Mechanisms of Drowning in Children: Influence of Cold Shock Response on Repolarization Patterns and Arrhythmia Burden in Healthy Children

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Abstract

INTRODUCTION: While drowning plays a particularly important role in children, the data on the physiology of drowning in this population are scarce. Both the cold shock response and the development of arrhythmias within the context of an autonomic conflict may be of particular significance during drowning. The cold shock response has now been outlined by our working group, while the effect of cold water on cardiac repolarization remains unclear. This study aims to provide a more detailed examination of the effects of cold shock response in healthy children, focusing on changes in repolarization patterns and the development of arrhythmias to enhance the knowledge on drowning mechanisms in children.

METHODS: Participants were first immersed up to the neck in warm water (34°C) and then in cold water (11°C), while skin temperature, heart rate and respiratory rate were continuously measured and ECG and Holter-ECG were recorded.

RESULTS: Heart rate variability parameters were lower in cold water compared to warm water. In cold water, the Tp-Te interval was significantly shorter compared to baseline in air. Additionally, QT interval did not adequately adapt to the sudden increase in heart rate during cold water immersion. Despite premature contractions regardless of immersion, no arrhythmias were detected.

CONCLUSION: The current study presents first data on repolarization patterns and arrhythmia burden in healthy children during the immersion into 11°C (52°F) cold water. Data showed, that cold water immersion represents a strong sympathetic stressor associated with mild QT hysteresis and a distinct influence on the transmural gradient of repolarization. Although no arrhythmias were detected during cold water immersion in healthy children, the cold shock response itself appears to have the potential to induce repolarization abnormalities in individuals with pre-existing conditions.

INTRODUCTION

Swimming and diving are popular recreational activities that support an active lifestyle and improve wellbeing as well as reduce cardiovascular risk and prevent obesity [1, 2]. In addition, learning to swim is essential to prevent drowning accidents especially in young people. Understanding the physiological responses to immersion and submersion as well as the mechanisms of drowning, is crucial for reducing drowning-related fatalities. Drowning is a leading cause of fatal accidents worldwide, with young age and lack of swimming skills as major risk factors [3]. While most drownings occur in water colder than body temperature, suggesting a link between physiological responses and cooling, it is believed to involve two distinct events triggering different physiological responses. At first immersion into cold water activates the sympathetic cold shock response, leading to tachycardia and hyperventilation. At second, submersion and especially facial immersion and apnea trigger the parasympathetic diving response causing bradycardia [4]. The simultaneous occurrence of both responses is assumed to carry the risk for arrhythmias due to an autonomic conflict between the two limbs of the autonomous nervous systems, which are also discussed as a reason for deaths in cold water. The risk of developing such arrhythmias

is increased in individuals with pre-existing heart conditions, such as congenital heart defects or congenital conduction system disorders [4–6].

Most data on drowning physiology are derived from adult populations, although drowning represents a particular risk during childhood. There are currently almost no data on the drowning physiology of children, including the reactions during cold water immersion, with the exception of two studies by Bird et al [7, 8], missing the effects of immersion on cardiac repolarization. Additionally, the data on swimming and diving in children with pre-existing heart conditions are currently scarce, while they are assumed to be at a particularly high risk. Due to limited experience and data on this topic, clear recommendations are lacking, often leading to restrictive patient counseling [9, 10]. In this context, our research group carried out two pilot studies on immersion and submersion effects in young adults with congenital heart defects [11–13]. To generate reliable comparative data from healthy children, we recently investigated the physiological diving response [14] and the adaptation to physical exertion during submersion and apnea [15]. The cold shock response in healthy children has now been described by our research group [16]. The current study aims to further investigate the effect of cold water immersion on repolarization patterns and arrhythmia burden. The key question is whether the cold shock reflex itself has arrhythmogenic potential even without facial immersion. It seeks to fill the existing data gap on swimming and diving physiology in healthy children and establish a structured data base for future studies involving children with cardiac preconditions. Furthermore, it intends to enhance the knowledge on drowning mechanisms in children to prevent drowning accidents.

METHODS

Participants

Healthy voluntary participants were recruited through local surveys. Inclusion criteria were age of 8-14 years, ability to swim and overall health, especially no restrictions of cardiopulmonary function. Exclusion criteria were signs of reduced general condition and acute illness, signs of limitations of cardiopulmonary function, e.g. a newly diagnosed heart murmur, and intellectual disability or genetic disease. The participants and their legal guardians gave their informed consent. The study received ethical approval by the ethics committee of University of Leipzig and is listed under the reference 233/24-ek.

Measurements

Anthropometric data were measured. Data on potential medical history and medication were obtained from personal interviews. The testing took place in two pools of the first division soccer club RB Leipzig e.V. in the Red Bull stadium in Leipzig. The pools were the same size with a depth of 1 m and two steps, and were located right next to each other in the same room. Ambient temperature was around 25°C, water temperature was 34°C in the warm pool and 11°C in the cold pool. The tests were supervised by two medical doctors, a pediatric nurse and a study nurse.

Prior to the start of the testing, all participants were instructed to the following protocol. The protocol consisted of two parts, one conducted in a warm pool, the other one in a cold pool. The participants wearing swimsuits or shorts quickly entered the warm water with the water reaching up to their necks. After the monitoring outside the pool, including drying and being wrapped in a towel, they were quickly lowered into the cold water in a seated position without moving themselves to avoid hesitation to fully enter the very cold water, again with the water reaching up to their necks.

Protocol:

1. 2 minutes of monitoring in a sitting position outside the pool
2. 1 minute of immersion until the neck in warm water
3. 2 minutes of monitoring in a sitting position outside the pool
4. 1 minute of immersion until the neck in cold water
5. 2 minutes of monitoring in a sitting position outside the pool

Skin temperature and ECG were conducted continuously by using a Dräger Infinity® 540 patient monitor (Dräger Medical GmbH, Lübeck, Germany). Additionally, a Lifecard CF® Holter-ECG-recorder was used to record heart rate and enable subsequent analysis of heart rate variability parameters and detection of arrhythmias (Spacelabs Healthcare GmbH, Nürnberg, Germany). Heart rate and respiratory rate were measured continuously using a Masimo Rad-97 ™ patient monitor with Masimo RD SET neo CS-3 sensors and RAS-45 rainbow acoustic sensors (Masimo Corporation, Irvine, USA).

For the arrhythmia detection, the ECGs were evaluated for arrhythmias and extrasystoles. The ECGs were then divided into respective phases (resting 1, warm water, resting 2, cold water, resting 3) based on the time indications. The times for atrioventricular conduction (PR interval), ventricular depolarization (QRS interval) and repolarization (QT interval) were measured four times per phase. Additionally, the QT interval was frequency-corrected with the RR interval (QTc). Furthermore, the QT dispersion was calculated as a measure of regional differences in the duration of ventricular repolarization and therefore as an indirect sign of electrical inhomogeneity. The Tpeak-Tend (Tp-Te) interval was quantified as an indicator of the transmural gradient of repolarization, as well as Tp-Te dispersion. To illustrate the dynamics of the QTc interval and Tp-Te interval, the average interval of the first 30 seconds and the last 30 seconds, as well as the difference between them, were determined.

For heart rate variability analysis, the following parameters were used: standard deviation of NN intervals (SDNN), number of pairs of successive NNs that differ by more than 50 ms (sNN50), root mean square of successive differences (RMSSD) and triangular index, that describes the distribution of normal NN intervals. The larger these parameters are, the greater is heart rate variability, reflecting the balance between the sympathetic and parasympathetic nervous systems. Low values suggest tension and

sympathetic activity, while high values indicate relaxation, parasympathetic activity or a healthy autonomic nervous system and a well-trained state.

Statistical analysis

For the statistical analysis, IBM SPSS Statistics for Mac (V29) was used. Anthropometric data and rhythmological parameters were analyzed and gender-specific differences were compared by conducting a Mann-Whitney U test. ECG parameters, heart rate variability parameters and repolarization parameters were compared between warm and cold water by using a t-test for dependent samples. Pearson's correlation was applied to examine the correlations between skin temperature, heart rate, respiratory rate, arrhythmias and heart rate variability parameters as well as repolarization parameters. The correlation coefficient r and p-value are included in the manuscript. The significance level was set at $\alpha = 0.05$.

RESULTS

In this study, 12 healthy children aged 9-13 years were enrolled, including 4 girls and 8 boys. All 12 participants finished the protocol including immersion into warm water (34°C) and cold water (11°C). Due to recording quality, the analysis of the Holter-ECGs and thus the examination of arrhythmias and repolarization patterns was only possible for 9 participants, 2 girls and 7 boys. No participant reported symptoms such as discomfort, dizziness, nausea, shortness of breath or heart palpitations. No adverse events were seen.

Table 1 shows the characteristics of the 9 participants including anthropometric and repolarization data. No significant differences between girls and boys could be observed.

Table 1: Anthropometric and repolarization parameters of the study population

	Total (n = 9) Mean (min; max)	Female (n = 2; 22,2%) Mean (min; max)	Male (n = 7; 77,8%) Mean (min; max)	p-value
Age (years)	10.67 (9; 13)	9 (9; 9)	11 (9; 13)	0.111
Height (cm)	146.67 (134; 162)	146 (146; 146)	146.9 (134; 162)	0.889
Weight (kg)	35.19 (26.7; 46.8)	34.35 (34.2; 34.5)	35.4 (26.7; 46.8)	0.889
BMI (kg/m^2)	16.29 (14.3; 19.7)	16.1 (16.0; 16.2)	16.3 (14.3; 19.7)	0.889
Mean PR (ms)	123.25 (110; 141.7)	112.81 (110; 115.6)	126.24 (110; 141.7)	0.222
Mean QRS (ms)	75.99 (68.5; 89.3)	73.33 (71.7; 75)	76.75 (68.5; 89.3)	0.5
Mean QT (ms)	297.33 (257.5; 317.5)	264.58 (257.5; 271.7)	306.68 (296.7; 317.5)	0.056
Mean QTc (ms)	382.22 (365.1; 421.1)	381.47 (379.2; 383.8)	382.43 (365.1; 421.1)	0.889
Mean Tp-Te (ms)	49.03 (40.75; 57)	49.06 (44.38; 53.75)	49.03 (40.75; 57)	1.000

Arrhythmias

One proband showed 5 premature ventricular contractions (PVC) and 1 premature atrial contraction (PAC) in warm water as well as 7 PVC in cold water and 9 PVC during monitoring outside the pool, without reporting any symptoms. Another proband showed 4 PVC during monitoring outside the pool but none in the water, also without reporting any symptoms. There was no pathological prolongation or shortening of PR interval, QRS interval or QTc interval. One participant exhibited a high-normal QTc interval with a maximum of 462 ms. As shown in Table 2 there are no significant differences in the rhythmological parameters between warm and cold water.

Table 2: Rhythmological parameters in warm and cold water

	Warm Water Mean (min; max)	Cold Water Mean (min; max)	p-value
Mean PR (ms)	125 (110; 145)	120.56 (105; 142.5)	0.237
Mean QRS (ms)	74.44 (62.5; 90)	77.22 (70; 85)	0.128
Mean QT (ms)	297.22 (245; 337.5)	293.24 (265; 317.5)	0.643

Repolarization patterns

Figure 1 shows the progression of the frequency-corrected QT (QTc) interval, Tpeak-Tend (Tp-Te) interval and the mean heart rate over time during immersion in warm and cold water, as well as the surrounding resting periods. As shown in Table 3, no significant differences were found in the parameters of repolarization between warm and cold water. When comparing baseline (resting 1) with warm water, no significant differences were observed in the repolarization parameters (Table 4). However, when comparing baseline with cold water, significant differences were found in the parameters mean Tp-Te and maximum Tp-Te, with both values being significantly shorter during cold water immersion than in air. Mean Tp-Te showed a decrease of 16.6%, while maximum Tp-Te decreased by 10.8% (Table 5).

Table 3: Comparison of the repolarization parameters between warm and cold water

	Warm water Mean (min; max)	Cold water Mean (min; max)	p-value
Mean QTc (ms)	387.89 (361.5; 428.3)	381.39 (359; 423.3)	0.297
Min QTc (ms)	365.11 (337; 397)	366 (346; 402)	0.876
Max QTc (ms)	412.33 (370; 358)	397.78 (365; 442)	0.185
QTc first 30 sec (ms)	389.89 (355.5; 444)	381 (348.5; 440)	0.357
QTc last 30 sec (ms)	385.89 (353; 429.5)	374.33 (342; 393.5)	0.272
Difference in QTc between first and last 30 sec (ms)	-4 (-68; 35)	-6.67 (-47.5; 23)	0.860
QT dispersion (ms)	22.22 (10; 40)	30 (10; 50)	0.228
Mean Tp-Te (ms)	47.01 (37.5; 60)	45.88 (36.25; 52.5)	0.667
Min Tp-Te (ms)	36.67 (25; 50)	35.56 (30; 40)	0.719
Max Tp-Te (ms)	58.33 (45; 75)	57.22 (40; 70)	0.753
Tp-Te dispersion (ms)	21.67 (5; 40)	21.67 (10; 35)	1.000
Tp-Te first 30 sec (ms)	47.78 (27.5; 70)	45.28 (35; 55)	0.573
Tp-Te last 30 sec (ms)	46.39 (32.5; 52.5)	46.67 (32.5; 52.5)	0.894
Difference in Tp-Te between first and last 30 sec (ms)	-1.39 (-25; 20)	1.39 (-22.5; 12.5)	0.491

Table 4: Comparison of the repolarization parameters between baseline and warm water

	Baseline Mean (min; max)	Warm water Mean (min; max)	p-value
Mean QTc (ms)	392.75 (352.8; 448.5)	387.89 (361.5; 428.3)	0.655
Min QTc (ms)	379.67 (349; 423)	365.11 (337; 397)	0.149
Max QTc (ms)	406.33 (358; 462)	412.33 (370; 358)	0.697
QT dispersion (ms)	25.00 (10; 40)	22.22 (10; 40)	0.415
Mean Tp-Te (ms)	55 (41.3; 72.5)	47.01 (37.5; 60)	0.163
Min Tp-Te (ms)	45.83 (35; 60)	36.67 (25; 50)	0.272
Max Tp-Te (ms)	64.17 (50; 80)	58.33 (45; 75)	0.062
Tp-Te dispersion (ms)	18.33 (10; 30)	21.67 (5; 40)	0.822

Table 5: Comparison of the repolarization parameters between baseline and cold water (*significant at a level of α = 0.05)

	Baseline Mean (min; max)	Cold water Mean (min; max)	p-value
Mean QTc (ms)	392.75 (352.8; 448.5)	381.39 (359; 423.3)	0.313
Min QTc (ms)	379.67 (349; 423)	366 (346; 402)	0.093
Max QTc (ms)	406.33 (358; 462)	397.78 (365; 442)	0.558
QT dispersion (ms)	25.00 (10; 40)	30 (10; 50)	0.661
Mean Tp-Te (ms)	55 (41.3; 72.5)	45.88 (36.25; 52.5)	**0.036***
Min Tp-Te (ms)	45.83 (35; 60)	35.56 (30; 40)	0.067
Max Tp-Te (ms)	64.17 (50; 80)	57.22 (40; 70)	**0.009***
Tp-Te dispersion (ms)	18.33 (10; 30)	21.67 (10; 35)	0.102

Considering the correlations with total heart rate and respiratory rate, only the following significant correlations among all repolarization parameters were identified: difference in Tp-Te between the first and last 30 seconds in warm water and total minimum respiratory rate (Pearson's r = 0.772, p = 0.015) and Tp-Te dispersion in cold water and total respiratory rate range (Pearson's r = -0.670, p = 0.048).

In warm water the difference in QTc between the first and last 30 seconds correlated positively with minimum respiratory rate (Pearson's r = 0.736, p = 0.024) and negatively with respiratory rate range (Pearson's r = -0.712, p = 0.031). Furthermore, the difference in Tp-Te between the first and last 30 seconds correlated negatively with heart rate range (Pearson's r = -0.798, p = 0.010) and positively with

maximum respiratory rate (Pearson's r = 0.670, p = 0.048). In warm water, no correlations between the repolarization parameters and the parameters of heart rate variability were detected.

In cold water, a significant negative correlation was observed between the difference in QTc between the first and last 30 seconds and the minimum respiratory rate (Pearson's r = -0.707, p = 0.033). Additionally, negative correlations were found between maximum Tp-Te and respiratory rate range (Pearson's r = -0.691, p = 0.039) as well as increase in respiratory rate (Pearson's r = -0.717, p = 0.030). Furthermore, negative correlations were observed between Tp-Te dispersion and respiratory rate range (Pearson's r = -0.686, p = 0.041) and increase in respiratory rate (Pearson's r = -0.732, p = 0.025). The difference in Tp-Te between the first and last 30 second correlated positively with the increase in skin temperature (Pearson's r = 0.674, p = 0.047) and negatively with the cooling rate of skin temperature (Pearson's r = -0.690, p = 0.040). Accordingly, the greater the drop in skin temperature (negative values) and the faster the cooling rate (positive values), the smaller the difference in Tp-Te between the first and last 30 seconds. In cold water, the following significant negative correlations between QTc and heart rate variability parameters were also found: mean QTc and SDNN (Pearson's r = -0.735, p = 0.024), mean QTc and RMSSD (Pearson's r = -0.769, p = 0.015), minimum QTc and RMSSD (Pearson's r = -0.883, p = 0.002) and maximum QTc and SDNN (Pearson's r = -0.732, p = 0.025). However, no correlation was found between the Tp-Te parameters and the heart rate variability parameters.

Heart rate variability

Table 6 shows the heart rate variability parameters including SDNN, sNN50, RMSSD and triangular index in warm and cold water, including significant differences.

Table 6: Heart rate variability parameters in warm and cold water (*significant at a level of α = 0.05)

	Warm Water Mean (min; max)	Cold Water Mean (min; max)	p-value
SDNN (ms)	77,89 (38; 107)	57,60 (19; 131)	**0.016***
sNN50	36,22 (12; 83)	29,50 (2; 129)	0.525
RMSSD	47,56 (26; 93)	41,10 (17; 65)	0.065
Triangular index	11,67 (4; 19)	7,50 (4; 11)	**0.031***

DISCUSSION

The present study provides first-real life data on the influence of cold shock response on changes in repolarization patterns and the development of arrhythmias during immersion of healthy children into 11°C cold water.

Physiology of cold shock response and diving reflex

Immersion of the human body with the upper airways above water leads to the cold shock response due to skin cooling and activation of cutaneous cold receptors. This sympathetic response triggers tachycardia, reflex hyperventilation and impaired breath-holding, increasing the risk of water aspiration and making the cold shock response a main cause of drowning in cold water, even in experienced swimmers. It begins at water temperatures below 25°C, peaks at 10-15°C, and lasts 2-3 minutes, with maximum intensity around 30 seconds [4–6, 17]. In adults, heart rate increases by 62.5% and respiratory rate by 450% within the first minute of cold water immersion [18]. In children, the cold shock response is much less pronounced, leading to only a 26% increase in heart rate and a 55% increase in respiratory rate after one minute [7]. This age-related difference may be due to higher oxygen uptake, greater metabolic heat production or lower limb skin temperature in children [7]. In our cohort, heart rate increased by 31% and respiratory rate by 58% within the first minute of immersion into 11°C cold water. The cold shock response peaked at around 30 seconds, with acclimatization beginning by 60 seconds as heart and respiratory rates started to return to baseline [16].

Submersion, especially facial immersion and apnea trigger the parasympathetic diving response, resulting in bradycardia to conserve oxygen and extend underwater time [4]. In adults, facial immersion reduces heart rate by 42% within 30 seconds [6]. Our recent study in healthy children showed a heart rate decrease of 16% during dry apnea, 28% during face immersion, and 25% during full submersion within 30 seconds [14].

When both antagonistic reactions occur simultaneously during submersion in cold water, an autonomic conflict may arise. The cold shock response triggers tachycardia via the sympathetic nervous system, while the diving reflex causes bradycardia via the parasympathetic nervous system. The simultaneous and intense activation of both branches of the autonomic nervous system is thought to increase the risk of cardiac arrhythmias. Arrhythmia incidence rises from 2% during cold-water immersion with free breathing to 82% when the face is submerged and breath is held. These arrhythmias may also contribute to potential cold water fatalities. Even non-fatal arrhythmias can cause unconsciousness, incapacity and inability to swim, leading to secondary drowning [4–6, 19].

Development of arrhythmias as a cause of drowning

With young age and the inability to swim being the greatest risk factors, drowning is one of the leading causes of accidental death worldwide [3]. It is associated with the two events of immersion and submersion and, since it often occurs in water colder than body temperature, also with cooling [4]. In fact, immersion in water is the second most common cause of accidental death among children and the third most common among adults, regardless of whether the individuals actually drown [20]. In the past, the presence of water in the lungs of a deceased person was taken as evidence of death by drowning, whereas the absence of water led to assumptions of death by hypothermia or "dry drowning," even though most immersions were too brief to induce dangerous hypothermia. Today, it is understood that the cold shock response, particularly the inability to hold one's breath and the accidental aspiration of water, is a major cause of drowning. Additionally, it is believed that cardiac arrhythmias triggered by

autonomic conflict and potentially leading to sudden cardiac death, may play a significant role in drowning but often go undetected. These arrhythmias cannot be identified post-mortem and may contribute to water aspiration due to incapacitation, resulting in a cause of death that closely resembles actual drowning [6].

Both sympathetic cold shock and parasympathetic diving reflex can independently trigger arrhythmias, but the risk increases significantly when both act simultaneously, leading to autonomic conflict [6]. They are typically atrial, nodal or ventricular premature contractions or bradycardic arrhythmias such as sinus arrest or AV block, alternating with short episodes of ventricular tachycardia, such as torsade de pointes. These arrhythmias are often respiration-related and occur especially when breath-holding ends or the heart shifts between sympathetic and parasympathetic dominance. The fact that these arrhythmias are mostly asymptomatic suggests that they go without major hemodynamic compromise [6, 21, 22]. It has been shown that during rapid heart rate changes, such as facial immersion in cold water, QT interval adaption is initially absent. Despite significant bradycardia, no QT interval prolongation occurred even after 30 seconds. This delayed or incomplete QT adjustment, known as QT hysteresis, may promote ventricular arrhythmias during autonomic conflict, possibly due to latency of the adaptation to the heart rate, or a unique incomparable vagal response triggered by facial immersion [6, 23–25].

Patients with channelopathies like Long QT Syndrome (LQTS), appear to be particularly vulnerable to drowning accidents with sudden cardiac death due to an increased risk of arrhythmias triggered by physical exertion or emotional stress, while swimming is considered the highest-risk activity, especially in children and adolescents. Several retrospective case reports and a small pilot study suggest a link between swimming and sudden cardiac death in LQTS patients [26–31]. Cardiac repolarization in LQTS patients appears to be more sensitive to autonomic influences than in healthy individuals. As the QT interval is strongly influenced by the balance between sympathetic and parasympathetic activity, autonomic conflicts or isolated reactions like cold shock reflex or diving response may trigger arrhythmias during swimming, increasing the risk of malignant arrhythmias, sudden cardiac death and drowning. Further research on the responses to immersion and submersion in children with congenital heart diseases, such as LQTS, requires reliable baseline data from healthy children.

Influence of cold shock response on cardiac activity in children

Significant differences in skin temperature, heart rate and respiratory rate are reported between warm water and cold water immersion. In warm water, heart and respiratory rates remained relatively constant, whereas in cold water, with a significant drop in skin temperature by 8°C, heart rate increased by 31% and respiratory rate increased by 58% [16]. The analysis of heart rate variability clearly shows that immersion into cold water is a strong stressor and triggers a significant sympathetic response. All heart rate variability parameters are lower in cold water, with some being significantly reduced, indicating decreased heart rate variability and therefore increased sympathetic activity.

The QT interval represents the duration of ventricular repolarization. It is dependent on heart rate and can be corrected for heart rate as QTc. In children aged 9 to 13 years, a QTc interval is considered

physiological if it is below 460 ms in girls and below 440 ms (or below 450 ms during mild exertion) in boys and above 350 ms [32, 33]. A prolonged QTc interval indicates a repolarization disorder and may promote the development of ventricular arrhythmias, particularly torsade de pointes tachycardia. In our cohort, the average QTc was 382 ms, with a slightly, but not significantly shorter QTc duration in cold water compared to warm water and compared to baseline. The difference in QT duration between warm and cold water was also not significant, although the QT interval was slightly lower in cold water. Normally, QT duration should decrease with increasing heart rate. However, despite a significant 31% increase in heart rate in cold water, this expected QT shortening does not occur. Thus, we were able to demonstrate a QT hysteresis during cold water immersion even without facial immersion. Nevertheless, the QTc interval also remains nearly unchanged. Regarding the difference between the QTc of the first 30 seconds and the last 30 seconds, there were no significant differences between warm and cold water, although QTc decreased slightly more over time in cold water than in warm water. This temporal dynamic appears to be primarily dependent on the development of respiratory rate in the present case, as the difference in QTc between the first and last 30 seconds only correlates with respiratory rate parameters. Thus, we can provide further evidence that the development of arrhythmias during drowning is primarily related to respiration. Additionally, in cold water, negative correlations between QTc interval and heart rate variability parameters are observed. With lower values in heart rate variability and thus greater sympathetic activity, there is a prolongation of the QTc interval. Normally, again, sympathetic activation and the resulting tachycardia would be expected to shorten the QT interval. However, if heart rate and heart rate variability increase while QTc also increases, this suggests that the QT interval does not adequately or quickly enough adapt to the sudden change in heart rate, again indicating the presence of QT hysteresis. The simultaneous occurrence of tachycardia and a prolonged, improperly adjusted QT interval could promote an increasing risk of ventricular tachycardias. Since there are no significant differences in QT and QTc between warm and cold water, QT hysteresis and thus the risk of arrhythmia development is likely to be minimal in these healthy children. However, this effect could be much more pronounced in children with preexisting heart conditions.

QT dispersion, defined as the difference between the longest and shortest QT intervals, serves as an indicator for the spatial inhomogeneity of ventricular repolarization. It is assumed that an increasing time difference in the repolarization process across different myocardial regions facilitates the occurrence of reentry phenomena and, consequently, the potential development of ventricular tachyarrhythmias. For this reason, QT dispersion is considered a risk marker for sudden cardiac death by some authors. Due to the lack of standardized methods for determining QT dispersion, as well as the absence of reference and pathological threshold values, its measurement is typically avoided in clinical practice. However, it can be assumed that a QT dispersion of < 65 ms indicates a physiological QT dispersion in adults. A pathological QT dispersion > 65 ms is commonly observed in patients with structural heart diseases or malignant ventricular tachyarrhythmias [34]. QT dispersion in our subjects ranged between 10 and 50 ms, with slightly but not significantly higher values in cold water compared to warm water. QT dispersion showed no correlation with any parameters and does not appear to be influenced by an increase in heart rate or respiratory rate in these heart-healthy children. The QTc

dispersion can also be calculated. However, it is recommended not to correct the QT dispersion for heart rate in children, as the QTc dispersion is influenced by the commonly occurring sinus arrhythmia in childhood [35]. Therefore, the authors also refrain from mentioning the QTc dispersion here.

The Tpeak-Tend (Tp-Te) interval, defined as the interval from peak to end of the T wave, represents the transmural gradient of repolarization. It is considered a reliable marker for predicting ventricular tachycardia, ventricular fibrillation and sudden cardiac death and is frequently used for risk stratification in patient groups with various cardiac conditions, such as congenital arrhythmias, ischemic artery disease, heart failure or hypertension [36]. An increased variation in repolarization between the heart's base and apex, either intramurally or within the interventricular septum, contributes to a higher risk of ventricular arrhythmias, particularly in individuals with channelopathies. In healthy children, the Tp-Te interval averages around 60 ms, with a range of 20–120 ms, while boys and older children tend to have longer intervals. The Tp-Te interval prolongs as heart rate decreases. Similar to QT dispersion, Tp-Te dispersion can be calculated as the difference between the longest and shortest Tp-Te interval. In healthy children, it averages approximately 40 ms, with a range of 6–80 ms, while Tp-Te dispersion increases with age but does not show differences between boys and girls [37]. The Tp-Te interval in our cohort averaged 49 ms and was slightly lower in cold water than in warm water but significantly lower than the baseline Tp-Te in air. Tp-Te dispersion showed the same mean value in both warm and cold water and was slightly higher than at baseline. The temporal dynamics of the Tp-Te interval, illustrated by the difference between the first and the last 30 seconds, showed a minimal decrease in warm water and an equally small increase in cold water. The Tp-Te interval, its dispersion, and its temporal dynamics appear to be primarily influenced by respiratory rate. A smaller difference in Tp-Te between the first and last 30 seconds can be expected with a large drop in skin temperature and rapid cooling. In contrast to QTc, no correlation between the Tp-Te interval and heart rate variability parameters was observed in either warm or cold water.

Although there is clear indication of a missing or insufficient adaptation of the QT interval to the suddenly increased heart rate (QT hysteresis) during cold water immersion, no significant differences in repolarization patterns between warm and cold water could be demonstrated. However, during cold water immersion, a significantly shorter Tp-Te interval was observed compared to the baseline value in air, suggesting a notable impact on the transmural gradient of repolarization. While two children exhibited non-pathological premature ventricular and atrial contractions regardless of immersion, no cardiac arrhythmias were observed during cold water immersion. This may be explained by the absence of facial immersion, as the risk of arrhythmias significantly increases during simultaneous cold-water and facial immersion with apnea, as a result of an autonomic conflict. Nevertheless, the cold shock response itself also appears to have the potential to contribute to the development of repolarization abnormalities and could promote the occurrence of life-threatening arrhythmias in predisposed individuals or patients with pre-existing conditions.

CONCLUSION

The present study is the first providing data on repolarization patterns and arrhythmia burden in healthy children during the immersion into 11°C (52°F) cold water. The data demonstrated that cold water immersion acts as a potent sympathetic stressor associated with mild QT hysteresis. Compared to baseline values in air, a significantly shorter Tp-Te interval was observed in cold water, indicating a significant influence on the transmural gradient of repolarization. Although no arrhythmias were detected during cold water immersion in healthy children, the cold shock response itself appears to have the potential to induce repolarization abnormalities.

LIMITATIONS:

The current study is limited by the small number of participants, the narrow age range of the subjects and the male dominance in the gender ratio, therefore a bias due to proband selection is possible. The small number of patients resulted from very restrictive ethical approval for a potentially harmful test protocol in children. Furthermore, the measurements were conducted using materials and devices not qualified for use underwater. Although the devices were well-adapted to be waterproof, we cannot completely exclude aberrant values because of off-label use.

STATEMENTS AND DECLARATIONS

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Conflict of Interest: The authors declare to have no conflicts of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and / or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study received ethical approval by the ethics committee University of Leipzig and is listed under the reference 233/24-ek.

Consent to participate: Informed consent was obtained from all individual participants included in the study as well as from their legal guardians.

Data Availability Statement: Due to privacy and data protection regulations, the data are not publicly available but can be provided upon reasonable request and with appropriate approvals.

Author contributions: Sophie Peter and Christian Paech supervised the study and developed the study protocol. Sophie Peter, Karoline Witte, Jacqueline Prautsch and Mia Bovet designed the test setting and the required material. Sophie Peter, Christian Paech, Karoline Witte and Jacqueline Prautsch conducted the measurements during protocol. Sophie Peter performed the statistical analysis. Sophie Peter and Christian Paech wrote the main manuscript text. All authors reviewed and approved the final manuscript.

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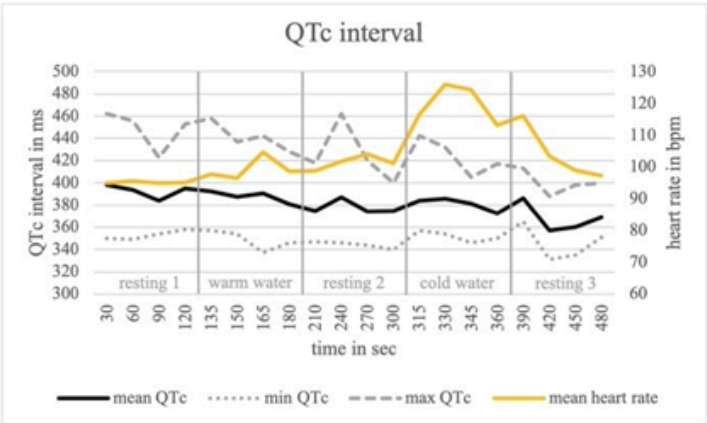
Figures



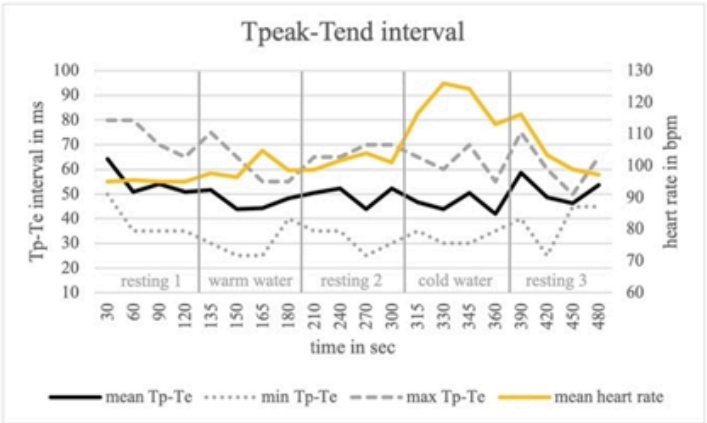


Figure 1

QTc interval, Tpeak-Tend (Tp-Te) interval and mean heart rate over the time