Ventricular response during lungeing exercise in horses with lone atrial fibrillation

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Summary

Reasons for performing the study: Atrial fibrillation (AF) is the most important dysrhythmia affecting performance in horses and has been associated with incoordination, collapse and sudden death. Limited information is available on ventricular response during exercise in horses with lone AF.

Objectives: To investigate ventricular response in horses with lone AF during a standardised lungeing exercise test.

Methods: A modified base-apex electrocardiogram was recorded at rest and during a standardised lungeing exercise test from 43 horses diagnosed with lone AF. During the test horses walked for 7 min, trotted for 10 min, cantered for 4 min, galloped one minute and recovered for 7 min.

Results: Individual average heart rate during walk ranged from 42 to 175 bpm, during trot from 89 to 207 bpm, during canter from 141 to 269 bpm, and during gallop from 191 to 311 bpm. Individual beat-to-beat maximal heart rate ranged from 248 to 492 bpm. Ventricular premature depolarisations were present in 81% of the horses: at rest (16%), during exercise (69%), and during recovery (2%). In 33% of the horses, broad QRS complexes with R-on-T morphology were found.

Conclusions: Exercising horses with lone AF frequently develop disproportionate tachycardia. In addition, QRS broadening and even R-on-T morphology is frequently found. QRS broadening may originate from ventricular ectopic foci or from aberrant intra-ventricular conduction, for example due to bundle branch block. This might explain the high number of complexes currently classified as ventricular premature depolarisations.

Potential relevance: Prevalence of QRS broadening and especially R-on-T was very high in horses with AF and was found at low levels of exercise. These dysrhythmias are considered risk factors for the development of ventricular tachycardia and fibrillation and they might explain signs of weakness, collapse or sudden death that have been reported in horses with AF.

Introduction

With a prevalence of about 2.5% [1], atrial fibrillation (AF) is the most important dysrhythmia affecting performance in horses. During AF in horses, multiple wavelets propagate through the atria at a rate of approximately 300 to 500 pulses per min [2; 3]. The term lone AF is used when there is no evidence of underlying structural disease and AF occurs in an otherwise healthy individual. The high parasympathetic tone in horses with lone AF causes the atrioventricular (AV) node to block most of these impulses, resulting in a normal ventricular rate at rest. The chaotic self-sustained electrical activity in the fibrillating atria causes independent activation of individual muscle fibres rather than the synchronous contraction seen during normal sinus rhythm [4]. As a consequence, atrial contribution to ventricular filling is lost, causing a decrease in stroke volume, especially during exercise. In addition, sympathetic tone prevails during exercise, reducing the blocking function of the AV node. This causes many of the atrial fibrillatory impulses to be conducted to the ventricles, resulting in a disproportionate tachycardia. Both factors reduce cardiac function and therefore athletic ability. Depending on the exercise load, AF can be an incidental finding or can result in performance loss or in signs of weakness and incoordination (9%) or even collapse during work (2%) [5].

Although numerous studies have been dedicated to AF and in particular its treatment options, limited information is available concerning electrocardiography (ECG) during exercise in horses with AF [6-9]. The aim of this study was to report the ventricular response and dysrhythmias in horses with lone AF during a standardised lungeing exercise test.

Materials and methods

Study population

Forty-three horses that were presented at the Department of Large Animal Internal Medicine, Ghent University for cardiac examination and were diagnosed with lone AF were included in this study..

Horses (17 mares, 5 stallions, 21 geldings; 39 Warmbloods, one Friesian, one Anglo Arabian, 2 French Trotters) had an age of 10.6 ± 3.6 years (mean ± standard deviation, s.d.) (range 4–20 years), a height of 170.2 ± 6.1 cm (range 152–181 cm) and a body weight of 584.5 ± 54;1 kg (range 468–710 kg). Presumptive AF duration was 3 weeks to one year; in 3 horses AF duration was not known. Horses were used for dressage (n = 7), jumping (n = 21), both (n = 3), eventing (n = 2), recreational (n = 6), trotting (n = 2), cross-country (n = 1) or driving (n = 1). Presenting signs were performance reduction (n = 28), epistaxis (n = 3) and weakness and collapse (n = 1). Eleven horses showed no signs.

In 36 horses, plasma ionised calcium, potassium and magnesium concentrations were determined. Thirty-six horses were successfully converted using transvenous electrical conversion (TVEC) (n = 33) or quinidine sulphate (n = 3). Three horses failed to convert by TVEC. In 4 horses no treatment was initiated.

Electrocardiography

Modified base-apex ECG was performed using a Televet 100® recording system[a] as described elsewhere [10]. Briefly, 4 self-adhesive electrodes were positioned under a girth[b] in a modified base-apex configuration: the right arm electrode was positioned 15 cm right of the withers, the left leg electrode on the thorax caudal to the left elbow. The left arm electrode was placed 10 cm above the green one. The reference electrode (right leg) was positioned 15 cm left from the withers. All electrodes were connected to the recording device in the girth.

The ECG was visualised in real time on a laptop computer and the signal was digitally stored to allow offline analysis.

Exercise protocol

Recording started as soon as the monitoring system was fitted, including a 15 min recording at rest. The exercise protocol was a standardised lungeing exercise test in which horses walked for 7 min, trotted for 10 min, cantered for 4 min, and galloped for one minute. The recovery period was 7 min. The 2 min walk to the exercise ring and back was included in the recording time during walk and the recovery phase, respectively.

Intra-atrial electrocardiography

In 37 horses, a bipolar temporary pacing electrode[c] was positioned in the right atrium in the standing horse. This allowed simultaneous recording of an intra-atrial electrogram and a base-apex ECG at rest using a modified Televet 100® recorder[d] or Pacemaker Programmer.[e] The signal was digitally stored to allow offline analysis.

Data analysis

Offline analysis of exercise ECGs was performed by an experienced observer (T.V.) using dedicated software.[f] All recorded ECGs were of diagnostic quality, and 16% showed important motion artefacts but still allowed accurate diagnosis. Standard gain (10 mm/mV) and paper speed (25 mm/s) were increased up to 20 mm/mV and 200 mm/s where necessary to allow accurate analysis. The number and type of dysrhythmias were documented by visual inspection. In each horse, the average heart rate at rest, walk, trot, canter and gallop was calculated; maximal heart rate was calculated from the single shortest RR interval obtained during the protocol. The duration of the QRS complexes and S waves was measured for 50 consecutive cycles at rest and during galloping, and in QRS complexes with an aberrant morphology (Fig 1). QRS complexes with abnormal morphology were categorised as ventricular premature depolarisations (VPDs), when changes in relative size of Q, R or S

waves leading to changes in morphology of the complex were observed or when duration of the QRS complex was altered. Slight changes in QRS amplitude due to respiration were not taken into account. When the R wave of the abnormal QRS complex was projected on the T wave of the previous QRS complex, QRS complexes were categorised as 'R-on-T' complexes.

In each horse, measurements of QRS and S-wave duration of normal complexes (rest and gallop), VPDs and R-on-T complexes were averaged over the measured cycles. The resulting means were compared between the complex types by a linear mixed model with complex type as fixed categorical effect and with the horses as subjects in a repeated measurements analysis.

Atrial fibrillation cycle length (AFCL) was calculated from intra-atrial electrograms as an estimate of atrial refractoriness by measuring the interval between successive atrial depolarisation waves from a 20 s window. Individual maximal heart rate was compared to AFCL using Pearson's correlation test. Data are presented as mean ± s.d.. Significance was set at $P<0.05$.

Results

Three horses had mild hypocalcaemia (1.4 mmol/L; reference range 1.5–1.8 mmol/L) and one was both hypocalcaemic (1 mmol/L; reference range 1.5–1.8 mmol/L) and hypokalaemic (1.8 mmol/L; reference range 2.9–4.4 mmol/L).

Forty-two horses completed the protocol. In one horse the protocol was terminated during walking to the exercise ring because of a high heart rate (297 bpm at walk). In 2 trotting horses the canter and gallop were replaced by trotting at increased speeds.

Individual average heart rates at rest, walk, trot, canter and gallop are shown in Fig 2. At rest and during walk, 35% of the horses with AF had an average heart rate above the normal reference range (reference range rest: 25–50 bpm; reference range walk: 60–80 bpm) [11]. During trot and canter the average heart rate was above reference range in 83% and 98% of the horses with AF, respectively (reference range trot: 80–120 bpm; canter 120–150 bpm) [11]. During gallop, all horses with AF in this study had an average heart rate above reference range (150–180 bpm) [11]. Individual maximal heart rate during the lungeing exercise test ranged from 248 bpm to 492 bpm (Fig 3), while the normal upper limits in maximal heart rate during vigorous exercise is 240 bpm.

In 81% of the horses with AF, QRS complexes with abnormal morphology, categorised as VPDs, were observed at rest (16%), during exercise (69%) or recovery phase (2%). Encountered abnormal morphologies were RS, rS, S or Rs in type. In 71% of the horses, different abnormal morphologies were observed. Both at rest and during exercise, abnormal QRS complexes were often associated with episodes of tachycardia due to increased sympathetic tone.

In 33% of the AF horses, broad QRS complexes with an ‘R-on-T’ morphology were observed (Fig 4). All QRS complexes with R-on-T morphology were associated with increased sympathetic tone: they occurred at rest when horses were aroused, or during fast galloping.

Episodes with R-on-T were short lasting, varying from one beat to 10 consecutive beats. Often R-on-T episodes were terminated by a long RR interval. Number of episodes per horse varied from 1 to 10.

Significant QRS shortening occurred during gallop ($P<0.0005$). Both VPDs and QRS complexes with R-on-T morphology were significantly longer than normal QRS complexes during gallop ($P<0.0005$) and shorter compared to normal QRS complexes at rest ($P<0.0005$). R-on-T complexes were not significantly different from VPDs ($P = 1.0$) (Fig 5). However, in R-on-T complexes the R wave is no longer discernible and only the S wave is measured. S wave duration was significantly longer for R-on-T complexes than for normal complexes at rest ($P = 0.012$) and during gallop ($P<0.0005$). Values for R-on-T complexes were also significantly longer compared to VPDs ($P<0.0005$) (Fig 6).

Average AFCL ranged from 128 to 207 ms. In 8 horses the recorded maximal heart rate was slightly higher than atrial fibrillation rate. There was no correlation between calculated AF rate at rest and individual maximal heart rate ($P = 0.591$).

Discussion

This study shows that in horses with lone AF, heart rate can raise high above the normal maximal heart rate. Excessively high heart rates are predominantly present during gallop and when horses were startled. Furthermore, QRS broadening is often found.

During AF, the AV node receives a high number of random electrical impulses from multiple wavefronts circulating in the atria. Ventricular response rate is determined by autonomic influences, the amount of concealed conduction and inherent AV nodal function [12; 13]. At rest, parasympathetic tone prevails and causes depressive effects on the AV node, hyperpolarisation and prolonged AV conduction time, which leads to conduction block [14; 15]. In this situation, concealed conduction takes place: atrial impulses reach the AV node during the relative refractory phase and hence only partially penetrate into the AV node without reaching the ventricles [16]. Concealed conduction of an impulse affects the conduction of a subsequent impulse by delaying it, blocking it entirely or causing repetitive concealed conduction [17]. It is supposed that during AF, many of the atrial impulses are concealed within the AV node [18]. During exercise or stress however, vagal influence diminishes and sympathetic tone becomes predominant [19]. The refractory period of the AV node shortens, which decreases the occurrence of concealed conduction and can lead to an increase in ventricular rate [20].

Another mechanism potentially contributing to increased heart rate during exercise is the dependency of the refractory period of the AV node on cycle length [21; 22]. The functional refractory period of the AV node shortens slightly with shorter cycle lengths [23; 24], increasing the rate with which atrial impulses can be propagated to the ventricles. Mendez *et al.* reported the occurrence of 'abnormally' short RR intervals after early atrial premature responses [21]. It seemed that the AV node responded to very early reexcitation with an abrupt shortening of its refractory period, thus leading to very short RR intervals. A possible

explanation for this phenomenon could be a cumulative effect of repeated short cycles on AV nodal refractory period.

QRS complexes with abnormal morphology, categorised as VPDs, were observed in 82% of the horses with AF, with 2 or more different morphologies present in 73%. In 36% of the horses with AF, QRS complexes with an 'R-on-T' morphology were observed. In comparison, the reported prevalence of VPDs during exercise in clinically healthy dressage and show jumping horses is 5% [25] and 18% [26]. In human patients, wide QRS complexes are frequently observed in AF [27]. Two different processes could be causing this broadening: ventricular ectopy or aberrant intra-ventricular conduction of supraventricular impulses [28]. Despite the difference in origin of these 2 processes (atrial or ventricular), differentiation is complicated in AF, since the relation between atrial impulses and QRS complexes is never recognisable. The differentiation, however, has prognostic and therapeutic importance, since aberrancy will disappear when sinus rhythm is restored, whereas ventricular ectopy can significantly affect both prognosis and treatment [27; 28].

The differentiation is very difficult based on surface electrocardiography alone but in human medicine, several criteria have been suggested amongst which QRS contour and resemblance of the initial deflection of the anomalous complex with that of flanking normal complexes seemed the most useful [28; 29]. Some of the broad QRS complexes in the horses with AF did fulfil the criteria for aberrant conduction. However, it is unknown whether or not these criteria also apply to horses. In 73% of the horses with AF, abnormal QRS complexes were present during exercise, a period in which sympathetic tone prevails. Sympathetic stimulation accelerates AV nodal conductivity [30] and shortens AV nodal refractoriness. With increasing heart rates, the refractory period of the AV node can become shorter than that of left or right bundle branch, such that atrial impulses conducted through the AV node may hit one of the bundles during its refractory period. When this happens, the impulse is forced to follow an

alternative pathway through the ventricles, leading to aberrant conduction caused by bundle branch block [27]. Twenty percent of the horses had abnormal QRS complexes at rest. In all but one of these horses, the QRS abnormality was observed when horses were distressed or excited, causing increased sympathetic tone and potentially leading to aberrant conduction. In the remaining horse, repeatedly a relatively long RR interval was followed by a short RR interval with altered QRS morphology. This phenomenon is described in human medicine as Ashman phenomenon and is caused by aberrant intra-ventricular conduction due to right bundle branch block. This is explained by the long refractory period of the right bundle branch at slow heart rates compared to the AV node or left bundle branch [27], and the fact that refractory periods are dependent upon the length of the previous RR interval. As such, when a short cycle follows a long one, the right bundle branch with its longer refractory period is still refractory, leading to a QRS complex with a specific aberrant morphology. A similar mechanism was thought to be present in this horse (Fig 7).

In many horses, broad QRS complexes had different morphologies, which were thought to be caused by ventricular ectopy. In 4 horses, concomitant hypocalcaemia and/or hypokalaemia was present, which may have contributed to the dysrhythmias [31; 32]. However, abnormalities were mild, and horses without electrolyte disturbances also had ectopic QRS complexes. Abnormal QRS complexes were most frequently observed during periods involving sympathetic stimulation. In human medicine, substantial evidence links enhanced sympathetic activity with ventricular dysrhythmias and sudden cardiac death in patients with various cardiac conditions [33]. Adrenergic facilitation of irregular ventricular activity has been attributed to increased automaticity, decreased diastolic threshold and decreased refractoriness. It has been shown in dog hearts that stimulation of the sympathetic nerves increases temporal dispersion of the refractory periods in ventricular muscle [34]. As a result, re-entry and fractionation of a ventricular wave front can be facilitated.

Many horses with AF had 'R-on-T' morphology on the surface ECG, a term which describes superposition of the ventricular depolarisation of an ectopic ventricular beat on the T wave of the preceding beat [35; 36]. In man, R-on-T is considered a high-grade risk factor for development of ventricular tachycardia or fibrillation [36; 37]. However, in man, atrial fibrillation is not typically associated with R-on-T. Although the morphology of the phenomenon observed in this study in horses with AF seems to be identical to what is described as 'R-on-T' in human medicine, it cannot be proven with certainty whether this rhythm was supraventricular or ventricular in origin. A recent study in healthy horses reported on what was called 'torsade-like polymorphic ventricular tachycardia' (T-PMVT) in the immediate post-race period [38]. Although QRS complexes described in that study showed similarities with the 'R-on-T' complexes seen in the current study, they occurred typically during race recovery. The authors also suggested autonomic influences as a potential cause for these dysrhythmias.

In human medicine, aberrancy is considered to be of limited clinical significance in AF, whilst VPDs are regarded as potential risk factors for the induction of ventricular tachycardia or fibrillation [28]. It is not known whether this is also the case for horses. Whilst R-on-T occurred relatively frequently, in none of the horses it deteriorated to ventricular fibrillation. This might suggest that R-on-T is caused by aberrancy rather than ventricular ectopy. However, signs of weakness, collapse and even sudden death have been observed in AF horses [5] and could have been associated with ventricular ectopy.

Individual beat-to-beat maximal heart rate was compared to AFCL in order to investigate the origin of the broad QRS complexes. If broad QRS complexes were due to bundle branch block, their origin would be supraventricular, and the shortest RR interval would approximate or be longer than the AFCL. If the shortest RR interval would be much shorter than the AFCL, broad QRS complexes would have to be ventricular in origin. Ten horses had a

maximal heart rate in excess of the atrial fibrillation rate. However, differences were small and could be explained by temporal and spatial dispersion in AFCL and by the fact that increased sympathetic tone shortens AFCL [18]. As such, the exact origin of the abnormal QRS morphology remained unknown.

A limitation of the study is the standardised lungeing exercise tests performed in horses with AF, meaning that for many horses workload was below their normal level. Still, a very high prevalence of dysrhythmias was found. Although maximal exercise was not studied, higher workload might be associated with more severe rhythm disturbances.

In conclusion, horses with AF frequently develop disproportionate tachycardia during exercise. QRS broadening and R-on-T phenomenon are often found and may originate from ventricular ectopy or aberrant intra-ventricular conduction. At this point, the origin of broad QRS complexes in horses with AF remains uncertain. The high number of VPDs in these horses might indicate that some of these complexes result from aberrant conduction rather than ventricular ectopy. However, in human medicine, R-on-T is always considered ventricular in origin. QRS broadening and R-on-T complexes might be a risk factor for exercise-associated weakness, collapse or even death. One should be aware of the high prevalence and potential risk factor of these dysrhythmias in horses with lone AF, even if they are used for low level exercise because sudden stress in a resting horse can elicit these dysrhythmias.

Authors' declaration of interests

The authors declared no competing interests.

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Author contributions

Study design: G. van Loon and T. Verheyen. Data collection and study execution: T. Verheyen, A. Decloedt and N. Van Der Vekens. Data analysis and interpretation: T. Verheyn, A. Decloedt and S.U. Sys. Preparation of the manuscript: T. Verheyen, A. Decloedt, N. Van Der Vekens, D. De Clercq, S.U. Sys and G. van Loon.

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Manufacturers' addresses

[a]Televet 100®, Kruuse, Marslev, Denmark.

[b]Orthohorse®, Mainat Vet, Barcelona, Spain.

[c]U.S.C.I. Ballinasloe, County Galway, Ireland.

[d]K. Engel, Engel Engineering Services GmbH, Offenbach am Main, Germany.

[e] Programmer 7990, Medtronic, Minneapolis, USA.

[f]Televet 100® software version 4.2.0, Kruuse, Marslev, Denmark.

FIGURE LEGENDS

Fig 1: Electrocardiogram showing calliper placement for QRS and S wave duration for a normal complex and S wave duration for a R-on-T complex.

Fig 2: Heart rate in 43 horses with lone atrial fibrillation at rest and during exercise. Grey boxes indicate lower quartile to upper quartile with horizontal black line indicating median. Sample minimum and maximum are shown by whiskers. Symbols indicate outliers. Blue bars indicate typical heart rate ranges for each speed in normal horses.

Fig 3: Individual beat-to-beat maximal heart rates during exercise as a function of calculated AF rate of 37 horses with lone atrial fibrillation.

Fig 4: Electrocardiogram showing R-on-T phenomenon (arrows) in a horse with atrial fibrillation during galloping.

Fig 5: Duration (mean ± s.d.) of normal QRS, abnormal QRS and R-on-T complexes at rest and during exercise. Different letters indicate significant differences.

Fig 6: Duration (mean ± s.d.) of S waves of normal QRS, abnormal QRS and R-on-T complexes at rest and during exercise. Different letters indicate significant differences.

Fig 7: Electrocardiogram showing a long-short cycle with broad QRS complex terminating the sequence, suggestive of Ashman phenomenon.

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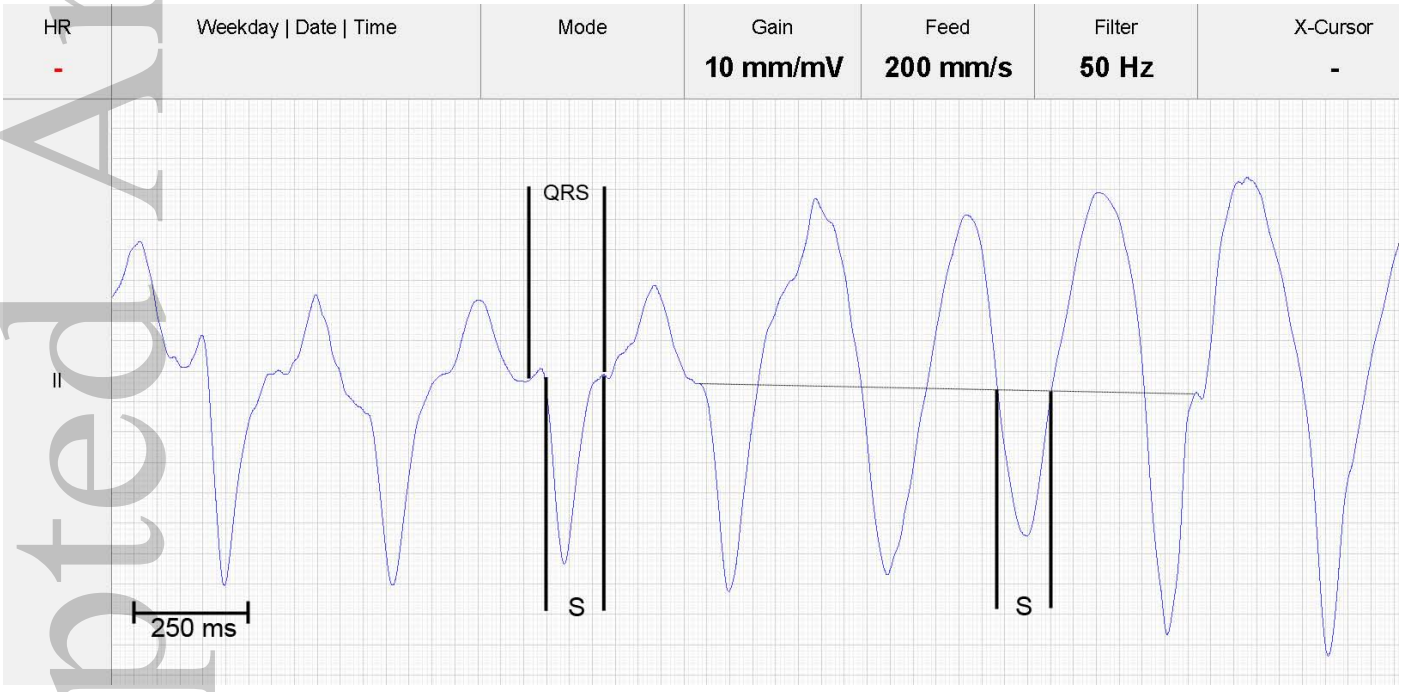

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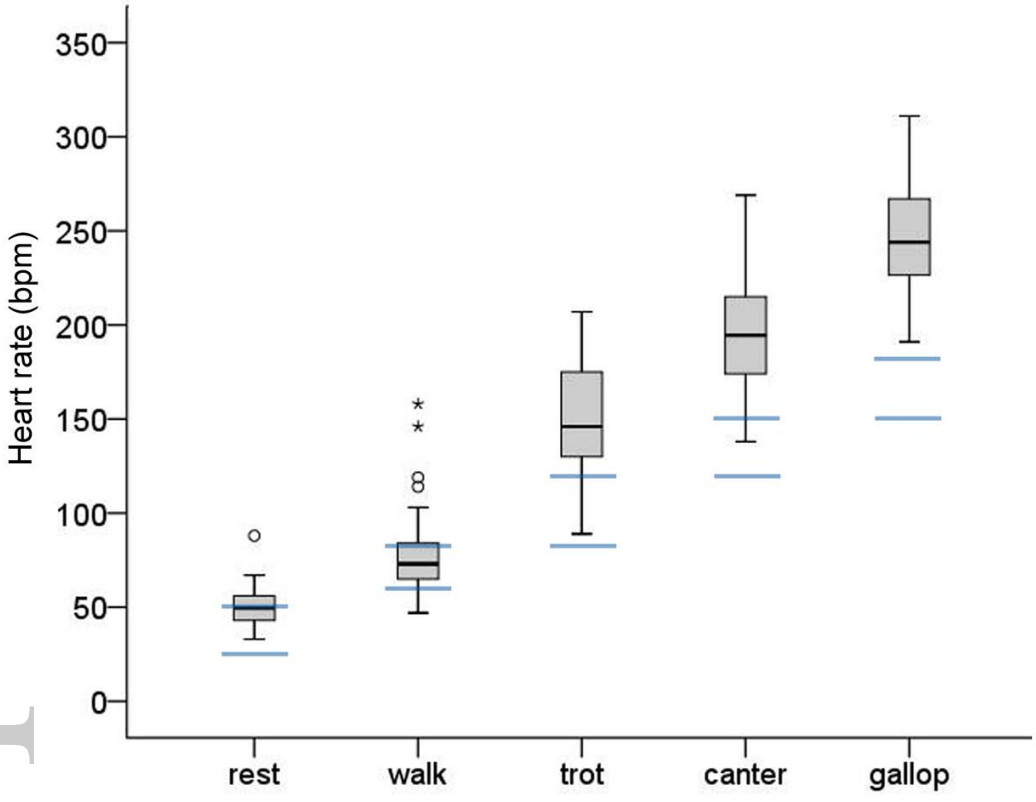

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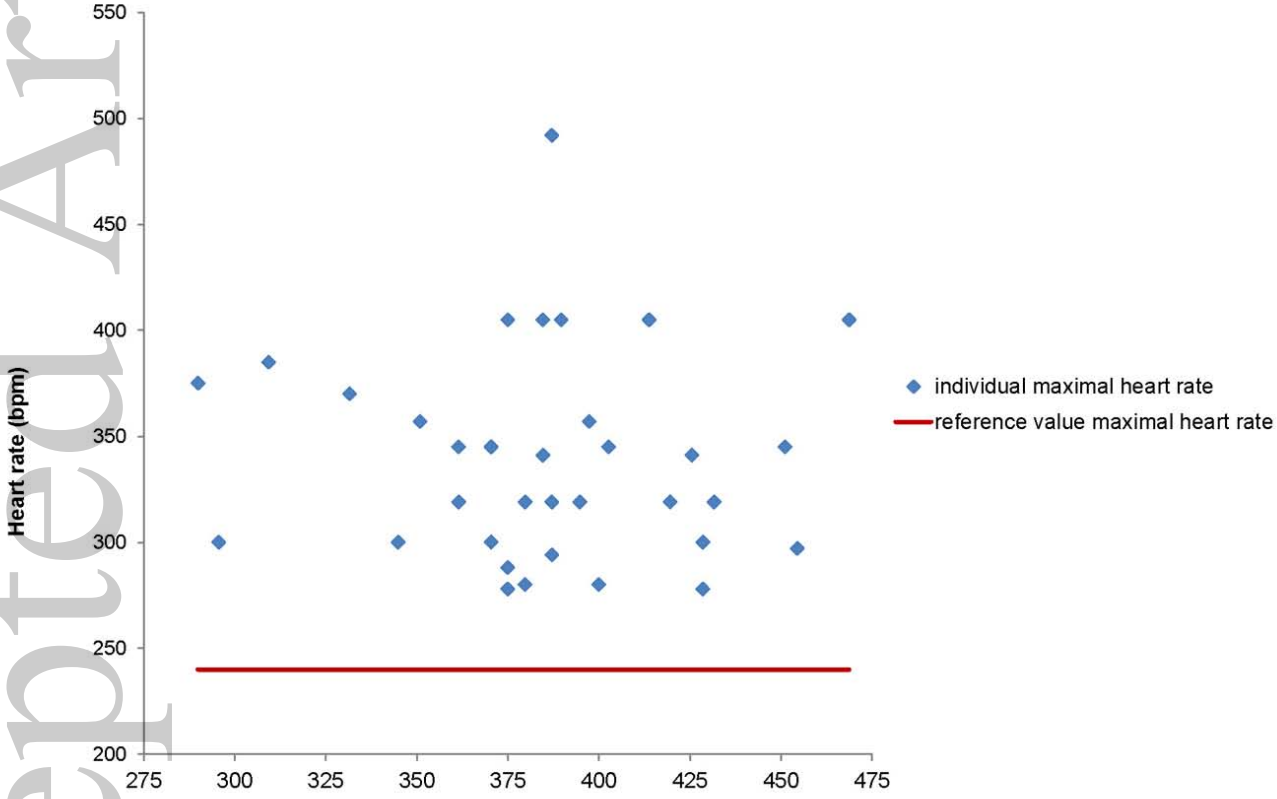

fig 3.tif

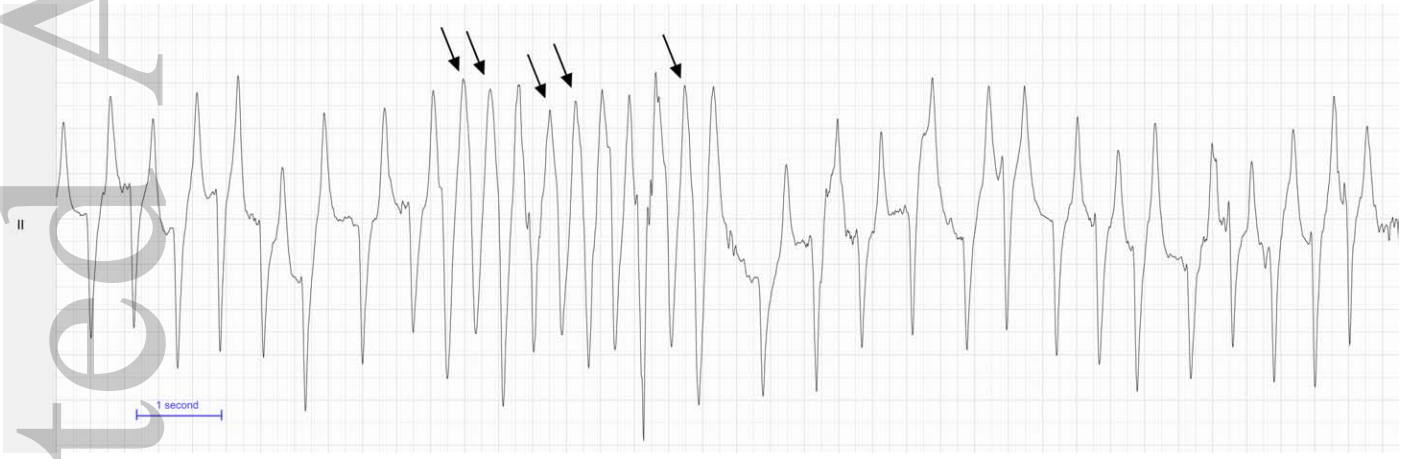

fig 4.tif

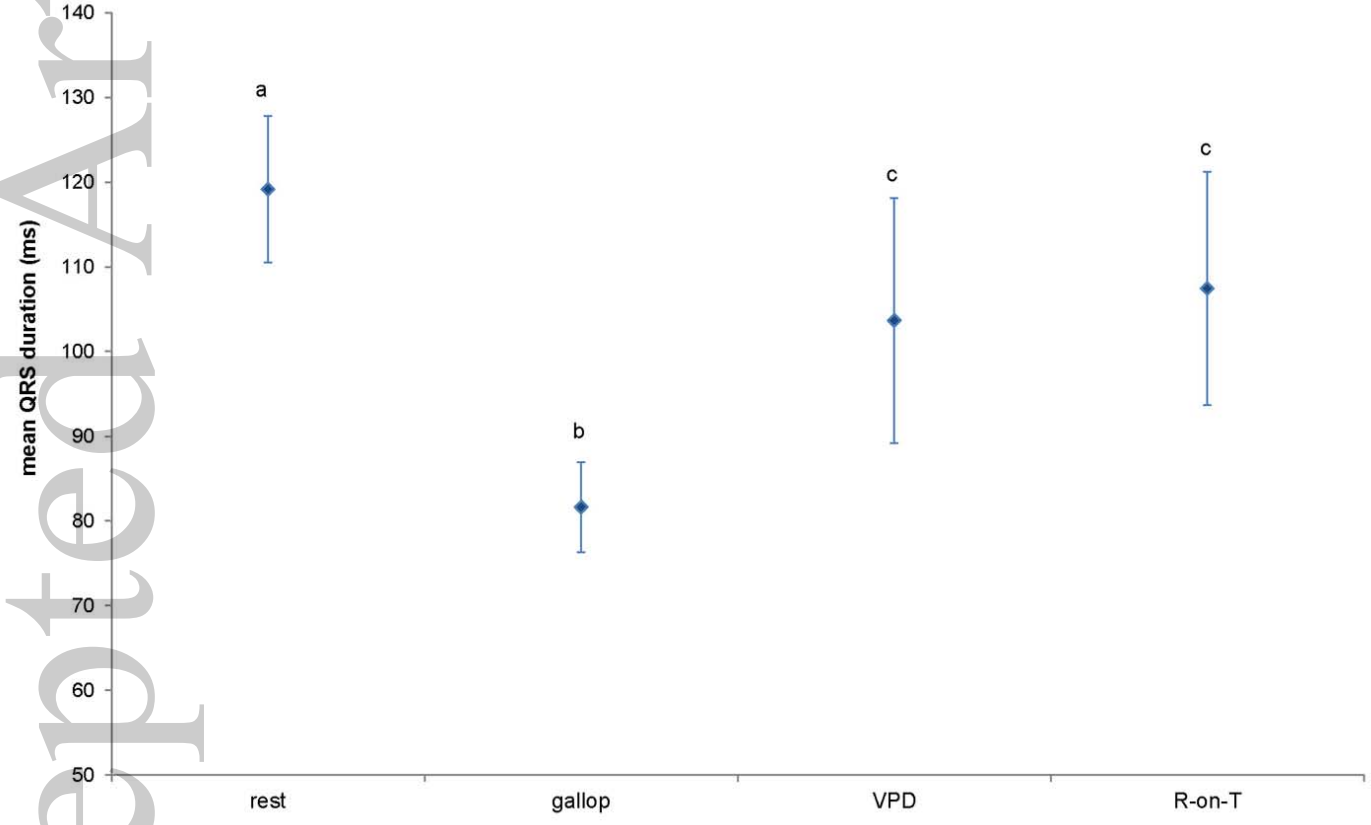

fig 5.tif

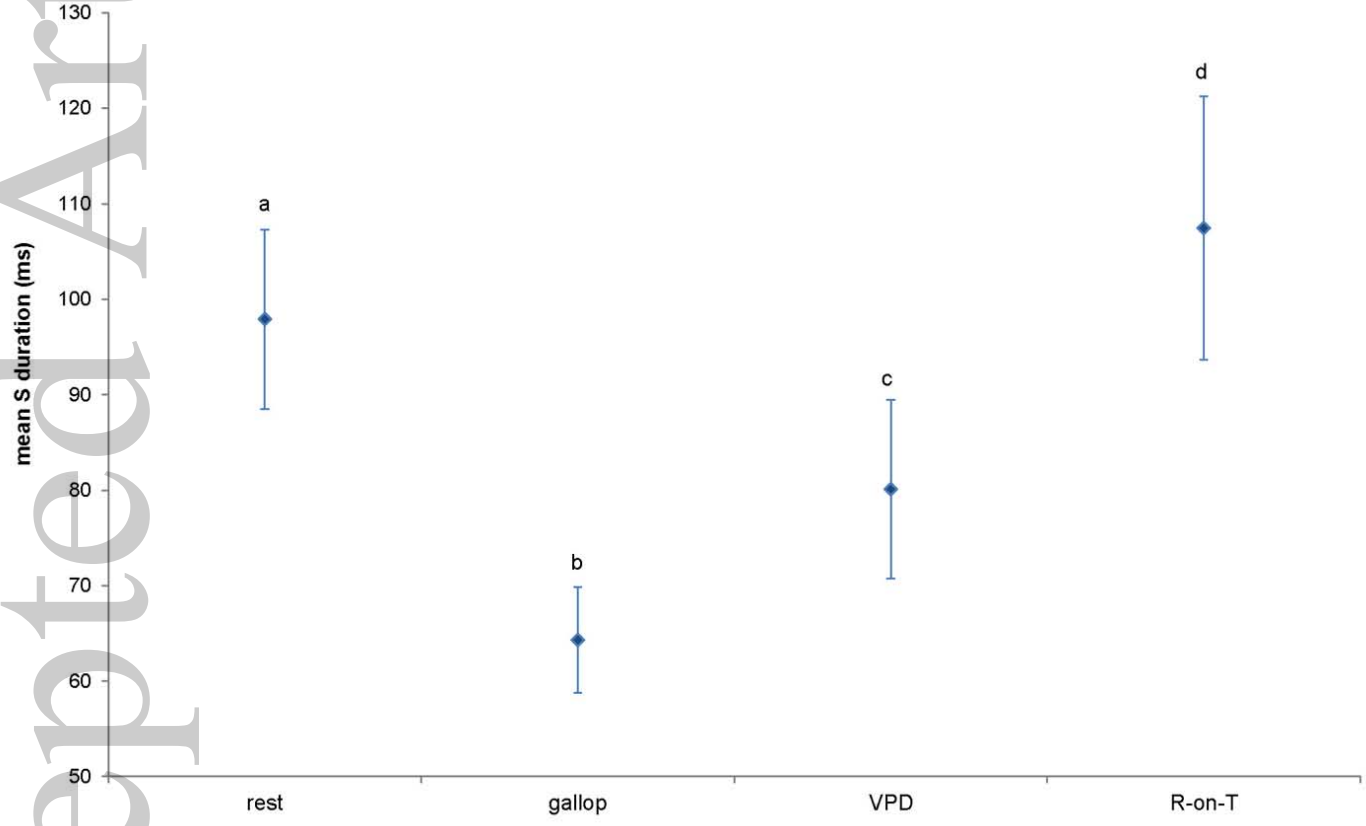

fig 6.tif

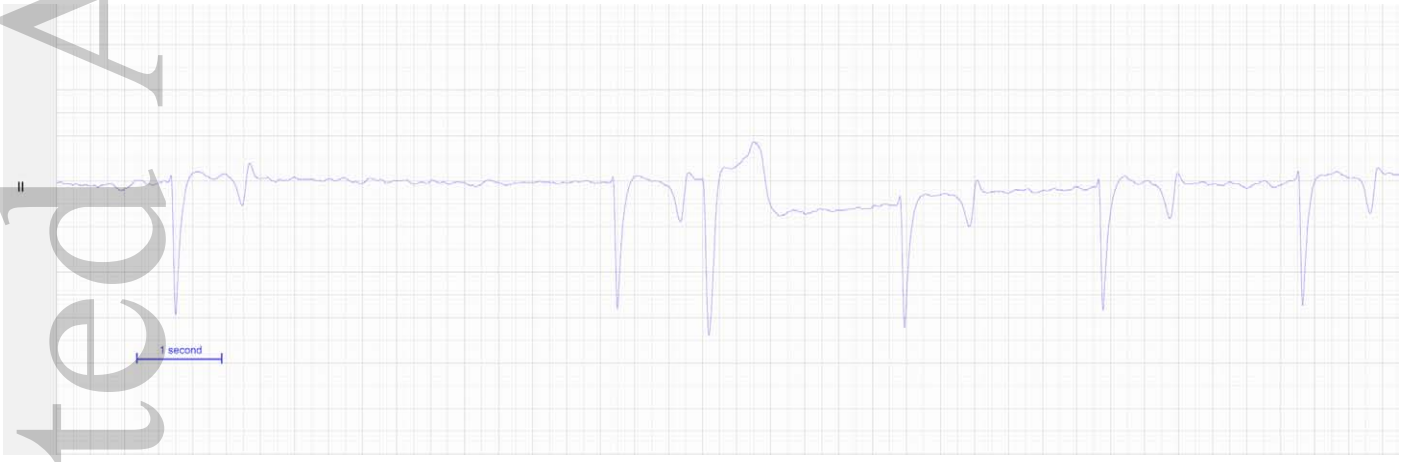

fig 7.tif