The use of low doses of acepromazine as an aid for lameness diagnosis in horses: An accelerometric evaluation

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Summary
Objectives: The aim of the present study was to quantify by accelerometry the trotting pattern of adult horses sedated with two different doses of acepromazine, in order to assess the use of this drug in equine lameness evaluations.

Methods: Seven mature horses were used and three treatments were administered to each horse: saline solution, acepromazine (0.01 mg/kg), and acepromazine (0.02 mg/kg). The portable gait analyzer used consisted of three orthogonal accelerometers that measure accelerations along the dorsoventral, longitudinal, and lateral axes. Baseline values were obtained and after treatment, accelerometric recordings were repeated every five minutes during the first 20 minutes after the injection and then every 10 minutes thereafter for two hours. Ground-to-lip distance was also measured.

Results: Administration of acepromazine decreased some of the variables investigated and differences between doses were observed. Speed, stride frequency, and stride length were significantly reduced following treatments. For coordination parameters, no significant differences among values were observed. Energetic variables suffered only weak reductions whereas ground-to-lip distance values were significantly increased up to 120 minutes after treatment.

Clinical significance: Acepromazine produces significant alterations in the gait pattern with differences between doses, but it does not affect coordination variables in normal unexcited horses, and at a dose of 0.01 mg/kg may be the tranquilizer of choice for evaluating lameness in this setting.

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Introduction
Lameness examinations and regional analgesia of the distal portion of the limb of most horses can be accomplished using minimal restraint, but for fractious horses or for horses that have previously been subjected to regional analgesia, using a lip twitch or lip chain is prudent (1). In other cases, tranquilization may be necessary. Sometimes horses are fresh and exuberant or become nervous when transported to veterinary facilities or during lameness examinations and this can mask lameness signs and prevent a correct examination. In these cases, drugs such as α2-adrenoceptor (α2-AR) agonists and phenothiazines are used, but because of the uncertainty of the effect of sedation or tranquilization on gait, a sedative or tranquilizer is best avoided, if possible (1). A low dose, such as 0.002–0.01 mg/kg of intravenously administered acepromazine maleate may be used (2).

The efficiency of accelerometry in detecting gait changes after sedation with α2-AR agonist drugs has been evaluated; it offers a practical, accurate, easy to use, portable, and low-cost method of objectively monitoring gait abnormalities in these circumstances (3, 4). The aim of the present study was to assess the use of acepromazine maleate in equine lameness evaluations, and to quantify by accelerometry its effects on the movement pattern of adult horses while trotting after sedation.

Materials and methods
Experimental animals
This study was approved by the Complutense University Animal Care and Use Committee. A total of seven mature horses with a mean (± SD) age of 13.2 (± 8.3) years (range: 4–21 years) and a mean (± SD) body weight of 425.8 (± 10.2) kg (range: 418–441 kg) were used. A complete clinical examination was performed on all horses to ensure they were healthy and free of lameness.
Treatment protocol

Each horse served as its own control, and three treatments were administered intravenously to each horse: saline solution (0.9% NaCl, 10 ml) (control treatment), and acepromazine maleate\(^b\) in two different dosages: 0.01 mg/kg and 0.02 mg/kg, diluted in saline solution to a volume of 10 ml. A minimum of seven days between each treatment was allowed, and the order of treatments was randomized.

The portable gait analyzer\(^c\) used included an acceleration sensor composed of three orthogonal accelerometers that measured accelerations along the dorsoventral, longitudinal, and lateral axes of the horse, a data logger and a scientific software program\(^d\). The data logger was introduced into a leather pocket fixed to an elastic girth positioned on the thorax. The accelerometer was always positioned by the same researcher (DG). Data were continuously collected while the horse was trotting, at a sampling rate of 100 Hz. Positive values were registered when acceleration signals were in dorsal, cranial and left directions. After the completion of the test, all data were transferred to a computer for further analysis.

All tests were performed in a quiet environment, and horses were familiar with the experimental conditions. On the day of the test, the three-dimensional accelerometric sensor was attached to the skin over the midline of the sacrum region at the level of the sacral tuber. Before administration of the test injection, horses were trotted at their own comfortable speed two times over a distance of 50 metres. Baseline accelerometric recordings (10 minutes) were then registered. A 16 gauge intravenous catheter\(^e\) was inserted into the left jugular vein and one of the three solutions was injected (minute 0). Accelerometric recordings were repeated every five minutes during the first 20 minutes after the injection (minutes 5, 10, 15, 20) and then every 10 minutes thereafter for two hours (minutes 30, 40, 50, 60, 70, 80, 90, 100, 110 and 120). Fifteen trials at the trot were performed, and each trial involved an accelerometric test and a sedation assessment.

Accelerometric and sedation parameters

The validation and reproducibility of the accelerometric measurements with the portable gait analyser have been previously described (3, 5-7). All the variables studied have also been described and included (3, 6, 8-12):

- Stride kinematic variables such as speed (m/s), stride frequency (cycles/s or Hz), and stride length (m).
- Coordination variables: Regularity to assess the similarity of dorsoventral acceleration patterns over successive strides, and symmetry, to assess the similarity of the acceleration pattern of right and left diagonals. Stability of the gait was calculated as the sum of symmetry and regularity, and used as an indicator of gait quality.
- Energetic variables: dorsoventral power or activity (W/kg); propulsive power, craniocaudal activity, or longitudinal activity (W/kg); mediolateral power, lateral activity, or side-to-side activity (W/kg); and total power (W/kg), defined as the sum of the three powers calculated in each axis. Also, the force of acceleration (N/kg) was calculated by dividing the total power of accelerations by speed to avoid potential bias due to different speeds. Finally, the mediolateral, dorsoventral, and propulsive power as a percentage of total power were calculated by dividing the different power components by the total power.
- The ground-to-lip distance (cm) was also determined against a scale before each trotting test as a sedation parameter.

The final value for each variable at each time point was calculated as the mean of three measurements.

Statistical analysis

All data analyses were performed by use of commercially available software\(^f\). Data were grouped and summarized as a mean ± standard deviation, and expressed as a percentage relative to baseline values. First, two-factor analysis of variance (ANOVA) with repeated measures in both factors was performed. If interaction was detected, a one-way ANOVA was also performed comparing groups at each time (with a Duncan’s multiple range test) and repeated measures one-way ANOVA comparing moments in each group. Values of \(p <0.05\) were considered significant.

Results

All horses completed the study, and no significant differences among control values were observed at any time. Administration of acepromazine decreased some of the variables investigated.

Stride kinematic variables

Significant reductions were observed for speed (\(p <0.0001\)), stride frequency (\(p = 0.0008\)) and stride length (\(p = 0.0018\)) following acepromazine maleate treatments. For speed, a significant reduction was observed between baseline values and values obtained 15 minutes after the injection of 0.01 mg/kg. After the administration of 0.02 mg/kg, differences were observed from five to 70 minutes, with the greater decrease (80.5 ± 6.5) occurring 15 minutes after injection. When compared to the effect of saline solution, differences appeared only 30 minutes after the administration of 0.01 mg/kg. Regarding the 0.02 mg/kg dose, differences were observed from 10 to 40 minutes and again at 70 minutes following treatment. Differences between both treatment groups were observed from five to 20 minutes after injection and again at 40 and 100 minutes following acepromazine maleate administration (Figure 1). For stride frequency, a significant reduc-

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\(^{a}\) Solución salina fisiológica 0.9%: B/BRAUN Medical S.A., Maddrid, Spain
\(^{b}\) Equiromacina, 5 mg/ml: Labiana Life Sciences S.A., Terrassa, Spain
\(^{c}\) Equimetrix-Centaur 3D Matlab 5: The MathWorks Inc., Natick, MA, USA
\(^{d}\) Surfio: Terumo Europe N.V., Leuven, Belgium
\(^{e}\) SAS 9.2 software for Windows: SAS Institute Inc., Cary, NC, USA

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tion was observed from 50 to 70 minutes after the administration of 0.01 mg/kg. After the 0.02 mg/kg dose, the significant differences appeared also from five to 70 minutes after drug administration. No differences were observed at any time point compared with the effect of saline solution for the 0.01 mg/kg dose, but in the 0.02 mg/kg group, differences appeared from 10 to 40 minutes and again at 60 and 70 minutes after acepromazine maleate injection. In this case, between both acepromazine maleate groups, differences appeared from 5 to 40 minutes after the injection of acepromazine maleate. Finally, for stride length values, differences were only observed after the administration of 0.01 mg/kg from 15 to 30 minutes after injection. Compared with saline solution, significant reductions occurred at 100 minutes for the 0.01 mg/kg group and at 15 minutes for the 0.02 mg/kg group. Differences were observed between both treatment groups from 15 to 20 minutes after injection, and again at 100 minutes following acepromazine maleate administration.

**Coordination variables**

No significant differences among values were observed in any of the three variables (regularity, symmetry and stability).

**Energetic variables**

Significant reductions were observed for mediolateral power (p <0.0001), total power (p = 0.0017) and force of acceleration (p = 0.0044), but not for dorsoventral power and propulsive power values. For mediolateral power, a significant reduction was observed between baseline values and values obtained five minutes after the administration of 0.02 mg/kg, whereas no differences were observed at any time point after the injection of 0.01 mg/kg. Compared with saline solution, differences appeared only at 15, 30 and 40 minutes after treatment with 0.02 mg/kg. Again, no differences were observed at any time point after treatment with 0.01 mg/kg. Between both treatment groups, differences were observed at five and 30 minutes following acepromazine maleate administration. For total power values, a significant reduction was observed from 10 to 20 minutes after the administration of 0.01 mg/kg. After the 0.02 mg/kg dose, significant differences appeared only five minutes after drug administration. No differences were observed at any time point when compared with saline solution in both treatment groups. Also, between both acepromazine maleate groups, no differences were observed. For force of acceleration values, a significant reduction was observed between baseline values and values obtained at 15, 20, 50, 60, 70 and 100 minutes after the administration of 0.02 mg/kg whereas after the 0.01 mg/kg dose, no differences were observed at any time point. Compared with the effect of saline solution, the differences appeared only 100 minutes after treatment with 0.02 mg/kg. Again, no differences were observed at any time point after treatment with 0.01 mg/kg. In this case, differences between both treatment groups were observed at 15 and 100 minutes following acepromazine maleate administration.
A redistribution of the three-axial power was observed with a significant decrease in the mediolateral power \((p = 0.006)\) and a significant increase in the dorsoventral power \((p = 0.0412)\). The propulsive force of the power did not change after the injection of acepromazine maleate.

**Sedation parameters**

Significant reductions were observed for ground-to-lip values \((p = 0.0003)\) following acepromazine maleate treatments. A significant reduction was observed between baseline values and values obtained from five to 120 minutes after the administration of 0.01 mg/kg whereas after the administration of 0.02 mg/kg, differences were observed from 10 to 120 minutes after drug administration. Compared with the effect of saline solution, the differences appeared from five to 120 minutes (none at 10 min) after both treatments. Differences between both treatment groups were only observed at 100 minutes following acepromazine maleate administration (▶Figure 2).

**Discussion**

In the present study, administration of acepromazine maleate only produced weak alterations while trotting the horses, with significant differences in duration of effect among doses. The clinical applicability of this observation is important.

Tranquilization is sometimes necessary when clinically assessing lameness in exuberant, nervous or excited horses, to avoid the masking of clinical signs. However, controversy remains regarding the use of tranquilizers during these examinations. Some authors indicate that a sedative or tranquilizer should be best avoided, because of the uncertainty of its effect on gait. Sedation of a fractious or exuberant horse may actually make a subtle lameness more obvious, depending on the degree of tranquilization, the severity of lameness and the experience of the clinician performing the examination (1).

There is also some disagreement regarding the drug of choice (1, 13–15). The use of α2-AR-agonists for sedation is not recommended by some, because these drugs induce some analgesia and may produce ataxia (2). The use of α2-AR antagonist to reverse the effect before re-evaluation has been described (1, 14, 15). Sedation with detomidine did not change the degree of lameness, but it did alter the general locomotion pattern and may be a better choice than xylazine because the drug lasts longer (13, 14). Xylazine can be more useful for restraint than detomidine because of its shorter duration of action; however mild ataxia is a possible side effect (1, 14). Regarding phenothiazines, low doses of acepromazine have been recommended for lameness examinations without apparent interference or negative effects (1, 2).

In the present study, stride kinematic parameters were affected by the administration of acepromazine maleate, although differences between both doses were present. The reduction in speed could be a potential benefit while examining an excited lame horse. Signs of lameness can be masked by velocity, and horses visually examined for subtle lameness on the straight should be evaluated at a slow speed (16). In a study determining velocity-dependent changes of time, force and spatial parameters in Warmblood horses walking and trotting on a treadmill, stride rate and stride length changed in a linear fashion with velocity, while stride length was the main variable contributing to the increase in velocity at the trot (17). In the over-ground situation, stride length was also the main contributor to changes in speed (18). After the administration of α2-AR agonists, a reduction in speed by reducing only stride frequency values occurred but, in this case, the administration of acepromazine maleate caused a reduction in speed by reducing both stride frequency and stride length (4, 19). This difference could probably be due to the greater inhibition of the locomotor activity produced by α2-AR agonists drugs, compared with phenothiazines. Differences between both dosages were evident during the first 40 minutes for speed and stride frequency and at 15 and 20 minutes for stride length with mainly weak reductions occurring after the administration of 0.01 mg/kg. Is important to consider that acepromazine maleate related stride length changes may alter the load of certain limb structures, thus changing some lameness characteristics. Thus, the use of the lower dose is probably more advisable.

All three coordination parameters, regularity, symmetry and stability, were preserved after the administration of acepromazine maleate. This finding is probably the most relevant result of this study. With the accelerometer system employed, the shape of the acceleration signals is compared between left and right stances and from one stride to the next (20). Regularity is an accelerometer-specific variable and refers to the stride to stride variability, whereas symmetry refers to the similarity of the left and right phases of a stride, and stability is described as an indicator of gait quality. In a study using the same equipment and similar protocols and methodology, the administration of xylazine produced a marked decrease in regularity values, and the authors concluded that this variable could potentially be a very sensitive parameter to detect and quantify uncoordinated movements at the walk (3). Unlike with α2-AR agonists, coordination parameters were not significantly affected in the present study after the administration of acepromazine maleate, indicating the potential usefulness of this drug to evaluate horses with lameness because no interference in the normal gait coordination pattern exists. Nevertheless, this study was performed using normal and not excited nor exuberant horses and a direct comparison with α2-AR agonists has not been performed in the same group of horses. Results should be judiciously transferred to a clinical situation because the effects of sedative drugs depend to a certain extent upon how excited or stressed the horse is prior to administration, and this fact could potentially change the expected effects of this drug in an over-exuberant horse.

In addition, weak, significant drug-related decreases in mediolateral power and total power values were detected. The significant reduction of force of acceleration values indicates that these effects were probably due to the peripheral and sedation effects of the acepromazine maleate, and that speed reduction was not an important factor for these power value reductions (21). Nevertheless, differences in power values between doses were not ob-
erved, and ultimately power and force alterations were weak and of short duration. Spontaneous locomotor activity, according to the stimulus, is able to suppress the sedative effect of some drugs (21). The same weak effects were observed for the redistribution of the powers. While the propulsive part of the power values were not affected, a significant decrease in the mediolateral part was observed mainly at the expense of the significant increase in the dorsoventral part. Although significant, the normal three-axial distribution of the power was globally maintained with around 70% for the dorsoventral power, 10% for the propulsive power and 20% for the mediolateral power approximately, without significant differences between doses.

Height of the head or ground-to-lip distance is one of the most frequently used parameters to assess sedation in horses. It has been used in the evaluation of the effects of α2-AR-agonists drugs alone or combined opiates, and through different routes, to determine the effects of phenothiazines or the effects of sub-anaesthetic doses of general anaesthetics, to develop constant rate infusions for standing procedures, to assess recovery after constant rate infusions, and to evaluate sedation after epidural administration of opiates (22-30). In our study, despite the fact that weak differences were observed for stride kinematic and energetic values, and no alterations appeared in coordination values, ground-to-lip distance values were significantly altered. After the administration of acepromazine maleate, ground-to-lip distance values decreased for up to 120 minutes after injection of both dosages. Even with the low dose of 0.01 mg/kg, enough sedation was achieved with minimal effect in stride kinematic and energetic values and with no effect in coordination parameters.

An important limitation of the present study refers to the use of acepromazine maleate in males. The evaluation of lameness in stallions is often challenging, not only by their sometimes exuberant behaviour. The administration of acepromazine maleate in male horses carries an extremely low risk of permanent penile dysfunction (1 in 10,000 cases), and this drug should be used cautiously in stallions (31).

In conclusion, our results indicate that although sedation with acepromazine maleate in normal, unexercised horses produces significant alterations in the gait pattern, with differences between doses, the coordination variables (regularity, symmetry and stability) are preserved. Thus a dose of 0.01 mg/kg may be the tranquilizer of choice for lameness evaluations in horses.

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Conflict of interest
None of the authors has any financial or personal relationships that could inappropriately influence or bias the content of the paper.

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