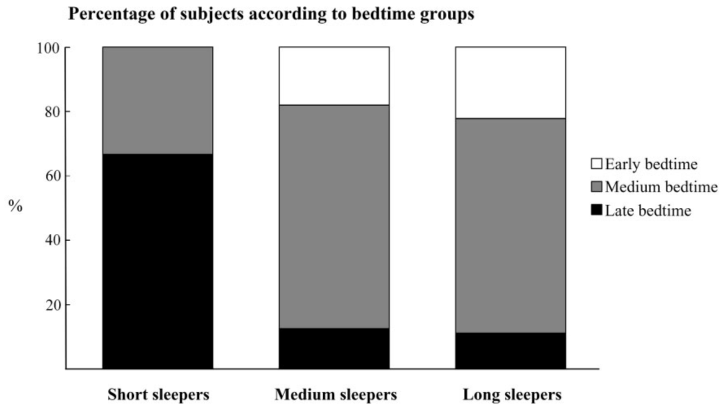



**Figure 2:** Histograms showing number of subjects according to bedtime, wake up time and sleep duration (number of hours of sleep). Extreme categories within each sleep variable (early and late categories in bedtime and wake up times as well as short and long sleeper categories) are indicated in light grey while the medium categories are denoted with dark grey.



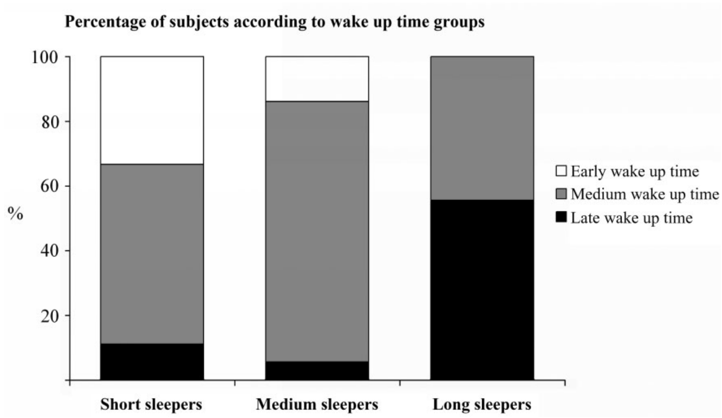




**Figure 3:** Histograms showing the distribution of subjects (as percentage) according to bedtime, wake up time groups across the sleep duration categories.

*III.3.1. Univariate analyses*

- Bedtime

ANOVA indicated significant group differences for bedtime (P = 0.007). Comparison of means indicated a progressive decrease in hippocampal volumes across the three groups from early to late **(Figure 4)**. T-tests revealed significantly smaller hippocampal volumes for the late bedtime subjects as compared with the medium bedtime (P = 0.033) as well as the early bedtime subjects (P = 0.005). Difference between the early bedtime and medium bedtime groups was marginally insignificant (P = 0.058). A scatterplot representing the relationship between relative hippocampal volumes and bedtime for each subject is presented in **Figure 5.**

- Wake up time

Neither ANOVA (P = 0.287) nor pairwise comparisons with t-test revealed significant differences between the three wake up time groups but there was a nonsignificant tendency for the late wake up group having smaller hippocampus as compared to the medium wake up group (P = 0.12; **Figure 4**).

- Sleep duration

ANOVA indicated a significant difference between groups (P = 0.009). Post-hoc t-test showed significantly larger hippocampal volumes for the medium sleep length group as compared with both short sleeper (P = 0.013) and long sleeper (P = 0.033) groups (**Figure 4**). Short sleepers and long sleepers did not significantly differ in hippocampal volume (P = 0.836).

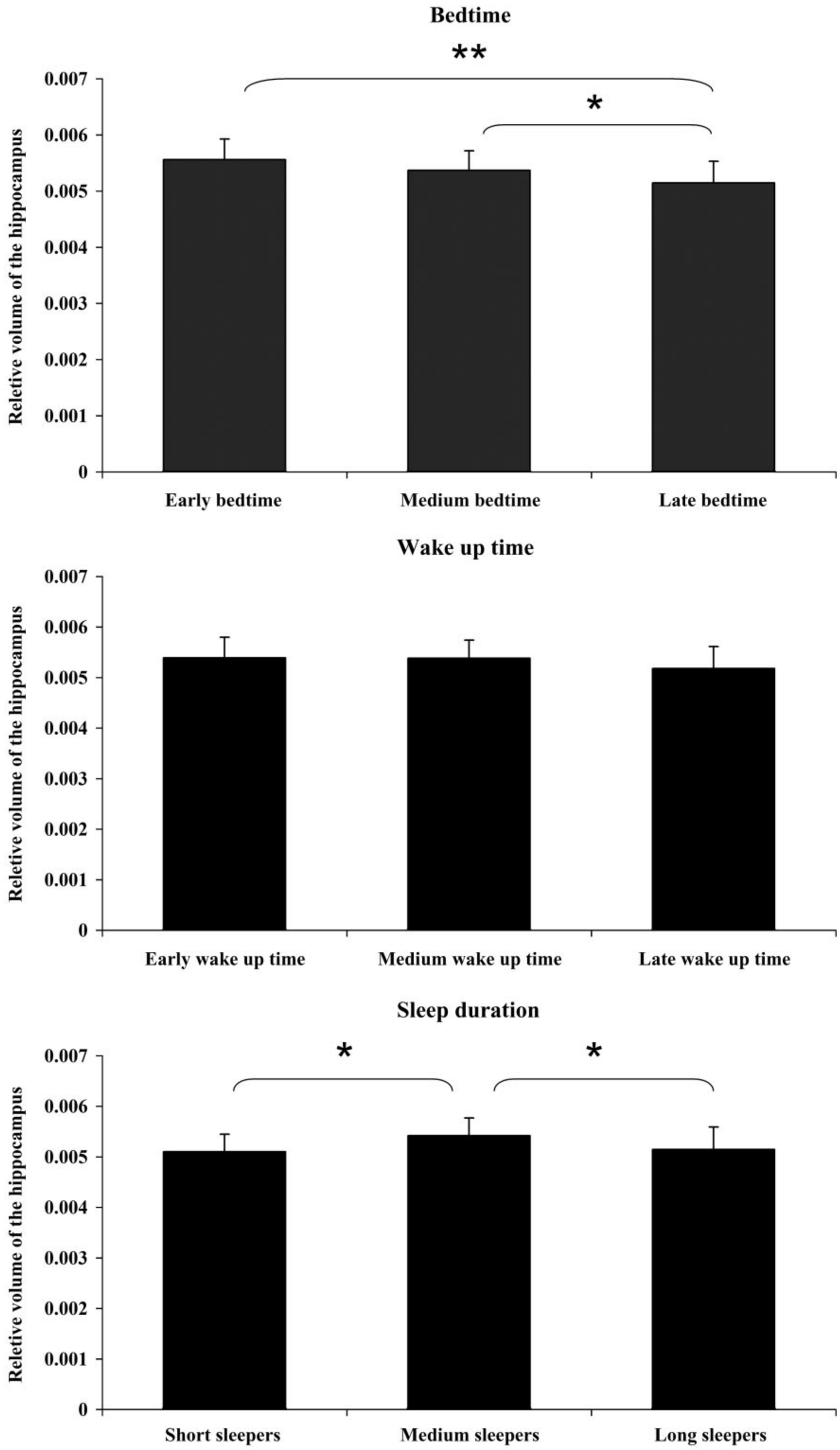



**Figure 4:** Mean±SD of relative hippocampal volumes in the three groups according to bedtime, wake up time and sleep duration. Asterisks indicate significant differences for pairwise comparisons (*p<0.05, **p<0.005).

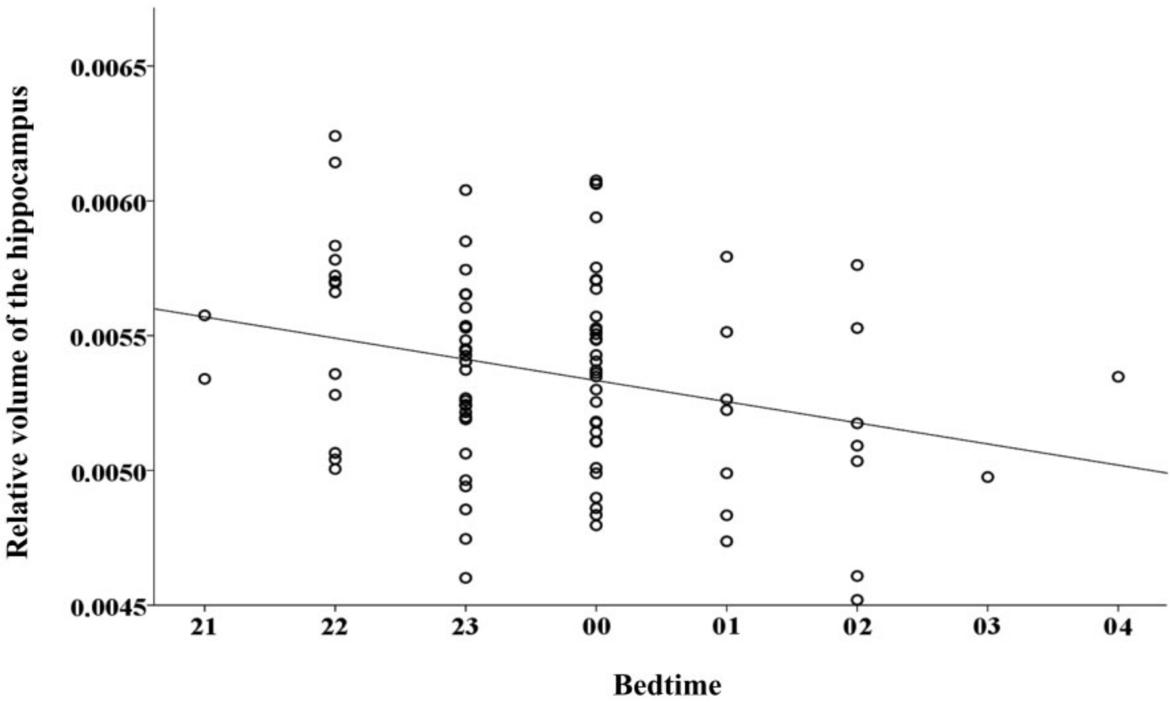



**Figure 5:** Scatterplot representing the relationship between the relative hippocampal volume and bedtime for each subject (Pearson correlation: r=0.269, p=0.01).

*III.3.2. Multivariate analysis*

A multiple linear regression model was created to assess the independent contribution of bedtime and wake up time variables to hippocampal volume. This model showed that only the bedtime group membership contributed significantly to hippocampal volumes ($\beta = -0.334$, $P = 0.004$). Statistical contribution of wake up time membership remained non-significant ($\beta = 0.017$, $P = 0.878$). Entering sex and age into the model as additional independent variables did not essentially change results: the contribution of bedtime group membership remained significant ($\beta = -0.31$, $P = 0.005$) and the wake up time membership remained non-significant ($\beta = 0.097$, $P = 0.39$). In this model sex was revealed to significantly contribute to hippocampal volume differences ($\beta = 0.377$, $P = 0.0003$) with females having larger hippocampal volumes. Age did not proved to be a significant predictor ($\beta = -0.118$, $P = 0.238$).

**III.4. Discussion**

To our knowledge this is the first study assessing the relationship between sleep timing and brain structure. The main finding from the study is that self-reported regular bedtime is significantly associated with the volume of the hippocampus even when wake up time, age and sex are controlled. Wake up time was not significantly related to hippocampal volumes; however, there was a non-significant tendency for smaller hippocampal volumes in the late rising group. Interestingly sleep duration exhibited an inverted U-shaped relationship with hippocampal volumes: short sleepers as well as long sleepers showed smaller hippocampal volumes as compared to those with medium sleep length. Age is known to be inversely related to hippocampal size. Presumably due to the relatively narrow age range in the present study age did not prove to be a significant factor determining hippocampal volume.

Hippocampal volume loss has been reported in numerous clinical and non-clinical conditions including sleep disorders, neuropsychiatric disorders, Cushing syndrome and aging. These conditions share a common feature of increased activity of the HPA axis hormones including cortisol. Administration of corticosteroids in patients with chronic inflammatory diseases has also been shown to decrease hippocampal volume. This vulnerability is due to large quantities of glucocorticoid receptors in hippocampal pyramidal cells. The hippocampus has also been proposed as the main regulator of HPA system feedback loops. Under physiological conditions cortisol levels exhibit a robust diurnal pattern with minimal concentrations during the first half of the night predominated with extended epochs of SWS. Across subsequent sleep cycles cortisol levels are increasing and reach their peak around awakening. Although maximal suppression of cortisol depends on SWS the magnitude of this suppression is further modulated by the phase of the circadian rhythm with most efficient suppression taking place around midnight. Delaying sleep onset may thus result in missing the optimal time window for maximal cortisol suppression, which in turn inhibits development of prolonged SWS episodes. Delay may lead to dissociations between the endogenous circadian pacemaker, HPA axis hormonal activity and timing of sleep stages, which may have adverse consequences. In Cushing syndrome, for example, chronic hyperactivity of the HPA axis is associated with the absence of early night cortisol nadir, reduced slow wave sleep, declarative memory impairment and hippocampal volume loss. A similar cluster of structural and functional abnormalities have been reported in depression, post-traumatic stress disorder and aging. A series of studies carried out by the group of Born are in support of a beneficial influence of SWS placed in the first half of the night with regard to the consolidation of hippocampus-dependent declarative memories. Impairment of hippocampal memory formation was also shown by experimental increase of cortisol during early SWS-rich periods of nocturnal sleep.

So far only a single study has assessed the relationship between sleep and hippocampal volumes in a nonclinical sample. This study was carried out in a large cohort of school-aged children and revealed bilateral hippocampal volumes to be correlated with sleep length. Other sleep variables such as timing of sleep were not assessed. However, assuming children's fixed morning school obligations we suppose that the correlation found with sleep duration in that study may also reflect an association with bedtime.

To examine the contribution of early and late bedtime and wake up time to differences in sleep duration we examined how they are linked. Doing this we found an uneven distribution of bedtimes and wake up times among the three sleep duration groups: short sleep was more frequently associated with late bedtime while long sleep with late wake up time. Thus it seems that the U-shaped association found with sleep duration actually reflects the influence of bedtime and wake up time. The significant decrease in hippocampal volume found for short sleepers likely results from delayed bedtime, while smaller hippocampal volumes in long sleepers results from delayed wake up times although the latter was revealed as a non-significant tendency ($P = 0.12$) only possibly due to the relatively small number of subjects in this group.

Of note, previous studies typically found a U-shaped association for sleep duration when assessing a number of health parameters such as risk for developing type 2 diabetes, cardiovascular diseases and mortality. These studies generally overlooked the possibility of sleep timing in determining these results. However, a recent study stressed the importance of adequate sleep timing (early bedtime and early wake up time) instead of sleep duration in determining optimal weight in children. From the cognitive viewpoint, the studies that are of importance are those indicating that evening-type subjects (also called "owls" in the chronotype literature) as compared to morning-type subjects ("larks") exhibit lower academic performance, as reflected in lower school grades. In the elderly, mild cognitive impairment

(MCI) is more common in those with poor sleep quality (Pittsburgh Sleep Quality Index > 5), difficulty falling asleep, or little sleep (≤ 5 hours). Atrophy of the medial temporal lobe is also more common in sleep-wake cycle fragmentation, and this has been shown to be a stronger predictor than age.

Mean difference in hippocampal volumes between early and late bedtime groups achieved 9% similar to that previously found for depression (~9%) and post-traumatic stress disorder (~7%). This may surprise given that we investigated healthy young university students without neurological or psychiatric diseases and self-reported sleep problems.

Since the present study is of correlative nature a formal conclusion regarding the direction of causality is not possible. However, given the extensive literature on brain structural changes in response to neurohumoral modulation – also in the context of sleep – an opposite causal relation seems unlikely. A limitation of the study is that the sleep variables used in the present study were self-reported and not confirmed by objective measurements. However this weakness is likely compensated by the relatively large number of subjects in the study.

### III.5. Conclusion

In sum we demonstrated that delayed bedtime and short sleep duration are significantly associated with smaller hippocampal volumes. Since bedtime preference is known to be a rather invariable trait of sleep behaviour, a regular delay in sleep onset may result in a cumulative loss of hippocampal volume. Results from the present study highlight the importance of adequate sleep timing, especially early bedtime, and the role of the adequate amount of sleep.

## IV. Sudden gamer death: non-violent death cases linked to playing video games

### IV.1. Background

Today video games provide relaxation and entertainment for billions with challenges to fulfill, new experiences to meet and new frontiers to explore. But attraction sometimes escalates to obsession or addiction. In the past two decades, year by year, reports could be read about people dying during playing video games, mostly young ones who had been playing for an extremely long period. Other reports cited homicide or suicide cases, where video games were involved in the motivation.

Between 1995 and 2017 penetration of internet use raised from below 1% to 46% of the world population, being much higher in developed countries among younger age groups. Growing of internet use was accompanied by growing of internet addiction. Addicted one can be overusing several modalities of internet (generalized internet addiction) or be focused on a specific internet-based activity like playing online video games. The latter phenomenon was nominated Internet gaming disorder (IGD) in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) in 2013. A metaanalysis of 113 epidemiological studies between 1996 and 2018 from 31 nations reported the averaged prevalence of generalized internet addiction to be 7% in the population, while the individual sources reported it wildly variable between 0.5 and 40% due to different definition and measurement method. An increasing tendency was demonstrated through years. IGD prevalence (based on sources from 2015 to 2018) was 2.5% (0.2-14.9%). The prevalence depends on the availability of internet and the internet culture, being much higher in Southeast Asia, where the prevalence of IGD among adolescents was estimated to be 5% according to a paper from 2014, and the prevalence is seven times higher among male adolescents than female adolescents. Someone with IGD often spend several hours a day, but in extreme cases the gamer may spend days online, consecutively, with little food or drink intake or sleep, which may lead to adverse (or fatal) physiological conditions.

## IV.2. Aims

While extensive debates can be found on the internet about the topic, according to our knowledge, it has not been systematically reviewed in the medical or health science literature, nor have we found any studies or case reports. We aimed to investigate the real size of the problem of death linked to playing video games, if these subjects were addicted to gaming as often stigmatized, the connection between gaming and death, the possible reasons leading to death.

## IV.3. Methods

We tried to collect all cases, where video gaming was associated with the death of the gamer. Search was started on the internet browsing (Google) for keywords “death”, “die” and “video game”. We found several cases and case compilations in online newspapers, blogs, and video portals. Obtaining specific keywords for individual cases, we gathered as much information as possible about them, preferring trustable online newspaper articles. Considerable cross reference was found among sources, which we could work along. We ended up with a moderately low number of detailed cases, which were frequently mentioned in several online newspaper and cited in compilations, and a few brief, undetailed references, which could not be further elaborated. We did not consider other death cases that could be associated to video games (accidents, suicides or homicides fueled by impulse, rage, revenge, frustration, negligence, carelessness or a game motivated pattern), only where the player itself died presumably connected to the action of gaming. Scientific search (Pubmed, Google Scholar) yielded no relevant publications.

## IV.4. Results and Discussion

Using the mentioned method, we found 24 relevant cases up until the end of 2021, and numbered them in chronologic order. We did not anonymize the victims since their names are publicly available. An isolated case was reported in the early 1980’s, but the cases of real interest started after 2002, with 1 or 2 cases every year or two years, but without trend for remarkably increasing incidence.

*Brief description of death cases*

- Case No. 0-1.

Multiple sources mention **Jeff Dailey** (19-year-old male) and **Peter Burkowski** (18-year-old male) as the first video game-associated deaths in 1981 and 1982 respectively, both guys having died playing „Berzerk” in an arcade in Chicago. Details about Burkowski’s death are more available: he was a good student, free of drinking or drugs, apparently healthy. He set up two top-ten scores in the game within 15 minutes, then turned to another arcade machine, collapsed, and died – 30 minutes within arriving to the arcade. Autopsy reported scar tissue on his heart, and stress of playing might have had an impact. Details about Dailey are much more lacking and controversial, his case might even be an urban legend.

- Case No. 2.

Some sources report **Kim Kyung-Jae** (24-year-old male) the first human to die from playing a video game too much. He died of deep vein thrombus and pulmonary embolism in October 2002 in an internet café in Gwangju (South Korea), after playing the video game “MU” for 86 hours with pauses only to purchase cigarettes and to use the bathroom.

- Case No. 3.

28-year-old male, **Seung Seop Lee** died on 5 August 2005 in an internet café in Taegu (South Korea). He was reported to be a gaming addict (often playing 14-18 hours a day), and recently lost job and broke up with his girlfriend. Lee was playing StarCraft for 50 hours with brief naps, reportedly ate and drank very little (if at all) and left his PC only to take restroom breaks. He fell off his chair onto the floor; a witness recalls he was conscious with closed eyes. He was rushed to nearby hospital where he died a few hours later presumably due to heart failure brought on by exhaustion and dehydration.

- Case No. 4.

26-year-old male from Jinzhou (Northern China) named **Zhang**, addicted to video games, died on 24 February 2007. He had been playing World of Warcraft at home for seven days during the lunar new year holiday, stopping only for eating, toilet breaks, and a few hours of sleep in his bed. Parents witnessed him twitching and slumping over his computer screen. Resuscitation attempt was unsuccessful. The death was supposed to be a consequence of heart failure due to his obesity (ca. 150 kg), poor blood circulation, and oxygen deprivation from sitting for too long.

- Case No. 5.

30-year-old **Chinese man** dropped dead at a cybercafé in Guangzhou (China) on 15 September 2007 after he had been playing games online for 3 days without considerable breaks. Paramedics tried to revive him, unsuccessfully. Further information was not disclosed.

- Case No. 6.

25-year-old „fit and healthy” male, **Tim Eves** collapsed and died while 'jogging' on a Nintendo Wii Fit games console on 4 March 2009 in Hopton-on-Sea (UK). He had just returned from Portugal a few hours before. Sudden Arrhythmia Death Syndrome was considered as cause of death.

- Case No. 7.

In February 2011 a 30-year-old **Chinese man** died at an internet cafe on the outskirts of Beijing after a three-day online gaming session not eating or sleeping.

- Case No. 8.

20-year old male, **Chris Staniforth** from Sheffield (UK) often played “Halo” online on his Xbox for periods up to 12 hours. He died in May 2011 after an interview at a JobCentre (he picked up a packet of chewing gum from the ground, he jolted back and began to spasm). Previously he was woken in the night by a ‘strange feeling’ in his chest. Cause of death was deep vein thrombosis and pulmonary embolism. Immobility was presumed to be a triggering factor.

- Case No. 9.

On 22 July 2011, 13-year-old girl, **Anna-Lee Kehoe** from Bridport (UK), was playing on her Xbox, when she stood up, complained about shortness of breath, and collapsed. 10 minutes before, she had gone to the toilet, and had been fine. She was resuscitated but remained brain-dead. The girl was known to have asthma, but otherwise was perfectly healthy. Heart attack was considered as cause of death.

- Case No. 10.

23-year-old male, **Chen Rong-Yu**, died in an internet cafe on 1 February 2012 in New Taipei City (Taiwan). He spent 23 hours almost continuously playing “League of Legends”, stopping occasionally only to rest his head on the table in front of his monitor and sleep for a little while, then picked up his game where he had left off. Nine hours after one such episode an employee tried to wake him, but found him dead, still reaching for the keyboard. Initial reports indicate he may have died due to cardiac arrest brought on by cold temperature, exhaustion, and lack of movement. According to his family he had been treated for a heart condition last year.

- Case No. 11.

18-year-old male, **Chuang** died on 15 July 2012 in Taiwan. He had been playing 40 hours with “Diablo III” in a private room of an internet cafe without eating or sleeping. He was found resting on the table. After the staff woke him up, he took a few steps and collapsed, then died shortly after arrival to hospital. Thromboembolism due to spending such a long time seated was suspected as cause of death.

- Case No. 12.

In August 2013, 35-year-old man, **Chang** was found dead in his seat after playing games for 10 hours at an internet cafe in Hualien City (Taiwan).

- Case No. 13.

In February 2014, 40-year-old man, **Wang**, died after playing games for 13 hours at an internet cafe in Greater Kaohsiung (Taiwan). Attendants found Wang dead, but his eyes were still open and staring at the screen as though he were still playing.

- Case No. 14.

38-year-old man, **Chu**, was found dead in the bathroom of a New Taipei (Taiwan) internet cafe on 1 January 2015, after a five-day-straight marathon of computer gaming. Except for going to the bathroom, taking cigarette breaks and occasional quick meals, the man did not leave his seat. Medicines to treat liver disease and gall stones were found in Chu’s belongings. Police officers said that Chu likely perished because of his medical condition, which was exacerbated by fatigue and physical exhaustion after five days playing computer games.

- Case No. 15.

32-year-old male, **Hsieh** in Kaohsiung (Taiwan), unemployed for longer time, regularly spent entire days in an internet cafe gaming. He used to take naps sitting in the chair or laying on the desk there. On 8 January 2015 he was found unresponsive laying on the keyboard, probably dead for several hours, after having played 3 consecutive days with combat computer games. Security camera footage showed Hsieh struggled with chest pains before collapsing. Cause of death was considered cardiac arrest, cold temperature, lack of movements and over-exhaustion from playing for so many hours non-stop being possible contributing factors.

- Case No. 16.

In March 2015, 24-year old male, **Wu Tai** died in an internet café in Shanghai (China) after sitting and playing 19 hours without a break with World of Warcraft. He was sitting in front of a computer, then started to cough violently. Witness saw him pale and to cough up blood, then he slumped in his chair. Paramedics tried to resuscitate him, unsuccessfully.

- Case No. 17.

17-year-old boy, **Rustam** in Russia's Republic of Bashkortostan died on 1 September 2015. The boy had been playing with “Defence of the Ancients” for 2000 hours in the past year and a half. After breaking his leg, and staying at home, he played it for 22 days almost all the time, stopping only to take a nap and grab a snack. Cause of death was presumed thromboembolism due the broken leg and not moving around at all.

- Case No. 18.

35-year-old male **Brian Vigneault** (alias Poshybrid) died on 19 February 2017 in Virginia (USA). He regularly made marathon gaming streams on Twitch. In this case he announced a 24-hour-long stream to raise money for charity. He was playing “World of Tanks”, repeatedly dozing off towards the end. At 22 hours he left for a cigarette break (he was known to be a heavy smoker) and never returned. Despite other speculations, cause of death later was reported as fentanyl overdosing.

- Case No. 19.

On 2018 October 29, 21-year-old male Swedish “Fortnite” pro-gamer and streamer **Bogdan Akh** passed away during sleep the night after finishing at 18th place at the Fall Skirmish finals at TwitchCon in San Jose (USA). His teammate found him dead in the morning. They have been playing Fortnite intensively every single day for the last two months to practice for TwitchCon. Cause of death was not revealed.

- Case No. 20.

11-year-old boy **Fahad Fayyaz** died on 5 February 2019 in Lahor (Pakistan) while playing “Fortnite”. Previously he returned home from school in a happy mood and had showed no signs of any sort of stress. Parents later found him unconscious in his room with a controller in his hand. He wanted to play with his friends, but one of them couldn’t join, which Fahad commented as “If I lose this game, I will get a heart attack.” He was reported to be addicted to this game, despite his parents trying to stop him, he would still play for hours. Heart attack was considered as cause of death.

- Case No. 21.

**Natsupon Arunrat** (32-year-old male) died on 27 April 2019 in an internet cafe in Samut Prakan (central Thailand). He started gaming at 4 am and was found dead in the evening probably 4 hours after having died, laying back on the chair, his mouth covered with blood from biting his tongue. He regularly spent the whole day there. His mother reported that he had been suffering from heart disease and high blood pressure for many years and could not work, and he had been addicted to computer games. Cardiac arrest was proposed.

- Case No. 22.

17-year-old male, **Piyawat Harikun** in Udon Thani (northern Thailand) was found dead, collapsed to the floor from his computer chair. During his school holiday, the boy had had all-night gaming sessions with multiplayer combat games, which he continued through the day until being found dead on the afternoon of 4 November 2019. Medics said the teenager died from a stroke, which they believe was caused by playing the computer constantly through the night.

- Case No. 23.

In October 2020, 12-year-old boy **Muhammad** from Egypt was found unresponsive (and dead before he arrived to the hospital) after playing “PlayerUnknown’s Battlegrounds” for hours on his mobile phone. The boy was reported to be obese and addicted to the game. Coroner’s preliminary examination attributed the cause of death to cardiac arrest from a sudden increase in blood pressure.

- Case No. 24.

A 16-year-old private school boy, **Dharshan**, collapsed and died on 1 February 2021 in Puducherry (India), while playing “Fire Wall” on his mobile phone for about 4 hours after school. Resuscitation attempt was unsuccessful. Autopsy revealed cerebral haemorrhage. Stroke expert neurology professor presumed unlikely that indulgence in video games was the reason for death in this case, though a surge in adrenaline spiking heart rate and blood pressure due to playing games, just as due overexertion of any kind can be fatal by an underlying vascular malformation.

*IV.4.1. Demographic and geographic characteristics*

Only one of the reported victims was female (No. 8), but we do not know about the length and intensity of her gaming. Internet addiction among females usually involves addiction to social media rather than gaming - IGD is seven times higher among male than female adolescents. It seems that deaths were connected to action-rich games, which are less popular among females. Competitiveness in games is more common among males, which may bind them for a long period to the game without pausing.

The victims were mostly adolescents or young adults (age ranging from 11 to 40 years). The first few victims died in their twenties; this was the age group that primarily got acquainted with computer games, and in whom IGD became an emerging problem. In the following years, age of victims broadened. The former teens and twenties aged to thirties. Further spread of computers, internet and games reached the very young age group, as well – nowadays kids often start to play video games before learning to read, and get their game-able smartphone before 10.

More than half of the cases originate from Southeast Asia (Taiwan, China, South Korea, Thailand) and most of them (12 cases) happened in internet cafes. It is not that surprising according to the popularity of these places. Buying gaming hours are cheap, and are far more economical alternative for young players than paying for an own PC, broadband internet connection, electricity and the games themselves. Moreover, internet cafes provide cheap food and drinks, some even private rooms with beds to sleep or to shower. With 0-24 opening hours a customer may not even need to move out for days. Without supervision, young people can get away from their parents, escape reality, and get lost in the game undisturbed without thinking about the pressures of school and work. On the other hand, in the cases from the western region the gaming event happened at home, as internet cafés never had such high popularity, due to the expansion of home-based e-mail and internet access points. In the recent years rapid spread of smartphones has been restructuring Internet access and gaming, as well, and the first gaming deaths linked to smartphones also appeared.

*IV.4.2. Incidence of death by gaming*

Using the above mentioned data, we tried to give a very rough estimation about the incidence of gaming related death. Number of internet users is growing, being around 2 billion (28% of 7 billion people in 2010) and 3 billion (41% of 7.38 billion people in 2015) Risk population seems to be males from 15 to 40 years, so about 360-540 million; we used 450 million for further calculation.

Using the 2014 Asian data, the prevalence of IGD among adolescents was estimated to be 5%, but since most of them were males, we used 10% for males. The population at risk (adolescent males with IGD) may be around 45 million. This means a roughly 1 death per 2 million gamers over about 15 years course, or 1 per 30 million yearly. Considering only the most avid gamers the incidence is probably higher.

*IV.4.3. Games involved in death cases*

In most cases the name (or the category) of the game the victim had been playing was reported. The common feature of these games is that they all need strong, strenuous mental concentration. The gamer may lock out the disturbing outside world, lose track of the passing time, and dimly notice hunger, thirst, tiredness or discomfort, which may lead to the adverse consequences. No one was reported to die while playing a *sandbox* game (like The Sims, Minecraft), where player use creativity instead of action, or an *adventure* game, which involves exploring and playing along a storyline (sprinkled with action and dexterity elements) in an enjoyably slow pace instead of the aforementioned rush. The games played were definitely or presumably multiplayer games, where the competitive factor or adaptation to the other players enforces the gamer into a faster pace and prevents him from stopping, contrary to single-player mode, where one can do it in his own pace.

*IV.4.4. Cause of death*

Ten victims were reported to have co-morbidities or risk factors: extreme obesity (No. 4), obesity (No. 8 and 23), asthma (No. 9), previous heart attack (No. 10) or heart problem (No. 21), high blood pressure (No. 21) liver disease/gallstones (No. 14), broken leg (No. 17), smoking (No. 2, 14 and 18), in the other cases such risk factors were not known.

Five sudden deaths were caused by **pulmonary embolism** (PE). A critically large embolus can lead to hemodynamic collapse, shock and death, which happens in about 10% of the cases. Autopsy can unequivocally prove or rule out the embolism, but preceding symptoms (sudden onset, stabbing chest pain, dyspnea, coughing up blood, swollen leg) may suggest the diagnosis, as well. Prolonged immobilization, bedrest or long sitting and dehydration are well- known risk factors for deep venous thrombosis (DVT) in the lower limb.

"Economy class syndrome" refers to DVT of aircraft passengers, where prolonged sitting cause venous stasis, may damage the endothelium of the veins, while dehydration due to dry atmosphere or drinking less, further increase risk of thrombus formation. Aforementioned gamers were similarly sitting long and moving little. Focused on the game they may be less aware of being stiff and sore, or thirsty. Obesity and smoking are further relevant risk factors. After thrombus formation, PE may strike later or in waves, like in case of Chris Staniforth (No. 8), who mentioned 'strange feeling' in his chest the previous night, and died at the JobCentre next day. Besides 22 days of sedentary gaming, Rustam (No. 17) had a broken leg, which increases risk of DVT over 10-fold on its own. Besides the extent of embolism, survival is determined by the ability to compensate for the increased resistance of pulmonary circulation, requiring good right ventricular function with adequate preload and autonomic regulation. Young subjects are expected to have better chances than elder ones. Autonomic dysfunction (explained later) and hypovolemia due to dehydration may have contributed to the death of the gamers.

In one case (No. 22) **stroke**, in another (No. 24) **cerebral haemorrhage** was reported as cause of death. Stroke was not further specified. It might have been ischemic stroke, which often causes disability but rarely sudden death, and is very hard to be explained at this age. It more probably could have been haemorrhagic stroke or subarachnoid haemorrhage. Haemorrhagic stroke in young adults can be caused by hypertension, vascular malformation, drug abuse, venous sinus thrombosis, hematologic conditions. According to the bleeding location and size, it may lead to herniation, coma or death. Subarachnoid haemorrhage is due to the rupture of saccular aneurysms in more than half of all cases. 25% of these patients die within 24 hours of the event; many die before they reach the hospital. Hypertension or acute elevation in blood pressure, smoking are risk factors for aneurysmal haemorrhage.

In many cases (No. 1,3,6,9,10,15,20,21,23) **'heart failure', 'heart attack' or 'cardiac arrest'** was named as cause of death, though the terms may not have been medically properly used. In other cases, definite cause of death was not even specified or speculations (like "overwork and obesity", "fatigue") were reported. Sudden cardiac death (SCD) developing such rapidly almost always happen due to onset of malignant ventricular arrhythmia (ventricular fibrillation, extremely fast ventricular tachycardia) or sudden severe dysfunction of the sinus or AV node without escape rhythm. Other possible specific causes (like extreme extent myocardial infarction and loss of pump function or aortic dissection leading to rapid bleeding or pericardiac tamponade) are improbable and could be easily identified during autopsy. Arrhythmia on the other hand often lacks obvious structural background. However, autopsy results or background medical information were available only in few cases, mostly the cases from the Western countries. For the Asian cases these were either not performed, or the international news agencies were not interested in writing follow-up articles. In many cases excitement, fatigue, physical exhaustion, sleep deprivation, dehydration, lack of movement, were named as contributing factors to the cardiac death.

Some cases seem out of the pattern. Tim Eves (No. 6) was playing on Wii Fit, where player actually moves and jogs, turning gaming into a sport, a mild to vigorous aerobic training. Circumstances did not suggest anything extraordinary either. His death is rather sport-related than game-related. Anna-Lee Kehoe's (No. 9) symptoms did not resemble an asthma attack, even complete airway obstruction would result in a longer agony. Symptoms rather suggest massive pulmonary embolism, and the source did not mention if examinations or autopsy was performed to rule it out. On the other hand, thrombosis at such young age is unlikely without the presence of thrombophilia. Though no obvious provoking factors were mentioned, arrhythmia-related death (heart attack) is possible in the presence of underlying disease (like arrhythmogenic right ventricular cardiomyopathy or channelopathy). Similarly, in Burkowski's case (No. 1) the half hour gaming session must have been no overexertion or overly stressful for the experienced player (who set up to top-10-scores). The scar on his heart, that probably was involved the lethal arrhythmia, is of unknown origin: cardiomyopathy, peri/myocarditis, mechanical injury or an unlikely myocardial infarction? He probably could have died due to any other physiological stressors or excitement, as well. Similarly, in other cases (No. 20, 21, 24), though the victims were gaming addicts, no extremity was reported about the last gaming session. If there is a very low chance of death during a gaming session, there is obviously a higher cumulative chance for ones who repeatedly do it.

Bogdan Akh's (No. 19.) death is not connected to uncontrolled gaming binge, but to a scheduled training for a competition, and we may consider it the first eSport related death (see below). Extreme exhaustion is unlikely, it was probably avoided in favour of the best performance on the competition. Strangely, death occurred not around the training or the competition, but after them, during rest, when all stress subsided. It is a question, if this change in balance could be the trigger, or there were other possible factors, like a celebration after the competition?

*IV.4.5. Sleep deprivation and death*

In 18 cases the gaming session before death was extremely long (around a day or even several days) with minimal rest, which results in acute sleep deprivation, or the victim was repeatedly playing quite long sessions, which suggests chronic sleep deficiency.

Sleep is a natural relaxing state for regeneration. Uncomfortable effects of acute or chronic sleep deprivation (SD) are experienced by almost everyone; impaired concentration, reduced mental and physical performance, mood alterations, irritability, to mention some. They may indirectly lead to fatal consequence, like falling asleep and causing a traffic accident. It is another question though if or when can SD itself trigger or contribute to a biological shock resulting in death, like in the aforementioned gamers. In an animal model of acute SD, all rats died within 2-6 weeks of continuous or paradoxical SD. The animal lost weight despite increased food intake, showed altered thermoregulation, but no obvious changes in brain morphology or function could be demonstrated. Experimental data of such drastic SD in human is not available. In a study, subjects after a night with sleep dept (still 1.7 hours sleep on average) showed increase of the QT interval and QT dispersion (still within the normal range), which may make more susceptible to lethal ventricular arrhythmias. A case report demonstrated spontaneous coronary dissection and myocardial infarction after 72 hours SD due to overtime work.

Several longitudinal human studies demonstrated a U-shaped association between sleep duration and all-cause mortality, optimal amount being around 7 hours sleep per day, with increased mortality of both short and long sleepers. Besides direct effect of SD, short sleep may also contribute to development physiological and social outcomes that may lead to increased mortality; e.g. cardiovascular disease, stroke, dyslipidemia, diabetes, hypertension, obesity, cancer, presence or development of stress, altered inflammatory cytokine levels and impaired immune response. Exact sleep habits of the gamers are not known, but it is presumable that the ones who were indicated as gaming addicts, and were doing regular several-day-long gaming binges or over 10-hour daily gaming sessions, were also taking away time from sleeping in favour of gaming, and are on the short-sleeper arm of the curve. The above results are also based on mainly middle-aged or elder subjects, and applying them on the mostly young gamers is questionable. On the other hand, chronic short-sleeping may have already done subclinical damage in these individuals, making them more susceptible to an acute event.

*IV.4.6. Sport and sudden cardiac death*

Eventual, unexpected, sudden cardiac death (SCD) cases are reported in another field, as well: sports and athletes. We tried to apply such experiences to our population. Public and medical attention is high for such events, the cases and causes are usually thoroughly investigated. Widespread registers offer more reliable data in contrast to the cases of video gamers. Due to inconsistencies of definitions incidence widely vary between 1 in 3000 and 1 in million athlete per year. Higher incidence was found among males (3-5 times) and blacks (3 times). Deaths occur most commonly in team sports, which have the highest levels of participation. In many cases structural abnormalities (hypertrophic cardiomyopathy or idiopathic left ventricular hypertrophy, dilated and restrictive cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, congenital coronary anomalies, aortic rupture due to Marfan syndrome, myocarditis, valvular disease, commotio cordis) were present, but individuals with morphologically normal hearts were common, as well, referred to as sudden arrhythmic death syndrome (SADS). In some of them primary electrical disorders or channelopathies (like Brugada syndrome, Wolff–Parkinson–White syndrome, long QT syndromes) could be identified, but about 30% remained unexplained.

*IV.4.7. eSports*

Outstanding performance attracts audience in gaming, as well, which up today turned into a rapidly growing industry, eSport, with over 1 billion audience, and with gamers doing it as a full-time profession. Average eSport player practices between 5.5 and up to 10 hours a day prior to competitions. 15% reported 3 hours or more of sitting and playing without standing to take a break. This sitting for hours staring the monitor with several hundred clicks and keypresses per minute results in chronic overuse (and sometimes career-ending) injuries (eye fatigue, neck or back pain, wrist and hand pain), but one case of deep venous thrombosis was also reported. As far as we know, up until today no case of death among eSport athletes linked to gaming was officially reported. On the other hand, eSport community is far smaller, and exists for a shorter time than the general gamer and IGD population, and the lower numbers may have just not produced a death case.

*IV.4.8. Stress and cardiac death*

Death of Chen Rong-Yu (No. 10), was a well investigated, still unexplained case, about which we have more detailed information from an interview with his physician, Dr. Ta-Chen Su in the book Death by video game. Rong-Yu had had a heart attack 3 months before. Extensive examinations (including ECG, echocardiography, 24-hour ECG, coronary angiography, cardiac electrophysiology study) did not show underlying abnormalities. Cardioverter defibrillator implantation was suggested which Rong-Yu refused. Dr. Su provided further hypotheses about his death, elaborated below.

*Acute autonomic dysfunction.* Most organs are regulated by the sympathetic and parasympathetic nervous system, their balance and reaction to stimuli adapt the organ's function (like blood pressure, heart rate, respiration, metabolism) to the actual needs. Prolonged or extreme stimuli may upset this balance, and result in so called acute autonomic dysfunction causing functional and sometimes morphological organ abnormalities, which can rarely lead to fatal consequences. Such manifestations in the heart can be various arrhythmias, myocardial infarction, takotsubo cardiomyopathy and sudden death.

Sleep deprivation is accompanied by a rise in sympathetic tone to maintain arousal and counteract parasympathetic impulses driving the body to a relaxing, regenerative state, ultimately resulting in a mentioned imbalance and autonomic disfunction. It can also be a part or trigger of acute or chronic stress reaction.

Gaming itself produce stress, according to cardiologist Robert S. Eliot, (M.D. at the University of Nebraska Medical Center), who used a video game (Pong) to replicate stressful situations in more than 1000 patients. Heart rate increases of 60 beats per minute and blood pressures as high as 220 was often observed within one minute of starting a computer game, without the patients being aware of that. Similarly, increase in heart rate and blood pressure was observed in eSport athletes, as well, although such high alteration was not pronounced. Acute elevation of blood pressure can trigger lethal arrhythmia in some cases. Present of stress during eSport activity can be demonstrated by the elevation of stress hormones, just like during physical sports.

Acute emotional distress (especially anger-like stress) may provoke ventricular arrhythmia, as well as acute myocardial infarction, but stress due to assault or natural disasters are reported as triggers for SCD, as well. 20 to 40% of sudden cardiac deaths may be precipitated by acute emotional stressors. A gamer may feel strong anxiety in an unfamiliar situation, panic in a high risk-high stake scenario, frustration when failing a challenge and lose progression or rage when repeatedly losing or getting “owned”.

*Overwork.* Even if the game is not especially stressful, extremely long gaming session could be compared to overtime at working, leading to exhaustion. In Japan several hundred cases were reported where people have died while repeatedly working overtime (termed as karoshi: death by overwork).

*Air pollution.* Dr. Su mentioned air pollution as another possible factor: Taiwan’s air relative humidity usually remains at 60-90%, that help fungi, bacteria and dust mites to flourish in a confined space. Taiwanese internet cafés were typically crowded, smoking regulation was more liberal at that time, poor ventilation and air conditioning may cooled but not improved the quality of air. Air-pollution index in internet cafés often exceeded safe levels. Severe air pollution was shown to trigger coagulation and thrombosis, increase heart rate and reduce heart rate variability, cause endothelial dysfunction, arterial vasoconstriction, apoptosis, and hypertension. In chronic exposures these contribute to the progression of atherosclerosis, but even acute exposures can lead to autonomic nervous system imbalance, plaque instability, and trigger acute cardiovascular events (myocardial ischemia and infarction, stroke, heart failure, arrhythmias, and sudden death). Air pollution may contribute to acute autonomic dysfunction, as well, just like sleep deprivation, acute and chronic, emotional or physical stress, which may explain the sudden unexpected death of gamers.

### IV.5. Limitations

It is unsure, how complete the search for cases was. A death case is more likely to be reported if it happens in public, happens to a celebrity or the case has extreme characteristics. In several cases, relatives provided information about death cases that happened at home, especially if they wanted to message to the community. It is quite possible though, that others wanted to mourn in private and refused media presence. We could only recover information from English language sources, like international electronic newspapers. If a case was not interesting enough for international media, and appeared only in local language news, it could have been lost to us. The demonstrated cases were reported in many news portals and added to various compilations. These "overhyped" cases appear in the frontline of an internet search, and they are the realistically visible ones. Others with less clicks, are squeezed out from the first few thousand search results, and are lost from sight among the several hundred million finds.

Quality of source data was sometimes debatable. Information from different sources were highly redundant with hardly any novelty. Sources must have shared or taken information from each other or worked with the same limited communiques. Details were often poor, the exact cause of death was unconfirmed or speculative, autopsy reports were rarely available.

### IV.6. Conclusion

We reviewed death cases linked to the action of playing video games. In several cases extreme length of sedentary gaming led to deep vein thrombosis and fatal pulmonary embolism. Lethal arrythmia due to acute autonomic dysfunction brought on by stress and sleep deprivation seem to be a frequent cause, as well. It mostly involved adolescent males, who were playing action-rich games. Most of them probably had internet gaming disorder. Incidence of gaming related death itself seems to be relatively low, much lower than sport related death in its risk population, but we should be aware that besides the low direct risk to life, gaming addiction can have adverse criminal and economical consequences, as well, and awareness of the problem should be maintained and prevention should be enforced.

## V. Summary of new results

Relationship between sleep habits and hippocampal volume:

- A significant correlation was found between late bedtime and smaller hippocampal volume.
- Significantly smaller hippocampal size was shown in both short and long sleepers compared to those who slept average amount (7-9 hours).

Sudden gamer death: non-violent death cases linked to playing video games:

- The victims were usually young males.
- Players typically played action-rich games.
- The length of the game before death was extremely long in most cases.
- The most common causes of death could be fatal arrhythmias, provoked by acute autonomic dysfunction that could be caused by acute and chronic sleep deprivation, exhaustion, and stress.
- The 2nd most common cause of death was pulmonary embolism.

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# VII. List of publications

**Publications related to the thesis:**

1. Kuperczkó D*, Perlaki G*(*megosztott első szerzők), Faludi B, Orsi G, Altbacker A, Kovács N, Dóczi T, Komoly S, Schwarcz A, Clemens, Zs, Janszky J. Late bedtime is associated with decreased hippocampal volume in young healthy subjects. Sleep and biological rhythms. 2015;13(1):68-75. doi: 10.1111/sbr.12077. **IF: 0.628 Q3**
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